Research Article

Effects of Type Two Diabetes Mellitus on Lung Function Parameters

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Abstract: Diabetic patients may have significant reduction in lung functions as chronic hyperglycemia in Type two Diabetes Mellitus (T2 DM) is associated with continuing damage, dysfunction, and failure of various organs, especially the eyes, kidneys, nerves, heart, lungs and blood vessels.   This study was carried out on One hundred T2 DM patients, age between 30-70 years of either gender who were subjected to Spirometry, their vital parameters were recorded, glycated hemoglobin (HbA1c) and fasting blood sugar (FBS) were analyzed and matched with healthy controls.Forced Vital Capacity (FVC) in diabetics ranged from 1.52 – 4 (Liters) mean 2.5 ± 0.7SD whereas in controls it ranged from 2.3 - 4.75 mean 3.15 ± 0.6SD with significant P value. ($P < 0.001$) Peak Expiratory Flow Rate (PEFR) in diabetics ranged from 189 – 460 (Liters per minute) mean 289 ± 71SD whereas in controls it ranged from 244 – 572 mean 374 ± 75 with significant P value. ($P < 0.001$) PEFR in female diabetics was 240 ± 39SD with significant P value when compared to male diabetics. ($P < 0.001$) In male diabetics spirometric indices were found insignificant as compared to healthy controls. ($P > 0.05$) HbA1c and FBS were found highly significant in patients when compared with controls in both sexes. ($P < 0.001$) Combined comparison of both sexes showed impaired FVC and PEFR. Lung function variable PEFR was seen impaired in Female Diabetics while male diabetics showed normal PEFR as compared to healthy controls.
Keywords: Diabetes Mellitus, Peak Expiratory Flow, Fasting Blood Sugar.

INTRODUCTION

We hypothesized that lung function impairment may be related to DM. Exercise and healthy eating habits should be More than 366 million people are suffering from Diabetes Mellitus (DM) worldwide, Pakistan ranking 8th globally [1]. DM is responsible for multi system damage and dysfunction. Pulmonary complications of DM have been poorly characterized [2].

Pulmonary damage at an early stage in most patients with DM is subclinical and rarely present with complaints. It is suggested that the increased systemic inflammation associated with DM may result in pulmonary inflammation which causes air way damage [3]. Diabetes increased the inflammation reaction and associated lung injury in mice [4]. Secondary reduction in the antioxidant activity of lung and increased susceptibility to environmental oxidants result in loss of lung function. Matsurba [5] demonstrated that pulmonary complications in DM are due to thickening of the walls of alveoli, alveolar capillaries and pulmonary arterioles, and these changes cause pulmonary dysfunction.Spirometry noninvasively quantifies the physiological reserves in a large micro-vascular bed that is not clinically affected by diabetes. Lung function may provide useful measures of the progression of systemic micro-angiopathy in diabetic patients [6]. Ford and Mannino reported that FVC and FEV1 were significantly and inversely associated with diabetes [7]. Hyperglycemia in DM may lead to a reduction in lung function due to diabetes associated systemic inflammation which results in pulmonary inflammation and air way damage [3]. Reduced antioxidant defense of lung and immune function impairment may also reduce lung function [8]. DM can cause pulmonary complications due to collagen and elastin changes as well as micro-angiopathy [9]. Breathlessness on exertion, orthopnea and increased susceptibility to respiratory infections result from respiratory involvement of T2DM.This increased susceptibility to pulmonary infection is due to an alteration in the chemotactic, phagocytic and bactericidal activity of polymorphonuclear leukocytes and impaired phagocytic function in diabetic patients [10]. Respiratory muscle weakness reduces inspiratory and expiratory capacity and this decreases vital capacity. Measurement of VC is therefore an excellent means of detecting respiratory muscle weakness. FVC may be reduced by airflow obstruction as well as by restriction. Electron microscopic study has shown that in diabetic patients, all parts of the lung are equally affected and the thickening of the basal lamina is of the same magnitude in both the lung and the kidney [7]. In diabetic patients Lung function provide useful measures of the progression of systemic micro-angiopathy [6] promoted in T2 Diabetics to maintain their BMI in

normal limits and to reduce its possible effects on lung functions.

MATERIALS AND METHODS

This Study was conducted in Baqai Medical University teaching hospital, Fatima Hospital and Combined Military Hospital (CMH) Malir Cantt. Karachi, Pakistan from December 2010 to June 2011, after obtaining written consent from the subjects and approval from Baqai university ethical committee. One hundred and sixty Subjects were recruited in the study. One hundred were suffering from T2 Diabetes Mellitus. They were compared with sixty healthy controls. Subjects with history of Asthma, Hypertension, Gross obesities, Smoking, COPD, Anemia, Cardiac Failure and complications of DM were excluded from the study. Healthy controls were selected from Fatima hospital Karachi, PAF Base Residential area Malir Karachi, Skin OPD and Eye OPD CMH Malir Karachi. All the Patients and Controls were subjected to Spirometry, their vital parameters along with height and weight were recorded. Blood samples were collected for Biochemical Analysis. Anthropometric measurements, BMI, Spirometric parameters (FVC, FEV_1, FEV_1/FVC, and PEF) and Biochemical Variables (HbA1c and FBS) were measured.

Statistical Analysis

Statistical analysis was done on SPSS version 13.0.

Comparison of FVC, FEV_1, PEFR and Percentage ratio, FBS and HbA1c was done by finding the means,

calculating the standard deviation and standard error of mean. Student T-test was applied to spirometric evaluates, FBS and HbA1c.

RESULTS

In Table 1 Spiro metric values, Forced Vital Capacity (FVC), Forced Expiratory Volume in 1st second (FEV_1), Peak Expiratory Flow (PEF) and the ratio of FEV_1 and FVC were compared between the T2 DM patients and healthy controls. The minimum value for FVC was 1.52 Liter per minute (L/min) and maximum 4L/min with mean 2.5 ± 0.7 in patients. In control FVC was between 2.3 and 4.75L/min with mean 3.15 ± 0.6. The minimum value for FEV_1 was 1.5 and maximum 3.51L/min with mean 2.1 ± 0.6 in patients. In control FEV_1 was between 1.6 and 3.96 L/min with mean 2.6 ± 0.5. The minimum value for FEV_1/ FVC was 70 L/min and maximum 99 L/min with mean 86 ± 8 in patients. In control FEV_1/ FVC ratio was between 78 and 98 L/min with mean 87 ± 6.6. The minimum value for PEF was 189 L/min and maximum 460 L/min with mean 289 ± 71 in Patients. In control PEF was between 244 and 572 L/min with mean 374 ± 75. All cases and controls were analyzed for comparison of biochemical variables such as Fasting blood Sugar and Glycated Hemoglobin. The minimum FBS level in cases was 84 and maximum 300 mg per dl with mean 174 ± 58. In Controls minimum FBS level was 70 and maximum 105 mg per dl with mean 92 ± 8.1. The minimum HbA1c level in cases was 6 and maximum 12.8 % with mean 8.8 ± 1.17. In Controls minimum HbA1c level was 4.5 and maximum 5.95% with mean 5.2 ± 0.3 (Figure 1).

Table 1: Comparison of Spirometric and Biochemical parameters between Patients and Controls

| Variables	Patients Mean± SD	Range	Control Mean± SD	Range	P value
FVC (L/min)	2.5 ± 0.7	1.52 – 4	3.15 ± 0.6	2.3 – 4.75	< 0.05
FEV_1 (Liters)	2.1 ± 0.6	1.5 – 3.51	2.6 ± 0.5	1.6 – 3.96	> 0.05
Percentage ratio (%)	86 ± 8	70 – 99	87 ± 6.6	78 - 98	> 0.05
PEFR (Liters/min)	289 ± 71	189 - 460	374 ± 75	244 - 572	< 0.05
FBS (mg/dl)	174 ± 58	84 – 300	92 ± 8.1	70 - 105	< 0.001
HbA1c (%)	8.8 ± 1.17	6 – 12.8	5.2 ± 0.3	4.5- 5.95	< 0.001
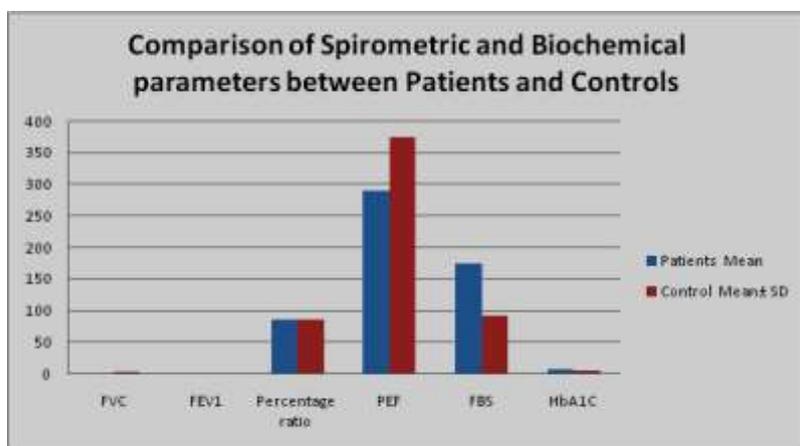
Fig. 1: Comparision between spirometric and biochemical parameters between patients and control

In Table 2 the Spiro metric values, Forced Vital Capacity (FVC), Forced Expiratory Volume in 1st second (FEV$_1$), Peak Expiratory Flow (PEF) and the ratio of FEV$_1$ and FVC were compared between the 50 diabetic female patients and 25 healthy control females. The minimum value for FVC was 1.52 L/min and maximum 2.88 L/min with mean 2.3 ± 0.3 in patients. In controls FVC was between 2.8 and 3.83 L/min with mean 2.9 ± 0.4. The minimum value for FEV$_1$ was 1.2 and maximum 2.85 L/min with mean 1.7 ± 0.2 in patients. In control FEV$_1$ was between 2 and 3.44 L/min with mean 2.6 ± 0.3. The minimum value for FEV$_1$/ FVC was 75 L/min and maximum 98 L/min with mean 85 ± 10 in patients. In control FEV$_1$/ FVC ratio was between 78 and 98 L/min with mean 88 ± 6.3. The minimum value for PEFR was 189 L/min and maximum 322 L/min with mean 240 ± 39 in Patients. In control PEFR was between 244 and 442 L/min with mean 346 ± 51. In the study group, all cases and controls were analyzed for comparison of biochemical variables, Fasting blood Sugar and Glycated Hemoglobin. The minimum FBS level in female cases was 84 and maximum 290 mg per dl with mean 157 ± 49. In Controls minimum FBS level was 79 and maximum 103 mg per dl with mean 94 ± 5.9. The minimum HbA1c level in cases was 6.5 and maximum 11 % with mean 8.7 ± 0.9. In Controls minimum HbA1c level was 4.5 and maximum 5.9 % with mean 5.2 ± 0.3 (Figure 2).

Table 2: Comparison of Spirometric and Biochemical parameters between Female Patients and Controls

| Variables	Patients Mean± SD	Range	Control Mean± SD	Range	P value
FVC (Liters)	2.3 ± 0.3	1.52 – 2.88	2.9 ± 0.4	2.8 – 3.83	> 0.05
FEV$_1$(Liters)	1.7 ± 0.2	1.2– 2.85	2.6 ± 0.3	2 – 3.44	> 0.05
Percentage ratio (%)	85 ± 10	75 – 98	88 ± 6.3	78 – 98	> 0.05
PEFR (Liters/min)	240 ± 39	189 - 322	346 ± 51	244 – 442	< 0.001
FBS (mg/dl)	157 ± 49	84- 290	94 ± 5.9	79 – 103	< 0.001
HbA1c (%)	8.7 ± 0.9	6.5– 11	5.2 ± 0.3	4.5 – 5.9	< 0.001
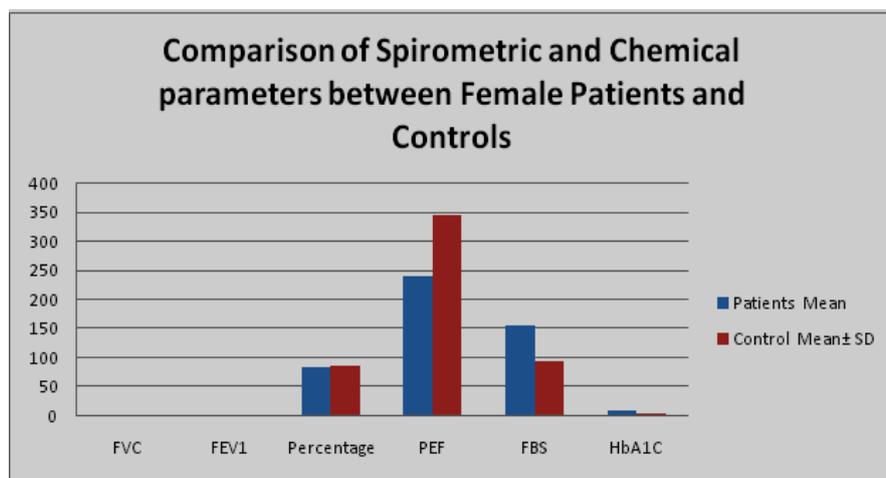
Fig. 2: Comparision of spirometric and chemical parameters between female patients and control

In Table 3 the Spiro metric values, Forced Vital Capacity (FVC), Forced Expiratory Volume in 1st second (FEV$_1$), Peak Expiratory Flow Rate (PEFR) and the ratio of FEV$_1$ and FVC were compared between the male patients and controls. The minimum value for FVC was 1.86 L/min and maximum 4 L/min with mean 3 ± 0.7 in patients. In control FVC was between 2.3 and 4.75 with mean 3.2 ± 0.7 L/min. The minimum value for FEV$_1$ was 1.19 L/min and maximum 3.91 with mean 2.4 ± 0.6 in patients. In control FEV$_1$ was between 1.10 and 3.96 L/min with mean 2.7 ± 0.6. The minimum value for FEV$_1$/ FVC was between 67 and 99 L/min with mean 87 ± 7.6 in patients. In controls the FEV$_1$/ FVC ratio was between 82 and 96 L/min with mean 87 ± 8.4. The minimum value for PEFR was 222 L/min and maximum 564 L/min with mean 345±76 in Patients. In controls the PEFR was between 200 and 520 L/min with mean 355 ± 83. In the study group, all cases and controls were analyzed for comparison of biochemical variables i.e Fasting blood Sugar and Glycated Hemoglobin combined for both sexes. The minimum FBS level in cases was 105 and maximum 300 mg per dl with mean 191 ± 8.7. In Controls minimum FBS level was 70 and maximum 105 mg per dl with mean 92 ± 9.3. The minimum HbA1c level in cases was 6 and maximum 12.87 % with mean 8.8 ± 1.35. In Controls minimum HbA1c level was 4.75 and maximum 5.75% with mean 5.2 ± 0.3 (Figure 3).

Table 3: Comparison of Spirometric and Biochemical parameters between male Patients and Control

Variables	Patients Mean± SD	Range	Control Mean± SD	Range	P value
FVC(Liters)	3 ± 0.7	1.86 - 4	3.2 ± 0.7	2.3 – 4.75	> 0.05
FEV$_1$(Liters)	2.5 ± 0.7	1.19 – 3.91	2.7 ± 0.6	1.10-3.96	> 0.05
Percentage ratio (%)	87 ± 7.6	67-99	87 ± 8.4	82 - 96	> 0.05
PEFR (Liters/min)	345 ± 76	222-564	355 ± 83	200 - 520	> 0.05
FBS (mg/dl)	191 ± 8.7	105 - 300	92 ± 9.3	70-105	< 0.001
HbA1c (%)	8.8 ± 1.35	6 -12.87	5.2 ± 0.3	4.75- 5.75	< 0.001
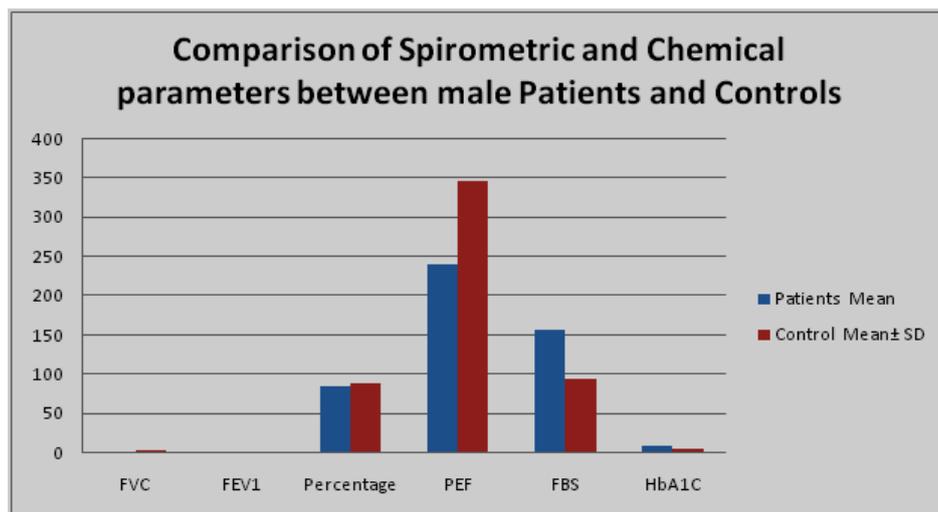
Fig. 3: Comparision between spirometric and chemical parameters between male patients and control

DISCUSSION

The hyperglycemia leads to glycation end products formation and their deposition in different tissues leading to diabetic retinopathy, neuropathy, nephropathy and lung impairment. In our study the mean FBS was 174 ± 58 SD in patients while controls showed 92 ± 8.1SD showing 59% change with significant P value. (P < 0.001) The mean HbA1c was 8.8 ± 1.17SD in patients while controls showed mean HbA1c 5.2 ± 0.3 SD showing 62% change with significant P value (P < 0.001). The findings of Agarwall [11] are consistent with our results. He found mean levels of fasting blood glucose, post prandial blood glucose and HbA1c significantly higher (P < 0.001) in T2 Diabetics whose lung functions were reduced.

McKeever and co workers [12] observed that an increase in mean HbA1c was associated with a decrease in FVC and FEV$_1$. However Lange [13] in the Copenhagen City Heart Study and Litonjua [14] in Normative Aging Study have shown that decline in lung function over time was similar between non-diabetic and diabetics but the results did not change after stratifying for smoking status. These finding were in opposition to our results which showed that participants who developed diabetes during the follow-up, had lower FEV$_1$ and FVC before disease onset as compared to the participants who did not develop diabetes.

Spirometry is a simple, reliable, non-invasive diagnostic tool and its use helps to take early preventive measures in diabetics and those subjects who are not diabetic but have impaired lung functions. In this study evaluation of Spiromtric values FVC, FEV$_1$, Percentage ratio and PEFR were statistically significant. Mohammad Irfan and co workers [15] demonstrated that diabetic patients had significant reduction in FVC and FEV$_1$ relative to their non diabetic controls. They concluded that reduced lung function is chronic complication of diabetes mellitus. This could be due to biochemical alterations in the connective tissue constituents of the lung collagen and elastin, and chronic hyperglycemia induced non enzymatic glycosylation of proteins resulting in micro angiopathy [3]. Respiratory muscle weakness due to autonomic and phrenic neuropathy was also suggested as a cause of reduced lung function, [7] however, the glycemic status was not compared in two groups. In our study glycemic status of patients and controls was assessed by Fasting Blood Sugar and Glycated hemoglobin with significant decrease in spirometric parameters. A study conducted b]y Meo [16] on Saudi diabetic patients showed significant reduction in FVC, FEV$_1$, and PEF as compared to their matched controls. They also showed a strong association with a dose–effect response of

duration of disease and decreased pulmonary function impairment in their diabetic patients. However a study conducted in India by Agarwall [11] failed to show any differences in pulmonary function parameters FVC, FEV_1, PEF, and maximal static inspiratory and expiratory pressures. The major limitation in the study was a very small number of patients in each group. But in our study appropriate number of subjects were recruited who showed significant reduction in FVC and PEF.

The FEV_1 was insignificantly impaired between patients and controls. (P > 0.05) Similar to our results Sanjeev [17] reported insignificant FEV_1 in female group who were not taking oral medication. Walter [3] and Litonjua [15] also showed insignificant FEV_1 in non smokers. Similiarly in our study FEV_1 was slightly reduced but not significant in two groups of patients showing disproportionate change in FEV_1 and FVC with mixed pattern of lung impairment. Engstrom and Janzon [18] demonstrated that decreased FVC and FEV_1 predicted the development of diabetes later on. This is in agreement to our speculation that impaired lung functions may be the future predictor of developing Diabetes Mellitus.

The FEV_1/FVC (Percentage ratio) ranged from 70 - 99 in patients with mean $86 \pm 8SD$ while in control ranged 78 - 98 with mean $87 \pm 6.6SD$ showing insignificant P value (P > 0.05). This finding is in concurrence with Sanjeev [17] who showed that the ratio of FEV_1 / FVC was statistically insignificant. Femognari [19] and co workers concluded that the restrictive but not obstructive dysfunction result in significant decrease in FVC, FEV_1 and percentage ratio (FEV_1/FVC). The possible explanation of insignificant percentage ratio in our study could be due to the restrictive type of pulmonary impairment caused by basal lamina thickening, [7] fibrosis, non-enzymatic glycosylation of collagen protein of chest wall and bronchial tree proteins.

The PEFR ranged from 189 – 460 in patients with mean 289 ± 71 SD while controls ranged from 244 – 572 with mean $374 \pm 75SD$ Showing 77% change with significant P value. (P < 0.05) The findings of Ozoh [20] are in agreement with our study. He showed PEFR significantly lower in diabetic patients compared with the healthy controls.

A study conducted on Indian Diabetics by Kanya Kumari [21] showed that FVC, FEV_1, FEV_1/FVC, PEFR, and FEF 25-75% were reduced when compared with predicted values. She also demonstrated that T2 DM was associated with restrictive pattern of respiratory abnormality. As the duration of diabetes increases the restrictive profile becomes more prominent.

However some studies have showed opposite results. Benbasat [22] showed that forced vital capacity, forced expiratory volume in first second and forced expiratory flow in mid expiratory phase were within the predicted values but the residual volume/total lung capacity ratio was slightly elevated. Sinha [23] reported that there was no difference among the three groups for pulmonary functions including forced vital capacity, forced expiratory volume in first second, peak expiratory flow rate, and maximal static inspiratory and expiratory pressures.

In our study FVC, FEV_1, FEV_1/FVC, PEFR of male T2 Diabetics were compared with healthy adult males and showed statistically insignificant difference (P > 0.05). The possible explanation of our finding may be due to exercise and healthy eating habits in our T2 Diabetic subjects who were soldiers. Their BMI and Lung functions remained unaffected by DM. This is favored by a study conducted by Dharwaker [24] showing that lung functions in T2 Diabetics were reduced due to Respiratory muscle weakness and suggested that strict glycemic control and regular breathing exercises to strengthen the respiratory muscles may improve the pulmonary function tests in Diabetics.

On the other hand when we compared FVC, FEV_1, FEV_1/FVC, PEFR of female T2 Diabetics with healthy adult females FVC, FEV_1 and FEV_1/FVC were found statistically significant (P < 0.05), whereas the PEFR was highly significant (P < 0.001). This finding is in agreement with the study conducted by Ozoh [20] which showed reduced PEF in female T2 Diabetic Nigerians with a predominant restrictive pattern.

CONCLUSION
Lung functions of T2DM patients showed impaired FVC and PEFR when combined for both sexes. PEFR is impaired in Female Diabetics while male diabetics showed normal PEFR as compared to healthy controls.

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