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Research Article

Pulmonary functions in type 2 diabetes mellitus patients: an observational study at a tertiary level hospital in Mumbai, Maharashtra, India

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ABSTRACT

Background: Pulmonary complications of diabetes mellitus (DM) have been poorly characterized. A reduction in lung capacity has been reported previously in diabetics. We undertook a study to check the association between pulmonary function tests in type 2 DM. Also to determine their correlations with body mass index (BMI), glycemic control and other clinically evident complications like peripheral neuropathy.
Methods: The study was conducted at tertiary care BYL Nair hospital, Mumbai where diabetic patients without any hypertension, cardiovascular disease, primary respiratory abnormalities and without any microangiopathic complications were enrolled. They were clinically evaluated for pulse, blood pressure, skin changes, BMI and various biochemical investigations. Blood sugar- fasting and post prandial, serum cholesterol, serum triglyceride, urinary proteins, electrocardiograph, X- ray chest were noted. Pulmonary function test was performed by spirometry. Peripheral neuropathy was looked for an association with pulmonary function tests (PFT).
Results: Out of 200 patients 68% (136) patients had normal PFT, mild obstruction 10.0% (20), mild restriction 10% (20) moderate obstruction 2% (4), moderate restriction 4% (8) and mixed 6% (12) were noted. FEV1, FVC values were statistically significantly reduced in patients with peripheral neuropathy and FEV1/FVC % significantly decreased with increasing duration of diabetes.
Conclusions: The present study shows that there is a statistically significant association between PFTs and type 2 DM in Indian patients. Pathologically it may be attributed to microangiopathic complications.

Keywords: Diabetes, Microangiopathy, Peripheral neuropathy, Pulmonary function test

INTRODUCTION

Diabetes mellitus (DM) is an endocrinological disease that typically consists of elevated blood glucose. DM is a micro-macro vascular disorder with debilitating effects on many organs. Type I DM (T1DM) is due to a total absence of pancreatic tissue and so no production of insulin whereas type II DM (T2DM) is caused due to peripheral resistance of tissues to the action of insulin. About 12.1% of the world's general population suffers from T2DM. There has been an alarming increase in the incidence and prevalence of this condition in India in the last few decades. From 40.9 million affected people in 2006, it is projected to reach 60.9 million till 2025.[1]

In a generalized condition such as diabetes that affects the osmolarity of all body fluids, functions of various parts of the body may be adversely affected by microangiopathic and macroangiopathic changes.

Macroangiopathic changes include atherosclerosis and hypertension while microangiopathic changes affect parts of the body like the eyes, kidney, and nerves leading to retinopathy, nephropathy and neuropathy respectively. The lungs, being one of the vital organs for survival, are at a higher risk of danger. The pulmonary alveolar-capillary network is the largest micro vascular organ in the body with a vast reserve. This means that a potentially large loss in function can be tolerated without developing any significant symptoms. Thus, this leads to the dysfunction persisting for a long time and being discovered only at a late stage.[2] As a result, pulmonary diabetic micro-angiopathy may be under-recognized clinically.

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. Our research is aimed towards studying the presence of pulmonary function abnormalities in patients with T2DM patients and to identify any correlations between duration of diabetes, glycemic control, peripheral neuropathy and pulmonary function parameters.

METHODS

Setting

Mumbai, the capital city of Maharashtra, is the most populous urban region of the world, with an estimated metropolitan area population of 20.7 million according 2011 census. Greater Mumbai has a literacy rate of 94.7%, which is higher than the national average of 86.7%.[3] Apart from Marathi, which is the native language, Hindi, Gujarati and English are spoken and understood well in this region. The religious groups represented in Mumbai include Hindus (67.39%), Muslims (18.56%), with Buddhists, Jains, Christians, Sikhs, Parsis and Jews making up the rest of the population. Topiwala National Medical College & BYL Nair Charitable Hospital is one of the foremost public medical colleges in India.

Study design

The study protocol was approved by an independent ethics committee prior to beginning patient interaction. Written, informed consent was obtained from all patients participating in the study and the study was conducted according to Good clinical practice guidelines. This was an observational, cross-sectional study evaluating pulmonary function in 200 T2DM patients at the outpatient clinic of B.Y.L. Nair Charitable Hospital. Patients of either gender, age above 30 years and suffering from T2DM were selected for the study. The patients that were selected were required to have no respiratory complaints.

Data collection and analysis

All patients were screened before being enrolled in the study. We excluded patietns who had a history of ischemic heart disease, hypertension or peripheral vascular disease. Other exclusion criteria for this study were patients with T1DM, patients having complaints of cough, sputum, or dyspnea, history of smoking, past or present history of tuberculosis, history of chronic obstructive pulmonary disease, asthma, interstitial lung disease or any other lung pathology, respiratory infection in the last 3 months, chest deformities and pulmonary surgeries, gestational Diabetes Mellitus. All enrolled patients underwent laboratory investigations like height, weight, blood pressure measurement, fasting and postprandial blood sugar, lipid profile, urinalysis, electrocardiography (ECG) and Chest X rays.

Patients were examined for peripheral neuropathy and was defined as >2 missing deep tendon reflexes in legs, diminished distal touch (assessed by cotton wool), pinprick or pressure sensation, distal vibratory sensation (assessed by graduated tuning fork of 128 Hz) and joint position sense. Other potential causes of peripheral neuropathy were excluded before attributing the peripheral neuropathy to diabetes. Microangiopathy was excluded as well. Histories of previous myocardial infarction or typical angina chest pain along with significant ECG changes were taken as indicative of presence of coronary heart disease (CHD). Cardiac evaluation was completed by clinical examination, electrocardiogram and echocardiograph. Any history of previous stroke or history suggestive of transient ischemic attack (blindness, dysarthria, or unilateral motor or sensory phenomenon) was taken as evidence of cerebral vascular disease. Peripheral vascular disease was defined as history of intermittent claudication or non-healing foot ulcers and/or absence of two foot pulses. Blood sugar and body mass index measurements were classified according to prevelant methods. Spirometry was done using Jaegger'spneumoscope and Forced Expiratory Volume in 1 second (FEV1) Forced Vital Capacity (FVC), FEV1/FVC % and Peak Expiratory Flow Rate (PEFR) were measured.

Approximate normality of data was confirmed and descriptive analyses of arithmetic means of lung function values were evaluated. Continuous variable data was used. Unpaired't' test, One way analysis of variance (ANOVA), Pearson correlation were used. The help of SPSS software was used. $P<0.05$ was considered statistically significant.

RESULTS

The study was conducted from January 2012 to August 2012. A total of 200 patients were investigated for the study. Out of the 200, 64 patients had an abnormal pulmonary function (32%). To break up the abnormalities into groups, 20 patients (10%) had mild restrictive

abnormality, 8 patients (4%) had moderate restrictive abnormality, 20 patients (10%) had mild obstructive abnormality, 4 patients (2%) had moderate obstructive abnormality and 12 patients (6%) had mixed abnormalities. (Table 1) On correlating FEV1/FVC% with the duration of diabetes in the patients, there was a statistically significant difference in the values in those that had a smaller time duration of suffering from diabetes from those that had been suffering from diabetes for a longer duration (p=0.009) (Table 2). On correlating the FEV1 values with the presence of peripheral neuropathy, there was a statistically significant finding. Patients with the presence of peripheral neuropathy (sign of micrvascular changes) had significantly lower values of FEV1 than those that did not have peripheral neuropathy (p=0.006) (Table 2). On correlating the FVC values with the presence of peripheral neuropathy, there was again a statistically significant difference between the FVC values in patients with the presence of peripheral neuropathy (lower values) and the values in patients with the absence of it (higher values) (p=0.005) (Table 2). Abnormal pulmonary function was seen to a greater extent in patients with a higher BMI. There was no statistically significant association of FEV1, FVC values with the duration of diabetes as was with fasting and postprandial blood glucose values.

Table 1: Baseline characteristics of patients included in the study.

Variable	Mean±standard deviation (n=200, males 88)
Age (years)	51.7±8.02
Body mass index (kg/m^2)	24.7±2.4
Fasting blood sugar (mg/dL)	138±14
Duration of diabetes mellitus (years)	18.4±2.7
2 hour post-prandial blood sugar (mg/dL)	221±18
Abnormal pulmonary function test	
Mild restrictive	20
Moderate restricitve	8
Mild obstructive	20
Moderate obstructive	4
Mixed	12

Table 2: Statistical associations with pulmonary function tests.

Pulmonary function test finding	p value
Duration of diabetes	
Forced expiratory volume during 1 second/Forced vital capacity	0.009
Forced expiratory volume during 1 second	0.8
Forced vital capacity	0.09
Peripheral neuropathy	
Forced expiratory volume during 1 second	0.006
Forced vital capacity	0.005

DISCUSSION

The significant finding of this study was the correlation of a microangiopathy like peripheral neuropathy with deterioration in lung function. Sinha et al also observed a significant change in lung function in diabetic patients with microangiopathy.[2] Marvisi et al found a significant reduction in diffusing capacity of the lungs for carbon monoxide (DLco) in diabetic patients with microangiopathies. In another study with a larger number of patients (n=80), there was again an association of decreased DLco with diabetic microangiopathy. Ljubic et al suggested a relationship between diabetic complications like microangiopathy with collagen and elastin changes in the lungs. Pulmonary function was found to be significantly reduced in patients with proliferative retinopathy as compared to background retinopathy in a study by Isotaniet al. However, some studies showed an absence of any correlation between pulmonary function tests and the presence of microangiopathy or glycemic control.

The mechanism by which the micro vascular changes occur is thought to be a combination of a few processes. Advanced glycation products are formed by enzymatic as well as direct processes in the periphery leading to changes in the elasticity and properties of materials leading to inability of the smooth muscle cells of the vasculature to dilate adequately. Also, abnormalities in the vascular endothelial cell function occur. In normal endothelial cells, active vasodilator substances are formed which lead to dilation of the micro and microvasculature. Due to dysfunction of the endothelial cells, such vasodilation does not occur leading to dysfunction. Platelet dysfunctions are seen as well.[5]

Hyper glycaemia induced advanced glycation products also induce oxidative stress on cells by stimulating superoxide dismutase. This enzyme leads to a cascade of steps that leads to great oxidative stress which results in the production of substances that antagonize the action of nitric oxide in the vasculature. Circulating levels of free fatty acids are often elevated in diabetic patients due to their excess secretion into the blood from adipose tissues due to lack of action of insulin. Free fatty acids have a detrimental effect on the endothelial function of the vasculature due to mechanisms such as oxidative stress and this again leads to vascular dysfunction and microangiopathies.[5,8]

As with the pulmonary function, the major contributory factor that may lead to pulmonary dysfunction is thought to be microangiopathic changes in the alveolar capillaries and arterioles. Other mechanisms are also thought to play a role. Chronic low grade inflammation as has been seen due to slightly elevated CRP and IL-6 levels may cause some damage to the endothelium of the alveoli and may ultimately lead to restrictive and obstructive changes. Aspirin as treatment can be thought to reduce this risk if established. Autonomic neuropathy related to the

respiratory muscle function is a possible cause of restrictive pulmonary changes. Insulin resistance syndrome may also play a role.[4]

Implications of this study include detection of pulmonary changes early in diabetic patients though yearly PFT check-ups. Chest physiotherapy, strict glycemic control and reduction of metabolic syndrome can be helpful as treatment if pulmonary abnormalities are detected. Treatment of patients with aspirin or statins may be helpful if pulmonary abnormalities with chronic inflammation is firmly established in a patient. Moreover, pre-anesthetic check-up of T2DM patients can include pulmonary function testing to determine the baseline pulmonary function for better monitoring during surgeries.

This study was performed at a tertiary level hospital with a specific socio-demographic profile. So the results of this study might not be generalizable to other geographical areas. Furthermore, we did not blind the clinicians or the patients, which would introduce bias in our observations. Our sample size is fairly small and randomized double-blinded control trials are warranted in future to confirm our findings. Furthermore, DLco could not be done for the patients, giving a more accurate pulmonary diffusion depiction.

CONCLUSION

Through this study it was determined that T2DM is associated with abnormal pulmonary functions. FEV1, FVC values were significantly reduced in patients with peripheral neuropathy and FEV1/FVC% significantly decreased as the duration of diabetes increased. The possible causes of these findings include microangiopathies, chronic inflammation, autonomic neuropathy and insulin resistance syndrome and warrants further research.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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