ORIGINAL ARTICLE

Association of Pulmonary Function Tests and Glycemic Control in Patients with Diabetes

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Abstract

Background: Pulmonary function impairment among diabetic patients has rarely been studied. Hence, the present study was undertaken to analyze the impact of diabetes and glycemic control on pulmonary function tests (PFT).

Materials and methods: A total of 120 patients were included in a cross-sectional study conducted at a tertiary care center in India. Formerly diagnosed diabetic patients with alteration in blood sugar levels were included. According to the duration of diabetes, there were three groups. Among all the patients, PFT was performed and correlated with the duration of the diabetic condition and glycated hemoglobin (HbA1c).

Results: Significant decrease was observed in the mean value of forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), and peak expiratory flow rate (PEFR) in relation to their predicted values with preserved FEV_1/FVC ratio, which is indicative of a restrictive pattern of ventilatory dysfunction. A significant negative correlation was found between the duration of diabetes, glycemic control, and PFT impairment.

Conclusion: Long-term diabetes worsens pulmonary function impairment and poor glycemic control. Hence early screening of the respiratory system and strict glycemic control may help to prevent the progression of pulmonary dysfunctions among individuals with diabetes mellitus (DM).

Keywords: Control, Diabetes, Glycemic, Pulmonary function test.

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Introduction

Diabetes mellitus (DM) arises owing to abnormalities in insulin secretion and fluctuating insulin resistance. Extensive biochemical, morphological, and functional complications associated with DM leads to several consequences which affect various organs and tissues, including the liver, skin, collagen, and elastin, as well as the nervous, cardiovascular, and renal systems.[1] These complications may emerge as a result of biochemical changes in connective tissue components, specifically collagen and elastin. Besides, vascular damage plays a key role in the pathogenesis of DM.[2,3] Although the lung has an extensive capillary network, respiratory complications related to diabetes are often neglected. This is primarily due to the alveolar-capillary system's enormous microvascular reserve and pulmonary impairment, which is usually asymptomatic in diabetic patients.[4] In daily clinical practice, while we evaluate cardiorespiratory manifestations such as dyspnea and easy fatigability among patients with diabetes, more emphasis has been given to the cardiovascular system; although cardiovascular diseases are the utmost prevalent reasons for mortality and morbidity among patients with diabetes, impairment of the respiratory system may also be accountable for the rising incidence of such cardiorespiratory manifestations among diabetic population.[5] Diabetes is not linked to any specific pulmonary symptoms. As a result, diabetic patients do not undergo routine lung disease screening. However, widespread connective tissue and microvascular circulation in the lungs raise the probability of being a target organ in diabetic patients.[6] Although extensive research has been conducted globally on the consequences of DM on pulmonary functions, the literature is not abundant in India. Thus, the present study was designed to assess pulmonary function impairment among patients with diabetes and its correlation with glycemic control and the duration of diabetic conditions.

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Materials and Methods

Study Design and Population

A cross-sectional study was conducted at a tertiary care center in India. Inclusion criteria include diabetic patients with fluctuating blood glucose levels. A total of 120 patients were involved in this study. Patients with occupational lung disease, cardiorespiratory illness, and smokers were excluded.

Ethical Statement

All the participants in this study provided written informed consent, and the study was approved by the Institutional Ethics Committee.

Methodology

Baseline demographics and medical history were recorded. Physical examination and relevant investigation were performed among all patients. Detailed information was collected from each patient regarding the duration of diabetes, various complications of diabetes, history of smoking, and occupational exposure. A detailed physical examination with special reference to the respiratory and cardiovascular systems was done. Chest X-ray, electrocardiography, echocardiography, and glycated hemoglobin (HbA1c) level were estimated in all patients. Pulmonary function tests (PFTs) were executed by spirometry, and the parameters, included (1) forced expiratory volume in 1 second (FEV_1); (2) forced vital capacity (FVC); (3) FEV_1/FVC, peak expiratory flow rate (PEFR); and (4) forced expiratory flow between 25 and 75% of vital capacity ($FEF_{25–75\%}$) were recorded.

Statistical Analysis

The statistical analysis was carried out using Statistical Package for the Social Sciences version 15.0. Continuous data were represented as mean, and standard deviation (SD), and the categorical data were expressed in terms of number and percentage. Comparison among the groups was done using paired *t*-test. The *p*-value of <0.05 was considered statistically significant.

Results

Comparison of Baseline Demographics

The study involved 120 patients. According to the duration of diabetes, that is, 5 years, 5–10 years, and >10 years, patients were classified into groups I, II, and III, respectively, including the 40 patients in each group. The average height, weight, and age in all three groups were equivalent, and statistically, no difference was observed among them. Demographic details of all the groups are depicted in Table 1.

Comparison of Subgroups of the Duration of Diabetes and PFT Parameters

In group I patients, we found that the mean observed values of FVC (2.33), PEFR (4.62), and $FEF_{25–75\%}$ (2.36) were significantly reduced compared to their predicted values. However, the ratio of FEV_1/FVC (0.84) was preserved. No significant difference was observed in the mean value of FEV_1(1.98) (Table 2). In group II patients, the mean observed value of FVC (2.17) was decreased, and the ratio of FEV_1/FVC was increased as compared to the predicted value. The observed mean value of PEFR (4.90) and $FEF_{25–75\%}$ was also decreased (Table 3). In group III patients, we observed a substantial fall in the mean of FVC and FEV_1 in relation to predicted values. However, the ratio of FEV_1/FVC was preserved (Table 4), which is pathognomonic to the restrictive pattern of ventilatory impairment.

Table 1: Demographic characteristics among all three groups

	Group I (n = 40)	*Group II (n = 40)*	*Group III (n = 40)*	
Parameter	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*p-value*
Body weight (kg)	60.1 ± 12.0	61.4 ± 7.85	64.5 ± 8.80	>0.05
Height (cm)	155.7 ± 7.7	155.5 ± 10.0	157.8 ± 10.0	>0.05
Age (years)	54.88 ± 8.28	53.90 ± 8.45	55.78 ± 7.87	>0.05

Table 2: Pulmonary function tests (PFTs) parameters in group I (duration of diabetes <5 years) subjects

	FVC	*FEV_1*	*FEV_1/FVC*	*PEFR*	*$FEF_{25–75\%}$*
Parameter	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*
Observed	2.33 ± 0.48	1.98 ± 0.44	0.84 ± 0.08	4.62 ± 1.68	2.36 ± 0.92
Predicted	2.47 ± 0.44	1.96 ± 0.34	0.80 ± 0.03	6.91 ± 1.24	3.35 ± 1.16
"*t*" (paired *t*-test)	–2.262	0.453	3.937	–8.621	–5.013
p-value	0.029	0.653	0.000	0.000	0.000
Significance	*	NS	***	***	***

$FEF_{25–75\%}$, forced expiratory flow between 25 and 75% of vital capacity; FEV1, forced expiratory volume in 1 second; FVC, forced vital capacity; NS, not significant; PEFR, peak expiratory flow rate; *$p < 0.05$; ***$p < 0.001$

Table 3: Pulmonary function tests (PFTs) parameters in group II (duration of diabetes 6–10 years) patients

	FVC	*FEV_1*	*FEV_1/FVC*	*PEFR*	*$FEF_{25–75\%}$*
Parameter	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*
Observed	2.17 ± 0.65	1.76 ± 0.58	0.82 ± 0.12	4.90 ± 2.19	2.16 ± 1.14
Predicted	2.42 ± 0.50	1.86 ± 0.43	0.78 ± 0.07	6.52 ± 1.21	2.96 ± 0.49
"*t*" (paired *t*-test)	–2.607	–1.309	2.224	–5.014	–4.262
p-value	0.013	0.198	0.032	<0.001	<0.001
Significance	*	NS	*	***	***

$FEF_{25–75\%}$, forced expiratory flow between 25 and 75% of vital capacity; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; NS, not significant; PEFR, peak expiratory flow rate; *$p < 0.05$; ***$p < 0.001$

Correlation of HbA1c with PFT Parameters

In our study, we found that the patients with HbA1c levels of <7 showed a significant reduction in the mean value of PEFR (4.61). Among those with HbA1c levels 7–9, a statistically significant reduction was revealed between observed and expected values for FVC and FEV_1. Whereas a significant rise was observed for the ratio of FEV1/FVC as compared to the predicted value. The mean observed values of PEFR and $FEF_{25–75\%}$ were also lower than their predicted values. In patients with HbA1c levels of >9, the observed mean FEV_1 decreased more significantly with preserved FEV_1/FVC ratio (Table 5).

Discussion

The negative effects of diabetes on the functioning of several organs are well-known facts. In the present study, the influence of diabetes on ventilatory function was analyzed. As depicted by a significant decrease in FVC and FEV1 with a preserved ratio of FEV_1/FVC, ventilatory dysfunction in diabetics was predominantly restrictive. Histopathological findings in diabetic patients' lungs revealed microangiopathic changes such as thickening of the pulmonary capillary basal lamina, alveolar, epithelial, and nodular fibrosis that will lead to restrictive lung disease.[7,8] Other possible mechanisms include glycation of chest wall/bronchial tree protein,[9,10] pulmonary autonomic neuropathy,[11,12] and respiratory muscle weakness due to defective muscle metabolism[13,14] could also be contributory factors. In our study, we compared the various parameters of PFT considering the duration of diabetes and found that patients with diabetes for <10 years displayed significant reductions in PEFR, FVC, and $FEF_{25–75\%}$ relative to their predicted values. However, FEV_1/FVC was preserved; this finding is suggestive of a restrictive type of ventilatory dysfunction. Patients having diabetes for>10 years presented a more significant decline in FVC ($p < 0.001$), and a significant reduction in the mean value of FEV_1 was also observed, representing that these parameters were reduced significantly with the duration of diabetes. However, PEFR, $FEF_{25–75\%}$, and FEV_1/FVC ratio were not significantly affected by the duration of diabetes. A significant negative correlation was found between FVC, FEV_1, and the duration of diabetes. This finding is supported by Yeh et al.[15] and Lange et al.[16] this negative correlation can be explained by the progression and the level of inflammation, which may advance with prolonged diabetes duration, as we concluded with increasing duration of diabetes ventilatory impairment worsens, like other complications of diabetes a periodic evaluation of pulmonary function should also be considered in diabetic patients. Among patients with stable blood glucose levels (HbA1c of <7), no significant difference was observed

Table 4: Pulmonary function tests (PFTs) parameters in group III (duration of diabetes >10 years) patients

	FVC	*FEV_1*	*FEV_1/FVC*	*PEFR*	*$FEF_{25–75\%}$*
Parameter	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*
Observed	2.11 ± 0.57	1.69 ± 0.43	0.81 ± 0.14	4.59 ± 1.72	2.23 ± 0.82
Predicted	2.44 ± 0.42	1.86 ± 0.34	0.77 ± 0.03	6.64 ± 1.56	2.78 ± 0.36
"*t*" (paired *t*-test)	−3.740	−2.657	2.231	−7.480	−3.912
p-value	0.001	0.011	0.032	<0.001	<0.001
Significance	***	*	*	***	***

$FEF_{25–75\%}$, forced expiratory flow between 25 and 75% of vital capacity; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; NS, not significant; PEFR, peak expiratory flow rate; *$p < 0.05$; ***$p < 0.001$

Table 5: Correlation of HbA1c levels with PFTs parameters

		FVC (L)	*FEV_1*	*FEV_1/FVC*	*PEFR (L/second)*	*$FEF_{25–75\%}$*
HbA1c levels		*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*	*Mean ± SD*
HbA1c <7 ($n = 41$)	Observed	2.42 ± 0.54	1.97 ± 0.52	0.80 ± 0.09	4.61 ± 2.08	2.45 ± 1.11
	Predicted	2.46 ± 0.50	1.89 ± 0.41	0.78 ± 0.05	6.87 ± 1.18	3.25 ± 1.14
	"*t*" (paired *t*-test)	−0.469	1.296	1.934	−7.873	−0.469
	p-value	0.642	0.202	0.060	0.000	0.642
	Significance	NS	NS	NS	***	NS
HbA1c 7–9 ($n = 36$)	Observed	2.15 ± 0.47	1.80 ± 0.47	0.85 ± 0.10	5.16 ± 1.45	2.26 ± 0.97
	Predicted	2.51 ± 0.39	1.96 ± 0.33	0.79 ± 0.04	6.99 ± 1.14	3.07 ± 0.45
	"*t*" (paired *t*-test)	−4.461	−2.238	3.853	−6.293	−4.461
	p-value	0.000	0.032	0.000	0.000	Significance
	Significance	***	*	***	***	***
HbA1c >9 ($n = 43$)	Observed	2.03 ± 0.62	1.66 ± 0.47	0.83 ± 0.15	4.41 ± 1.93	2.05 ± 0.79
	Predicted	2.36 ± 0.45	1.84 ± 0.36	0.78 ± 0.06	6.27 ± 1.56	2.79 ± 0.47
	"*t*" (paired *t*-test)	−3.866	−2.704	2.508	−6.382	−3.866
	p-value	0.000	0.010	0.016	0.000	0.000
	Significance	***	**	*	***	***

$FEF_{25–75\%}$, forced expiratory flow between 25 and 75% of vital capacity; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; HbA1c, glycated hemoglobin; NS, not significant; PEFR, peak expiratory flow rate; *$p < 0.05$; **$p < 0.01$; ***$p < 0.001$

in the PFT parameters in relation to predicted values except for PEFR, which was significantly reduced. Significant fall in FVC, FEV_1, PEFR, and $FEF_{25–75\%}$ in relation to their predicted values was found in patients with HbA1c levels 7–9. Nevertheless, the mean value of FEV_1/FVC was significantly increased as compared to their predicted value. The result showed an inverse correlation between HbA1c and FVC, FEV_1, PEFR, and $FEF_{25–75\%}$ concluding that poor glycemic control has a detrimental effect on lung function impairment. Protein's nonenzymatic glycosylation in the lungs and chest wall reduces the collagen's susceptibility to proteolysis and results in collagen buildup in lung connective tissue.[17,18] Hyperglycemia primarily triggers this pathway. Thus, it is frequently observed among individuals with poor glycemic control.[16] Glycemic control is crucial for curtailing complications of diabetes comprising lung function impairment. Hence, clinicians must monitor HbA1c levels while treating diabetic patients. Comparable results were shown by many other studies.[19,20] It is unknown whether improving glycemic control leads to improvement in lung function impairment. Future studies need to be done to evaluate the benefits of improved glycemic control on lung function impairment.

Study Limitations

Our study has several limitations. First, we did not include a healthy control group for comparison of pulmonary function abnormalities between diabetic and nondiabetic. Second, we did not perform any investigations to rule out unknown and subclinical preexisting respiratory disease in the study population, which may contribute to spirometry changes and could be the confounders affecting the results of our study. Third, we have not performed diffusion studies diffusing capacity of the lungs for carbon monoxide (DLCO) which may provide more detail about the severity of obstructive and restrictive lung diseases and pulmonary vascular diseases.

Conclusion

In our study, the majority of diabetic patients had restrictive pulmonary dysfunction. Duration of diabetes and poor glycemic control could be the contributory factors. Medical practitioners should be aware of the pulmonary complication of diabetes, and routine screening of pulmonary function must be done in diabetic patients, especially in patients suffering from diabetes for a long period and having poor glycemic control, so that early intervention can be done to reduce morbidity.

Clinical Significance

Diabetes mellitus (DM) is positively correlated with a decline in lung function as measured through PFTs, including decreased FVC and FEV_1. Therefore, PFT should be performed regularly in individuals with DM to monitor the progression of respiratory complications and to allow for early intervention and treatment.

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