ORIGINAL RESEARCH

Are diabetics prone for restrictive lung disease like pulmonary fibrosis and higher hba1c lead to more harm?

Dr. Venkatesh Deshpande

Consultant Pulmonologist, Dr. Hedgewar Hospital, Aurangabad, Maharashtra, India

Corresponding Author
Dr. Venkatesh Deshpande
Consultant Pulmonologist, Dr. Hedgewar Hospital, Aurangabad, Maharashtra, India
Email: venkypande72@gmail.com

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Abstract

Introduction: Diabetes mellitus is a group of metabolic diseases characterized by persistent hyperglycemia having rising prevalence and incidence in all parts of the world. In view of its micro-vascular complications, it affects all major organs of the body *viz*. heart, kidney, eyes etc. Its complications in lungs were less known and less understood. There is increasing evidence in literature about diabetes affecting lungs. Our study designed to study the effects of diabetes on lungs.

Objectives: To evaluate and compare the pattern of pulmonary dysfunction amongst diabetics and non– diabetics. To assess the effect of HBA1c levels and duration of diabetes on pulmonary dysfunction**.**

Methods: Subjects with diabetes (after applying exclusion criteria) were posted for pulmonary function testing. For control group, people for wellness centre were selected who are non-diabetic.

Results: There was statically significant difference in PFT parameters between diabetes and control group. Poor glycemic control (rising HbA1c) showed significant changes in FVC, FEV1 with duration of disease.

Conclusion: Amongst diabetics, pulmonary dysfunction represents in the form of restrictive abnormality i.e. decrease in FEV1, FVC and increased or normal FEV1/FVC ratio. Our study supports to the theory of pulmonary fibrosis as one of the complications of diabetes.

Keywords: Diabetics, lung disease, pulmonary fibrosis, HbA1c

Introduction

Diabetes mellitus is a group of metabolic diseases characterized by persistent hyperglycemia which prevalence and incidence have raised sharply in India and worldwide. Diabetic complications affect many organs in a person. Along with Lung has been hypothesized as one of the target organs in Diabetes Mellitus along with the known kidneys, eyes, heart, liver etc. There is emerging evidence indicating diabetes can increase the risk of pulmonary dysfunction. As lung consists of abundant alveolar-capillary network and connective tissue, it may be targeted by diabetic micro-vascular damage. Early epidemiological studies from different populations on whether diabetes was as independent risk for pulmonary dysfunction were inconclusive.

Few studies could establish a relation between diabetes and asthma i.e. obstructive airway disease.[1,2,3] While other studies conclude with hyperglycemia lead to pulmonary fibrosis which a restrictive lung disease.[4,5,6,7] Explanation was over nutrition, insulin resistance and inflammation or ROS (reactive oxygen stress) and AGE (advanced glycation end products) leading to fibrosis of lungs and kidneys. In late 70's Schuyler *et al*. first demonstrated loss of pulmonary elastic recoil in the diabetics and proposed the abnormalities might be manifestations of extensive abnormal collagen and elastin depositions(7). Later, a prospective observational study by Davis *et al* demonstrated a decline of lung volumes and airflow limitation (decreased FVC, FEV_1, VC, and PEF) in diabetics.[8]

With this chronic disease, unresolved important clinical question is whether diabetes causes pulmonary fibrosis (restrictive) or Asthma (obstructive airway disease). Hence this present study was carried out with following objectives.

Objectives

- To evaluate and compare the pattern of pulmonary dysfunction amongst diabetics and non– diabetics.

- To assess the effect of HBA1c levels and duration of diabetes on pulmonary dysfunction.

Materials and Methods

This study was carried out amongst 135 patients (includes cases – 45 and controls – 90) during the period of June 2021 to May 2022. All patients studied were from outpatient department at Dr. Hedgewar Hospital, Aurangabad Maharashtra and controls group were from wellness center (Health checkup center AT Dr. Hedgewar Hospital), Aurangabad. All the subjects went through the protocol of informed consent, explanation of study purpose. History along with vital parameters like temperature, pulse, BP taken for all the participants of this study. Respiratory examination was also done. Sixty five individuals with Type 2 DM and 90 individuals without DM (from above 40 years annual health checkup) who underwent Pulmonary Function Tests during 12 months period. Data of HbA1c of diabetic individuals collected. Pregnant, breast feeding women, persons with disability to perform pulmonary function test, persons with pre-existing respiratory disorder and / or cardiac dysfunction were not included in the study. Forty five (45) individuals with Type 2 DM (cases) and ninety (90) individuals without DM (control) were selected. Effect of glycemic control (HbA1c) and duration of diabetes on pulmonary functions were studied. Subjects without diabetes were studied for their pulmonary functions.

Statistical Analysis: The collected data was entered in Microsoft Excel 2007 and then transferred to SPSS version 19, where it was numerically coded and entered. The qualitative was expressed as proportions whereas quantitative data was expressed as mean and standard deviation. Discrete data was analysed using Pearson's Chi-square test for difference in proportions (Fischer's exact test in case if the expected count in any cell was less than 5) to find the association of Diabetes Mellitus with various factors. P-values less than 0.05 were considered as significant and less than 0.001 were considered as highly significant.

Results

Table 1: Comparison of Baseline Variables

Parameters	Case (n=45)	Control (n=90)	p-value
Age	59.62 (±11.69)	45.46 (±5.50)	0.00
Height	163.02 (±5.60)	163.32 (±8.81)	0.193
Weight	64.26 (±10.68)	73.85 (±11.63)	0.001
BMI	24.16 (±3.77)	33.28 (±3.15)	0.098

As Table 1 shows comparison of baseline variables like age, height, and weight and body mass index amongst control and case study groups. As age and weight are statically significant.

Table 2: Comparison of PFT parameters between cases and control

Parameters	Case (n=45)	Control (n=90)	p-value
FVC	79.62 (±22.32)	102.22 (±14.69)	0.000
FEV1	86.71 (±20.33)	110.92 (±13.81)	0.000
FEV1/FVC	110.63 (±14.65)	94.57 (±11.09)	0.000
FEF 25-75%	93.86 (±34.13)	128.97 (±37.03)	0.000

As shown in Table 2 that the comparison of Mean and SD of Pulmonary Function Tests of Diabetic (case group) & control groups using unpaired t- test. Results reveal a significant difference in FVC (p-0.000), FEV1 (p-0.000), FEV1/FVC (p-0.000) and FEF 25-75 (p-0.000).

Table 3: Comparison of PFT parmeters between groups according to Duration of DM and HBA1C Levels

Lung Function Parameters	A	B	C	I)	E	p - value
	Duration <5	Duration <5	Duration <S	Duration >5	Duration > 5	
	HBA IC <7%	HBA1C7%.9.9%	HBA1C >10%	HBA1C <7%	HBA IC7%.9.9%	
FVC	83.81(±17.18)	74.42 (±11.01)	82.20(±27.51)	94.28 (±40.53)	67.11 (±14.21)	0.130
FEV1	86.63 (±13.20)	81.28 (±13.12)	9132 (±27.81)	100 (±26.44)	78.49 (±20.50)	0.242
FEV1FVC	111.0 (±1125)	115.42 (±11.44)	106.56 (±14.82)	114.42 (±21.04)	106.25 (±1399)	0.665
FEF 25%. 75%	85.63(±37.62)	102.71(±44.24)	93.34(±19.59)	101.85(±29.15)	91.40(±35.12)	0.834

As Table 3 shows that the effect of duration of diabetes and HbA1c on pulmonary functions. There seems to be an obvious relation between duration of diabetes & HBA1c levels on pulmonary functions in the form of reduced FVC and FEV1. But this is statically not significant.

Discussion

In routine practice, incidences of diabetes and idiopathic pulmonary fibrosis are rising. This causes an additional burden on patient's health and economy as well. Objective evidence has found a link between the two diseases. Relying on limited research, we speculate that the sustained hyperglycemia in the body promotes the development of pulmonary fibrosis, through various mechanisms like directly damaging the alveolar epithelial cells (AECs), participating in the generation of other pro-inflammatory and pro-fibrotic factors,failure of re-epithelialization and re-endothelialization, and epithelial-mesenchymal transition (EMT, increase of fibrotic markers such as α-smooth muscle actin (α-SMA) and vimentin, and the reduction of epithelial markers such as E-cadherin [9,10] leading to destroyed lung architecture and pathological pulmonary fibrosis.

Although the lung is not the main organ of diabetic complications, patients suffering from both diseases are reported a worsen prognosis.[7-10] Increasing number of studies have found an anti-fibrotic effect of some anti-diabetic agents, and more attention and deeper studies on mechanism and intervention are needed for diabetic pulmonary fibrosis as well as an integrated follow-up system.

Limitations

Further studies with larger sample size are required for better understanding this relationship of diabetes and pulmonary fibrosis. Follow up of these study subjects will also be helpful to get an idea for end stage pulmonary compaction.

Conclusion

There was significant difference in PFT parameters between diabetes and control group. Poor glycemic control (rising HbA1c) showed significant reduction (though statically not significant) in FVC, FEV1 with duration of disease. Amongst diabetics, pulmonary dysfunction represents in the form of restrictive abnormality i.e. decrease in FEV1, FVC and increased or normal FEV1/FVC ratio. Our study supports to the theory of pulmonary fibrosis as one of the complications of diabetes.

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