

Research Article

Pulmonary function changes in type 2 diabetic lungs

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Received: 19 February 2016

Accepted: 23 March 2016

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ABSTRACT

Background: Diabetes is a systemic disease with well-known complications involving eyes, kidneys and nerves. The presence of an extensive pulmonary micro vascular circulation and abundant connective tissue raises the possibility that lung may also be a target organ in diabetes. The purpose of this study was to evaluate pulmonary functions in patients with diabetes mellitus and to determine their correlation with glycemic control, duration of diabetes and its complications.

Methods: One hundred type 2 diabetic patients, aged 30-60 years, with 1-20 year duration of diabetes were included in the study. Pulmonary functions were performed with Helios spirometer and Smart PFT-CO transfer equipment. Glycemic levels assessed by measuring FPG, PPG and HbA1c. All patients were evaluated for diabetic microangiopathies: nephropathy (by 24-hour protein excretion), retinopathy (by direct ophthalmoscopy) and neuropathy (by clinical examination).

Results: All the spirometry values decreased in diabetic patients of which FVC, FEV1% show significant reduction. Majority have restrictive ventilation pattern. Poor lung functions are in correlation with high sugar levels and long duration. Diffusion capacity significantly reduced in micro vascular complications like retinopathy, nephropathy and neuropathy.

Conclusion: The study shows reduced dynamic lung functions in diabetes mellitus. Lung function parameters are negatively correlated to glycemic status and duration of diabetes. Hence strict glycemic control may improve pulmonary functions.

Keywords: Spirometry, Diabetes, Glycemic control, Micro vascular complications

INTRODUCTION

Man may be the captain of his fate but he is also the victim of his blood sugar as said by Wilfrid Oakley. Diabetes is fast gaining the status of a potential epidemic in India with more than 62 million diabetic individuals currently diagnosed with the disease.¹ According to Wild et al the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030 with a maximum increase in India.² India is going to face a big challenge posed by the rising prevalence of DM and

its complications with the rapid rate of industrialization and urbanization occurring in the country.³

Each and every system is affected by complications of diabetes but attention is usually paid to angiopathy, retinopathy and nephropathy. One of the systems most neglected in diabetes is the respiratory system, except for the recognition of increased infection prevalence like tuberculosis.⁴

The pulmonary function tests are age old, time tested parameters for assessing respiratory health of a person.⁵

This work is intended to study the effect of type 2 diabetes on dynamic pulmonary function tests.

METHODS

One hundred diabetic patients of the age 30 years and above, both newly diagnosed as well as previously detected were randomly selected in the department of pulmonary medicine over a period of one year.

Diabetics who have never smoked, with no active or past history of lower respiratory illness and whose chest roentgenogram was clear at the time of the examination were included. Subjects with a past history cardio respiratory diseases, respiratory allergies and smokers were excluded from the study protocol.

All the participants were informed about the study protocol and written consent has been taken. A detailed clinical history, through medical examination was conducted. Glycemic status was determined by measuring fasting and prandial plasma glucose levels by glucose peroxidase method. Glycated hemoglobin (HbA1c) was estimated by ion exchange resin method. All patients were evaluated for diabetic microangiopathies: nephropathy (by 24-hour urine protein excretion), retinopathy (by direct ophthalmoscopy) and neuropathy (by clinical examination). Pulmonary function tests were performed with turbine flow sensor-based Helios Spirometer according to American thoracic society guidelines.⁶ All patients performed spirometry three times at the interval of 15 minutes and the best of the three was taken into account and parameters like forced vital capacity (FVC) in liters, forced expiratory volume in 1 second (FEV1), FEV1/FVC in percentage (%), and peak expiratory flow rate (PEFR) were recorded. Lung diffusion Capacity for carbon monoxide (DLCO) was measured with single breath technique using Smart PFT-CO transfer machine (Medical equipment, Europe).

All data were collected in a data collection form and Microsoft word and Excel have been used to generate graphs, tables etc. Statistical analysis was done with SPSS 15.0. Correlation and regression were used to examine strength of association between glycemic status and duration of diabetes mellitus with dynamic pulmonary function tests. Groups are compared with student t test and f test.

RESULTS

Majority of patients belong to age group 41-60 years. Females were more than males. Mean diabetes duration was 6.5 years. Micro vascular complications seen in 48% (n=48). Of them, non-proliferative diabetic retinopathy was the most common complication (36%) followed by diabetic nephropathy and neuropathy (Figure 1). All pulmonary function values reduced in diabetics with statistical significance reduction in FVC indicating

restrictive ventilation. High glycemic levels were in accordance with poor lung functions. Diffusion capacity was significantly reduced in patients with microangiopathic complications. Mean FEV1/FVC (measured %) according to Diabetic duration, diabetic treatment, diabetic complications and DLCO in Type 2 DM patents showed statistical significance with diabetic duration, complication (Table 1).

Figure 1: Microvascular complications of diabetes.

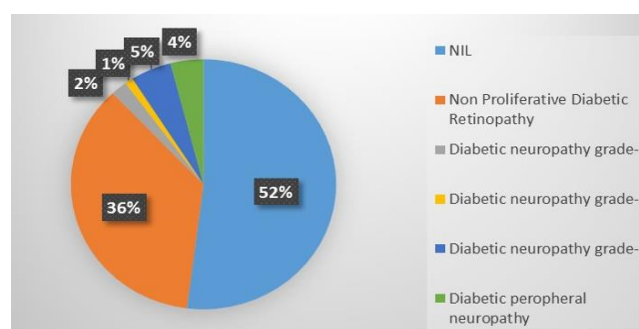


Table 1: Mean FEV1/FVC (measured %) according to diabetic duration, diabetic treatment, diabetic complications and DLCO in type 2 diabetes mellitus patients.

Variables	FEV1/FVC (measured %) in type 2 diabetes		Statistical values
	Min-max	Mean \pm SD	
Diabetes duration			
<2 years	81.49- 96.79	91.29 \pm 4.53	f=3.017
<5 years	61.85-92.07	80.94 \pm 11.29	
5- <10 years	60.65-99.71	78.26 \pm 9.69	p=0.039
>10 years	65.41-95.92	79.03 \pm 9.48	
Type of treatment			
OHD	61.85-99.51	81.29 \pm 10.08	t=0.293
OHD & Insulin	63.32-92.05	80.28 \pm 9.64	p=0.768
Microvascular complications			
Present	58.8 -92.79	73.03 \pm 9.04	t=2.302
Absent	60.85-99.71	80.85 \pm 9.95	p=0.026
Diffusion capacity			
>80 %	65.41-74.16	71.28 \pm 3.53	t=1.934
<80 %	56.85-71.44	66 \pm 5.16	p=0.085

OHD= Oral hypoglycemic drugs; p value <0.05 is statistically significant. DLCO= Diffusion lung capacity for carbon monoxide. FEV1/FVC= Forced expiratory volume in 1st second/ forced vital capacity.

DISCUSSION

Diabetes mellitus is a systemic disease that produces changes in the structure and functions of several tissues particularly connective tissue with complications that affects the eyes, kidneys, capillaries and nervous system. The presence in the lung of an abundant connective tissue and extensive micro vascular circulation raises the possibility that lung may be a target organ in diabetic patients.⁷ Several biochemical and physiological changes occur in diabetes, including non-enzymatic glycosylation

of connective tissue which might be responsible for end organ damage and diabetic myopathy. These could lead to loss of elasticity, altered perfusion characteristics and weakness of the respiratory muscles responsible for ventilation.⁸ Lung function may provide useful measures of the progression of systemic micro-angiopathy in diabetic patients.

In this study of 100 diabetic people, majority belong to the age group 41-60 years with a mean age of 54.48 yrs. There were large number of females than males (60% vs 40%). The probable cause for this female preponderance was the fact that many males were excluded on account of their smoking history.

Duration of diabetes ranged from 1 month to 10 years with a mean period of 77.28 ± 46.62 months. The mean fasting and prandial glucose levels were 150 and 210 mg respectively. A recent international study reported that diabetes control in individuals worsened with longer duration of the disease (9.9 ± 5.5 years).⁹ The mean HbA1c levels was 7 ± 0.68 which shows that subjects had a poor glycemic control. McKeever et al have observed that an increase in mean HbA1c is associated with a decrease in the lung function parameters FVC and FEV1. They hypothesize that impaired glucose auto regulation is associated with impaired lung function.¹⁰

Diabetic retinopathy was the common sequelae followed by nephropathy and neuropathy in the present study. In a south India study by Pradeepa et al showed neuropathy is the most common complication (24.6%) followed by cardiovascular complications, nephropathy, retinopathy and foot ulcers.¹¹

All pulmonary function values decreased in diabetics. The mean forced vital capacity (FVC) values are 2.27 ± 0.70 lit (predicted 3.52 ± 0.60 lit). The mean forced expiratory volume in first second (FEV1) are 1.80 ± 0.45 lit (predicted: " 1.90 ± 0.3 " 0 lit). The mean measured FEV1/FVC ratio was 91 ± 12 lit showing restrictive ventilation defect (predicted: 78 ± 8.4). In one study by Davis et al demonstrated decline of $>10\%$ of FVC & FEV1 in the 125 prospectively studied patients.¹² Absolute measures continued to decline at an annual rate of 68 & 71 ml/year for FVC, FEV1 respectively. They also said that air flow limitation was an important predictor of mortality in type 2 diabetic patients.

Reduction in FVC was much higher than reduction in FEV1. The effect on the FVC was even more pronounced in diabetics who had duration of disease longer than 3 years and subjects with poor diabetic control have worse pulmonary functions. FEV1 fall was more pronounced among diabetic females than males. Poor diabetic control was associated with poorer lung function.¹³ There was a rough association between greater declines in FVC and higher values of FPG and PPG. The possible mechanism for significant reduction in FVC, FEV1% may be due to respiratory muscle weakness because of non-enzymatic

glycosylation of connective tissue proteins such as collagen in the chest wall and pulmonary tree.¹⁴

In our study, we found a predominantly restrictive pattern (80%), with almost all males having a FVC less than 80% of the predicted value, while only 36% of females had FVC $<80\%$ of predicted. An obstructive pattern indicated by an FEV1/FVC ratio less than 70% was seen in 15% and mixed defect in 5% of patients. In Framingham heart study by Robert E Walter demonstrated an association between glycemic state & reduced FVC and FEV1.¹⁵ The consequent larger FEV1/FVC ratio in subject with diabetes suggest restrictive physiology. In contrast, when those with diabetes on therapy were excluded, higher levels of fasting blood glucose were associated with larger reduction in FEV1 than FVC indicating obstructive pattern. Similar results were shown by van den Borst et al studies.¹⁶

Diffusion capacity of lungs for carbon monoxide was decreased ($<80\%$) in 65% patients which have a mean FEV1 % of 71 ± 4 . In Marico Guzzi et al¹⁷ study the mean DLCO was $84.2 \pm 7.9\%$. They mainly focused on alterations in diffusing capacity (DLCO) and their relationship with duration of diabetes, in insulin dependent diabetes mellitus. They found that there was reduction in lung function that was slightly more pronounced in insulin dependent than in non-insulin dependent diabetics. In the studies of Hiroshi Mori et al, DLCO was negatively correlated with duration of diabetes and patients treated with insulin had significant decrease in DLCO compared to those taking oral hypoglycemic drugs.¹⁸ No relation was noted between treatment with FVC, FEV1%. No such difference between insulin treated and OHA treated individuals was noted in our study, but the numbers were too small to draw any conclusions. Differences could be explained by the differences in duration of diabetes and diabetic control with insulin treated type 2 diabetics likely to have had diabetes for a longer duration with higher sugars needing a change from OHAs to insulin. Agarwal et al showed reduced diffusion capacity in patients with micro albuminuria and retinopathy.¹⁹

Several studies have analyzed the association between impaired lung function and death and found that a 10% decrease in FEV1 was associated with a 12% increase in all-cause mortality in type 2 diabetes.²⁰

CONCLUSION

All spirometric values were consistently lower in diabetes patients but the differences reached statistical significance only for the forced vital capacity. Majority have restrictive ventilator defect with low diffusion capacity. The effects were marked when the duration of hyperglycemia was more than 3 years and poor sugar control have worse lung functions. Hence, we conclude that strict glycemic control and regular breathing

exercises to strengthen the respiratory muscles may improve the pulmonary function tests in diabetic patients.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the institutional ethics committee

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Cite this article as: Mandava V, Gopathi NR. Pulmonary function changes in type 2 diabetic lungs. *Int J Adv Med*. 2016;3:378-81.