Frequency of Restrictive Pulmonary Function in Type 2 Diabetes Mellitus

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Abstract

Objectives: The aim of this study was to determine the frequency of restrictive pulmonary dysfunction in type 2 diabetic patients.
Study Design: Cross-sectional Study.
Setting: Outpatient clinic of Department of Medicine, King Edward Medical University, Lahore.
Subject and Methods: One hundred and seventy patients of Type 2 Diabetes Mellitus, presented in outpatient department of Mayo Hospital, Lahore with inclusion and exclusion criteria were included in the study. After taking informed consent, pulmonary function tests were performed. Patients were explained about the risks and benefits while their identity was kept confidential. The demographic information of the patients like name, age, sex, height and weight were collected. Digital spirometer was used to perform pulmonary function tests. FEV1 / FVC Ratio more than 80% or normal, was considered as restrictive defect and Ratio less than 80%, was considered as obstructive defect. All collected information was recorded on pre-designed Performa (attached). Effect modifying factors like duration of type 2 diabetes mellitus and smoking status (smoker and non smoker) were addressed through data stratification.

Results: In this study, we included one hundred and seventy type 2 diabetic patients. The mean age was 54.32 ± 19.08 years. There were 122 (71.8%) males and 48 (28.2%) females. The mean height was 161.59 cm. The mean FVC was 107.78 ± 20.31. The mean FEV1 was 94.09 ± 27.72. The mean FEV1 / FVC% was 104.762 ± 24.93. In 28 (16.5%) cases restrictive pathology was observed, 3 (1.8%) cases had obstructive pathology and 139 (81.8%) cases had normal lung function tests.

Conclusion: In this study we concluded that the target organ for diabetic injury was lung. It was responsible for restrictive diseases of lung. More research work required to rule out pathophysiologic mechanisms and clinical significance.

Key Words: Diabetes Mellitus, Pulmonary function test, Restrictive pulmonary dysfunction.

Introduction

Diabetes mellitus is a metabolic disorder because of insulin deficiency, inappropriate hyperglycemia generates or may be because of insulin resistance inside the body and insufficient insulin secretion to recompense with the body glucose. Type 2 Diabetes mellitus is
dominant type and resulting from insulin resistance with compensatory insulin secretion dysfunction. T2DM is common in > 90% cases.1

In recent year it has been noticed with the evidences that pulmonary function of T2DM patients is reduced. Pulmonary factors associated with vital capacity warrant consideration as potential risk factors for insulin resistance and T2DM.2 The Fremantle Diabetes Study showed that in start of study, among 125 T2DM candidates, 29 candidates had FEV1 < 70% of predicted value and FVC < 80% of predicted value without previously documented pulmonary dysfunction.3

Lung functions are compromised in patients with T2DM like decrease in FVC, FEV1 and PEF as compared to non-diabetics. Stratification of results by duration of disease shows a dose – response effect on lung function parameters.4 Patients with T2DM have significantly lower FVC and FEV1 than those without T2DM. FVC decreased in T2DM patients faster than non-diabetics.5

Chronic complications of T2DM are decreased lung volumes and airflow limitation severity of which correlate with the exposure of glycemic level. After adjusting other risk factors, airflow restriction is predictor of death in T2DM.3 Expression of adhesion molecules increases due to hyperglycemia in T2DM patients. Lower pulmonary volumes in T2DM patients are due to compromised pulmonary microvasculature. Sensitive markers for endothelial activation and damage is adhesion molecules appearance in patients with T2DM.6

Pulmonary function tests have been proved to be affected by T2DM. However no research work has been done in Pakistan so far. My study would like to record the frequency of pulmonary dysfunction in patients with T2DM, so that early pulmonary function changes can be picked up and thus improve the patient care by strict glycemic control. We can reduce morbidity in patients with T2DM due to lung dysfunction by assuming lung as another target organ.

Smokers or patients with a history of acute or chronic respiratory disease, history of cirrhosis of liver and autoimmune diseases, history of occupational exposure like petrol pump workers or working in chemical or wood factory, neuromuscular or cardiovascular diseases or kyphoscoliosis, pectus excavatum and morbidly obese patients with BMI > 30 kg/m2 or patients having complaints of cough, sputum, or dyspnea were excluded. After taking informed consent, pulmonary function tests were performed. Patients were explained about the risks and benefits while their identity was kept confidential. The demographic information of the patients like name, age, sex, height and weight were collected. If FEV1 / FVC Ratio is more than 80% or normal it was considered as restrictive defect and if this Ratio is less than 80% it was be considered as obstructive defect. All information was recorded on pre-designed Performa. All Data analyzed by using SPSS version 21.0 for windows. Variable like age was given as mean and standard deviation. Variables like sex and pulmonary dysfunction (restrictive) were given as frequency and percentage.

Results
The study included one hundred and seventy patients with the mean age of 54.32 ± 19.08 years. There were about 122 (71.8%) males and 48 (28.2%) females as shown in Table 1. The mean height was 161.59 cm.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. FVC liter / minute</td>
<td>109.28 ± 20.22</td>
<td>106.28 ± 20.4</td>
</tr>
<tr>
<td>2. FEV1 liter/minute</td>
<td>94.5 ± 28.07</td>
<td>93.06 ± 27.08</td>
</tr>
<tr>
<td>3. FEV1 / FVC %</td>
<td>105.36 ± 24.46</td>
<td>103.25 ± 26.29</td>
</tr>
</tbody>
</table>

Table 1: Age distribution of patients according to Gender; (n = 170).

<table>
<thead>
<tr>
<th>Gender</th>
<th>Mean Age (Years)</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>54.30</td>
<td>6.49</td>
<td>38</td>
<td>70</td>
</tr>
<tr>
<td>Female</td>
<td>54.39</td>
<td>6.52</td>
<td>40</td>
<td>70</td>
</tr>
</tbody>
</table>

Table 2: Spirometry results and gender; (n = 50).

Material and Methods
This cross sectional study was conducted at Department of Medicine, King Edward Medical University Lahore from 01-02-2015 to 31-07-2015. One hundred and seventy non smoker ages 38 – 70 years both male and female with type 2 Diabetes Mellitus, fulfilling the inclusion and exclusion criteria were included in the study through diabetic clinic of Mayo Hospital Lahore.
The mean FVC was 106.28 ± 20.4%. The mean FEV\textsubscript{1} was 94.09 ± 27.72%. The mean FEV\textsubscript{1} / FVC\% was 104.762 ± 24.93. Spirometry results according to gender are given in Table 2. In 28 (16.5%) cases, restrictive pathology was observed, 3 (1.8%) cases had obstructive pathology and 139 (81.8%) cases had normal lung function tests as shown in Figure 2.

The cross-sectional studies have shown that vital capacity is lower in T\textsubscript{2}DM as compared to non-diabetics.\textsuperscript{7} Our study included 170 T\textsubscript{2}DM patients. 16.5% were found to have restrictive pathology, 1.8% had obstructive pathology and 81.8% had normal lung function tests.

The results are similar to previously published data. Atherosclerosis Risk in Communities (ARIC)\textsuperscript{8} study of adults ages 45 – 64, with hypothesis that T\textsubscript{2}DM is associated with reduced pulmonary function parameters. In cross-sectional analysis, middle – age T\textsubscript{2}DM patients have significantly lower pulmonary function parameters than predicted. These associations are categorized by fasting glucose, HbA\textsubscript{1c}, duration of diabetes and treatment. In prospective analysis, FVC decreased faster in T\textsubscript{2}DM patients as compared to non-diabetics. These correlations were independent of risk factors for lung function dysfunctions. This study showed annual decrease of FVC by 58 ml/year.

Results are consistent with cross-sectional studies which also have shown that diabetic patients have reduced FEV\textsubscript{1} and FVC as compared to non-diabetics,\textsuperscript{9,10} with respect to the duration of diabetes. Insulin treatment becomes mandatory, when diabetic patients have co-morbidities. While non diabetic patients have lower FVC and FEV\textsubscript{1} due to high fasting glucose, hyperinsulinemia and insulin resistance.

Lange et al,\textsuperscript{11} followed 506 Danish adults in the Copenhagen City Heart Study for 15 years. Diabetic patients had lower FVC and FEV\textsubscript{1} with difference of > 8% in FVC between diabetics and non-diabetics. However, Diabetes had declined FVC 24 ml/year in females and 39 ml/year in males.

Davis et al,\textsuperscript{12} followed 125 Australian T\textsubscript{2}DM patients for duration of 7 years. FVC and FEV\textsubscript{1} declined at annual rates of 68 and 71 ml/year, respectively. FVC and FEV\textsubscript{1} were declined in patients with higher baseline HbA\textsubscript{1c} with no non-diabetic control group.

Litonjua et al,\textsuperscript{13} conducted a case-control study in 352 patients with T\textsubscript{2}DM and 352 controls. This study showed that T\textsubscript{2}DM patients had lower FEV\textsubscript{1} and FVC. They had only 5.4 ml/year decline after diagnosis of diabetes as compared to non-diabetics.

Primary mechanism lung dysfunction in diabetes remains unclear. Glycosylation of chest wall, thickening of basal lamina,\textsuperscript{14} increased susceptibility to respiratory infections and bronchial tree proteins were mechanism suggested in previous studies. However, hyperglycemia, inflammation and diabetes – related oxidative stress have association with muscular dysfunction.\textsuperscript{15} The pro-inflammatory master regulator
molecules could mediate these effects which is further mediated by hyperglycemia.\textsuperscript{16,17}

Other studies of pulmonary dysfunction in the prediabetic cases obscure causal extrapolations. Recent studies showed that compromised lung function is an independent factor of T\textsubscript{2}DM incidence.\textsuperscript{18} Cross sectional studies showed significant association in diabetics and lung functions as compared to prospective studies. These results showed that abnormalities in lung function predate diabetes and continue after onset of diabetes.

In a study conducted by Sharma B et al,\textsuperscript{20} a mixed restrictive – obstructive pattern of pulmonary dysfunction has been observed in T\textsubscript{2}DM patients which become more severe with course / duration of the disease and poor glycemic control. Strict glycemic control over 12 weeks is not adequate to progress this pulmonary dysfunction. Losartan (diabetes medication) with strict glycemic control does not improve the pulmonary function. Pulmonary dysfunction should be considered as a precise derangement induced by T\textsubscript{2}DM. Further studies may elucidate whether this should be included as a long term complication of T\textsubscript{2}DM. The role of strict glycemic control and losartan therapy on pulmonary function in diabetics with incipient nephropathy is another interesting aspect and needs further studies.

In a study done by Nakajima K et al,\textsuperscript{21} the most believable factor for the association between Restrictive Pattern and Metabolic syndrome is insulin resistance, an essential component that aggravates metabolic abnormalities. The association between pulmonary dysfunction and insulin resistance, and insulin deficiency has been verified by many investigators over several decades.\textsuperscript{158-21}

This study has shown lung dysfunction, especially reduced vital capacity found in T\textsubscript{2}DM patients. Further research work required for pathophysiologic mechanisms and clinical importance of this association. Moreover, physicians must pay close attention to T\textsubscript{2}DM patients regarding their pulmonary functions. Cross sectional studies have been conducted in T\textsubscript{2}DM with respect to their pulmonary functions till today. Some T\textsubscript{2}DM patients have shown abnormalities of pulmonary function parameters, however more information of the association required to be sought out. The influence of duration of diabetes and glycemic control have major role in the development of restrictive pulmonary dysfunction through randomized trials.

**Conclusion**

In this study we conclude that the target organ for diabetic injury is lung. It is responsible for restrictive diseases of lung. More research work required to rule out pathophysiologic mechanisms and clinical significance.

**References**