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RESEARCH ARTICLE

Effect of Type 2 Diabetes Mellitus on Pulmonary Function

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ABSTRACT

Diabetes mellitus (DM) is a chronic metabolic and vascular disorder affecting various organs and systems. Many studies have shown impairment of pulmonary functions in diabetics subjects, whereas some studies did not show any changes in pulmonary functions. Therefore, objective of the present study is to find out alterations in the pulmonary functions. **Methods Design, Setting, and Participants:** This cross-sectional study was conducted in a tertiary care hospital among patients attending medicine department. The sample size was 200. A total of 100 known cases of DM without any acute or chronic lung disease and 100 healthy controls were included in the age group of 40–50 years. History of smoking was excluded in both groups. The diabetic subjects had at least 1 year of duration of disease. **Intervention:** Pulmonary function test (spirometry) was performed with NND TrueFlow Easy One™ diagnostic spirometer. **Main Outcome Measures:** The forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) were the primary outcome measures to assess the pulmonary functions. **Results:** In Phase 1 analysis, diabetic subjects did not show any changes in both FVC and FEV1 when compared with controls. In Pearson correlation test, a significant negative correlation between duration of disease and pulmonary functions, FVC at the level of 0.05 and FEV1 at the level of 0.01 were observed. However, in Phase 2 analysis, a significant reduction in FVC and FEV1 was observed in diabetic subjects with duration of diabetes more than 5 years. **Conclusion:** The decline in FVC and FEV1 in diabetic subjects is more likely to be the effect of DM. The decline is more pronounced with the duration of the disease.

Keywords: Spirometry, pulmonary function test, duration of diabetes

INTRODUCTION

Diabetes in all forms imposes an unacceptably high human, social, and economic cost on countries at all income levels. Despite the numerous tools available to tackle the disease, diabetes and its complications are more and more prevalent.[1] The highest numbers of people with undiagnosed diabetes are the same countries with largest number of people with diabetes: China, India, and the United States.[2]

Persistently, high blood glucose levels cause generalized vascular damage affecting the heart, eyes, kidneys, and nerves. Diabetes is one of the leading causes of cardiovascular disease, blindness, kidney failure, and lower-limb amputation. In pregnancy, poorly controlled diabetes increases the risk of maternal and fetal complications. Chronic microvascular complications are nephropathy, neuropathy, and retinopathy, whereas chronic macrovascular complications are coronary artery disease leading to angina or myocardial infarction, peripheral artery disease contributing to stroke, diabetic encephalopathy, and diabetic foot. In addition,

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diabetes has also been associated with increased rates of cancer, physical and cognitive disability,[3] tuberculosis,[4] and depression.[5]

The association of reduced lung function and diabetes has been described for many years, and many reports have suggested that the lung is a target organ of diabetic microangiopathy.[6] The spirometry and lung diffusing capacity of the lungs for carbon monoxide are used as primary outcome measures to assess the effect of diabetes on pulmonary functions.[7]

There is a significant reduction in forced vital capacity (FVC) and forced expiratory volume in the first second (FEV1) among diabetic subjects. The reduction in pulmonary functions is influenced by the duration of illness and glycemic exposure. Some studies showed significant association of pulmonary functions with other manifestations of diabetic microangiopathy, i.e., the reduction in pulmonary functions is more pronounced in diabetic subjects with either retinopathy or nephropathy.[8,9] Some studies suggested that impairment of pulmonary function as a predictor of the incidence of diabetes and showed the subsequent development of diabetes in subjects with lower vital capacity.[10]

The history of smoking was excluded from most of the studies, to avoid the deteriorating effect of smoking on pulmonary functions. Subjects with acute or chronic pulmonary diseases were also excluded from the study.

The large prospective studies showed the association of lung functions with glycemic exposure hemoglobin A1C than the duration of diabetes.[11-13] These results were inconsistent, as many studies did not show changes in pulmonary functions when compared with controls.[14-16] Hence, it was envisaged to take up a study in our tertiary care hospital and find out the influence of diabetes mellitus (DM) on FVC and FEV1.

Objectives

- The study aims to determine the FVC and FEV1 of these subjects and compare FVC and FEV1 of diabetic subjects with the FVC and FEV1 of controls
- And the study aims to find out the correlation of pulmonary functions in diabetic subjects with the duration of diabetes.

MATERIALS AND METHODS

The study was conducted on 200 subjects. A total of 100 patients with type 2 DM and 100 healthy matched controls were taken from medicine department. The study was conducted after obtaining institutional ethical clearance. A written informed consent was obtained from the study subjects before their participation in the study. A detailed history was obtained, and physical examination was carried out. Subjects with smoking, abdominal, thoracic, surgery, and with spinal deformity were excluded from the study and also subjects with lung pathology such as bronchial asthma, chronic obstructive pulmonary disease, and pulmonary tuberculosis were also excluded from the study. Healthy non-diabetic subjects and type-2 diabetic subjects with minimum 1 year duration were included in the study. Anthropometric measurements: Height was measured in centimeters and weight was measured in kilograms and body mass index (BMI) was calculated.

Spirometry

NND TrueFlow Easy One™ diagnostic spirometer, made in Zurich Switzerland, is used to measure FVC and FEV1. The individuals were made to sit comfortably, and instruction was given in English or in Tamil. Individuals were asked to close the nostrils with thumb and index finger and were told to take a deep and deeper breath through his/her mouth and breath out with maximum effort through the mouthpiece which is connected to the easy one spirometer. A long beep indicates completion of the test. The procedure was repeated until the spirometer displays "session complete" after at least three attempts. Individuals were given adequate rest in between the attempts. NND Easy One™ diagnostic spirometer was connected to the personal computer in which the EasyWare software 2.22.0.0 Version was installed, and the test results are obtained as hard copy. The best value displayed was taken for analysis.

FVC

The maximum volume of air can be exhaled with maximum forced expiratory effort from the maximum inspiration.

FEV1

The fraction of the FVC expired during the 1st s of forced expiration.

Statistical analysis

Student *t*-test was applied to compare the means between diabetic subjects and control group for the selected variables such as age, sex height, FVC, and FEV1 with the selected variables (age, height, weight, and duration). Regression analysis was applied to predict mathematical equations for FVC and FEV1 separately based on age, height, weight, and duration.

RESULTS

Hundred known cases of DM without overt lung disease and hundred healthy controls, nonsmokers without any lung disease were included in the study. The duration of illness was elicited from the subject. Number of diabetic subjects with the duration of diabetes 1–5 years was 45 and with the duration of diabetes, more than 5 years was 55.

Phase 1 analysis

There are 64 males and 36 females in the diabetic group and 75 males and 25 females in the control group. The means and the standard deviation of the variables were compared by applying Student's *t*-test. The mean values of age sex, height, weight, and BMI are shown in Table 1 *P*-values obtained showed no significant difference; all the above-mentioned variables were not statistically significant. Chi-square was applied for comparison of sex distribution, and *P*-value shows no significant difference.

A comparison of FVC and FEV1 between the diabetic subjects and controls is given in Table 1.

The mean FVC of diabetic subjects was found to be 2.76 ± 0.58 L, and the mean FVC value for control group was found to be 2.91 ± 0.55 L. The mean FEV1 of diabetic subjects was found to be 2.35 ± 0.53 L, and the mean FEV1 value for control group was found to be 2.4 ± 0.49 L. The Student's *t*-test was applied to compare the two means. *P*-value shows no significant change in FVC, FEV1 values in diabetic group when compared with control group

Phase 2 analysis

Pearson correlation test was applied in diabetic subjects to find out the relationship of FVC and FEV1 with the selected variables. (Age, height, weight, and duration) Pearson correlation analysis is given in Table 2. Correlation of age and height with FVC and FEV1 was significant. However, there was no correlation between weight and BMI with FVC and FEV1.

Correlation of duration with FVC and FEV1

There was significant correlation between the duration and FVC at the 0.05 level (two- tailed) and also duration strongly correlates with FEV1 at the 0.01 level (two-tailed).

Table 1: Comparison of anthropometric and pulmonary function test data of diabetic patients with their healthy controls

Variables	Diabetic subjects (*n*=100) mean±SD	Controls (*n*=100) mean±SD	*t*-value	*P*-value
Age (years)	45.36±3.70	44.84±3.60	0.999	0.319 (NS)
Height (cm)	165.50±7.00	167.05±6.60	1.558	0.121 (NS)
Weight (kg)	72.51±13.50	74.66±14.50	−1.089	0.277 (NS)
BMI	26.41±0.58	26.41±0.58	0.122	0.903 (NS)
Forced vital capacity (L)	2.76±0.58	2.91±0.55	−1.825	0.069 (NS)
Forced expiratory volume in the first second (L)	2.35±0.58	2.44±0.49	−1.323	0.187 (NS)

P-value <0.05 is considered to be significant. NS: Not significant, SD: Standard deviation

Regression analysis

Table 3 shows the results of multiple linear regression analysis of FVC and FEV1 with the age, height, weight, and duration of diabetic subjects. The purpose of a multiple linear regression model is to analyze all selected variables simultaneously. In correlation analysis, the variables are analyzed separately. Another purpose of the multiple linear regression models is to predict the dependent variable based on the selected independent variables. The results of regression analysis indicate that age of the subject, height of the subject, and duration of illness are highly related to FVC and FEV1 levels, after adjusting with other variables. However, weight of the person has no significant relationship with FVC and FEV1. The regression coefficient square value of 46.2% indicates that 46% of FVC and FEV1 have been explained by age, height, and duration of DM.

The Pearson correlation coefficient and regression analysis indicate increase in duration of disease decreases the FEV1 and FVC levels [Figures 1 and 2]. Hence, to get more clarity, the diabetic subjects with duration of illness more than 5 years are compared with the controls.

Table 2: Correlation of FVC and FEV1 with age, height, and weight and duration in diabetic subjects

Variables	FVC	FEV1
Age	−0.299**	−0.276**
Height	0.491**	0.429**
Weight	0.163	0.150
Body mass index	−0.280	−0.007
Duration	−0.244*	−0.293**

*Correlation is significant at the 0.05 level (two- tailed), **Correlation is significant at the 0.01 level (two- tailed), FVC and FEV1 strongly correlate with the age, height, duration. FVC: Forced vital capacity, FEV1: Forced expiratory volume in the first second

Table 4 shows the mean and standard deviation of FVC and FEV1 in controls and diabetic subjects with duration of disease more than 5 years. The mean FVC level for the control group was found to be 2.91 ± 0.55 L and for the diabetic subjects with duration more than 5 years 2.64 ± 0.48 L. Student's *t*-test was applied to compare the two mean values. *P*-values indicate that there is a significant reduction in FVC and FEV1 in diabetic subjects with more than 5 years duration when compared with controls [Figures 3 and 4].

DISCUSSION

The major findings of this study are a significant reduction in FVC and FEV1 in diabetic subjects with a duration of more than 5 years. There is a significant negative correlation of both FVC and FEV1 with duration.

However, in Phase 1 analysis, where all the 100 diabetic subjects with a duration of 1–15 years were compared with the matched controls. There were no statistically significant changes in FVC and FEV1 between diabetic subjects and controls.

Some studies did not show a significant reduction in FVC and FEV1. However, they observed significant reduction in diffusing capacity in type 2 diabetes subjects with microangiopathy.[17,18,14]

However, several studies reported a significant reduction in FVC and FEV1 in both sexes.[19-22] Agarwal *et al*.,[15] in their study conducted in Northern India, showed significant reduction FVC and FEV1 in males than females and they observed significant reduction in peak expiratory flow rate and maximum voluntary ventilation in female subjects. However, the present study shows

Table 3: Multiple linear regression analysis of FVC and FEV1 with age, height weight and duration of diabetes mellitus

Mode	Regression analysis result of FVC value					Regression analysis result of FEV1 value				
	B	SE	Beta	*t*-value	*P*-value	B	SE	Beta	*t*-value	*P*-value
Constant	2.763	0.042		65.74	0.000	2.348	0.040		58.800	0.000
Age	−1.600	0.045	−0.273	−3.560	0.001	−0.150	0.043	−0.281	−3.511	0.001
Height	0.396	0.048	0.677	8.234	0.000	−0.320	0.046	−0.601	7.006	0.001
Weight	−0.099	0.048	−0.170	−2.065	0.420	−0.680	0.046	−0.127	−1.481	0.142
Duration	−0.116	0.045	−0.198	−2.576	0.012	−0.127	0.043	−0.239	−2.974	0.004
	R^2=0.505 (50.5%)					R^2=0.462 (46.2%)				

*Significant value *P*<0.05 For the independent variables, Z values are called to overcome the normality. FVC: Forced vital capacity, FEV1: Forced expiratory volume in the first second

Table 4: Comparison of FVC and FEV1 between the controls and diabetics having diabetes mellitus for more than 5 years

Variables	Diabetic subjects (*n*=55) mean±SD	Controls (*n*=100) mean±SD	*t*-value	*P*-value
FVC	2.64±0.48	2.91±0.55	2.940	0.004*
FEV1	2.22±043	2.4±0.49	2.710	0.007*

*Highly significant *P* value. FVC: Forced vital capacity, FEV1: Forced expiratory volume in the first second, SD: Standard deviation

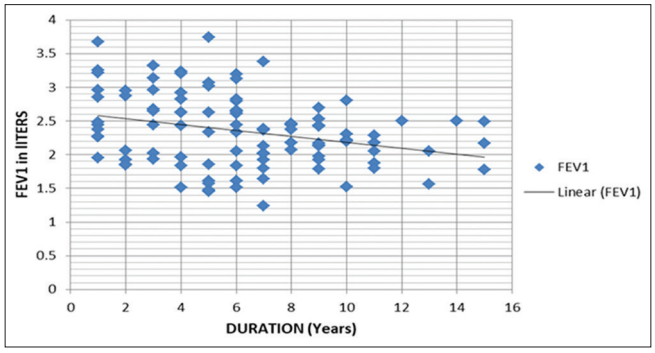

Figure 1: Regression analysis for forced expiratory volume in the first second (FEV1) against duration of diabetes mellitus. A significant negative correlation was found, between FEV1 and duration of disease

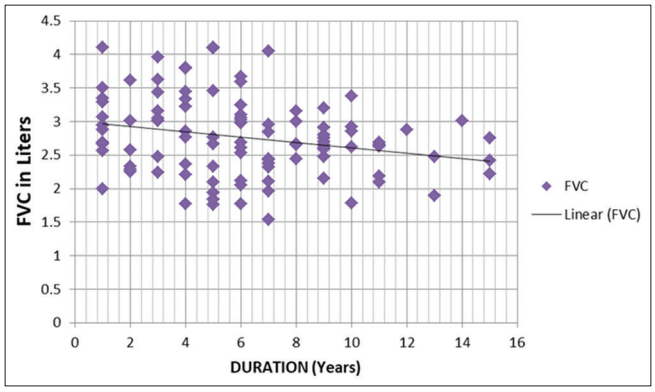

Figure 2: Regression analysis for forced vital capacity (FVC) against the duration of diabetes mellitus. A significant negative correlation was found, between FVC and duration of disease

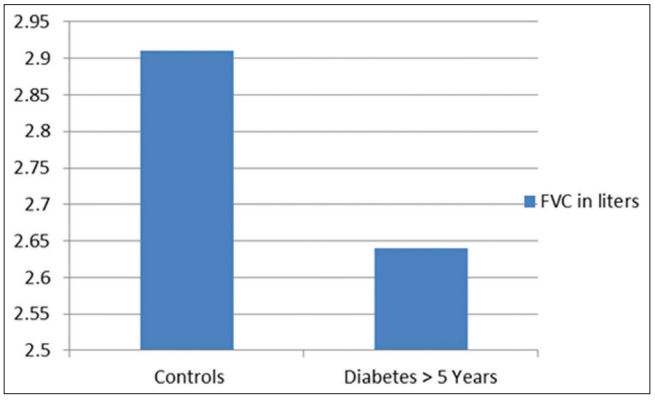

Figure 3: Comparison of forced vital capacity values between diabetes mellitus subjects and controls

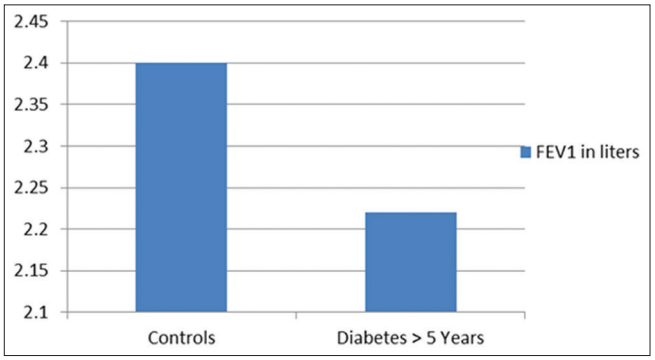

Figure 4: Comparison of forced expiratory volume in the first second values between diabetes mellitus subjects and controls

no significant difference in pulmonary function between males and females diabetics.

The Phase 2 analysis was focused on the possible correlation of pulmonary functions with the duration of illness. In the Pearson correlation analysis, there was a strong association of FVC and FEV1 with duration of illness among diabetics. The correlation of FVC was at the 0.05 level and FEV1 was at the 0.01 level. Davis *et al*.,[23] in their large prospective study in type 2 diabetics, observed significant reduction in both FVC and FEV1 ($P < 0.001$) in the follow-up spirometry when compared with baseline FVC and FEV1 values. Earlier studies conducted by Meo *et al*.,[24] and Asanuma *et al*.[19] also showed significant strong correlation with duration of the disease. But the study conducted by Verma *et al*[21] and Shah *et al*[25] showed significant reduction in all the parameters of pulmonary function tests except FEV1/FVC in patients of type 2 DM as compared with the healthy controls but did not show correlation of FVC, FEV1 with duration of disease, and glycemic levels.

The Pearson correlation coefficient and regression analysis indicate increase in duration of disease decreases the FEV1 and FVC levels. Hence, to get more clarity, the diabetic subjects with duration of diabetes more than 5 years were compared with controls to find out any changes in lung functions. The diabetic subjects showed highly significant reduction

in FVC and FEV1 when compared with controls.

The pathophysiological mechanisms involved in the reduction of pulmonary functions in DM are still not clear. The earlier histopathological studies[26,27] showed features of microangiopathy in the lungs.

In the present study, pulmonary functions did not show any statistically significant differences in diabetic subjects with a duration of diabetes <5 years when compared with controls.

Limitations of the present study

First, the glycemic status of the diabetic subjects was not correlated, second, the relationship with other microvascular complications, and third, the present study is a cross-sectional study. A prospective study will be worthwhile to understand the role of glycemic status, duration, and other comorbid conditions and also to understand possible pathophysiological mechanisms.

CONCLUSION

The present study suggests that the impairment in pulmonary functions is more likely to be the effect of DM. As a significant reduction was observed in diabetic subjects with duration more than 5 years, spirometry has to be done periodically to assess the pulmonary functions.

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REFERENCES

1. International Diabetes Federation. The Diabetes Atlas. 8th ed. Brussels: International Diabetes Federation; 2017. p. 12.
2. Dall TM, Yang W, Halder P, Pang B, Massoudi M, Wintfeld N, *et al.* The economic burden of elevated blood glucose levels in 2012: Diagnosed and undiagnosed diabetes, gestational diabetes mellitus, and prediabetes. Diabetes Care 2014;37:3172-9.
3. Carstensen B, Jørgensen ME, Friis S. The epidemiology of diabetes and cancer. Curr Diab Rep 2014;14:535.
4. Riza AL, Pearson F, Ugarte-Gil C, Alisjahbana B, van de Vijver S, Panduru NM, *et al.* Clinical management of concurrent diabetes and tuberculosis and the implications for patient services. Lancet Diabetes Endocrinol 2014;2:740-53.
5. Roy T, Lloyd CE. Epidemiology of depression and diabetes: A systematic review. J Affect Disord 2012;142 Suppl: S8-21.
6. Goldman MD. Lung dysfunction in diabetes. Diabetes Care 2003;26:1915-8.
7. Kaminsky DA. Spirometry and diabetes: Implications of reduced lung function. Diabetes Care 2004;27:837-8.
8. Weynand B, Jonckheere A, Frans A, Rahier J. Diabetes mellitus induces a thickening of the pulmonary basal lamina. Respiration 1999;66:14-9.
9. Davis TM, Knuiman M, Kendall P, Vu H, Davis WA. Reduced pulmonary function and its associations in Type 2 diabetes: The Fremantle diabetes study. Diabetes Res Clin Pract 2000;50:153-9.
10. Yeh HC, Punjabi NM, Wang NY, Pankow JS, Duncan BB, Cox CE, *et al*. Cross-sectional and prospective study of lung function in adults with Type 2 diabetes: The atherosclerosis risk in communities (ARIC) study. Diabetes Care 2008;31:741-6.
11. Litonjua AA, Lazarus R, Sparrow D, Demolles D, Weiss ST. Lung function in Type 2 diabetes: The normative aging study. Respir Med 2005;99:1583-90.
12. Lange P, Parner J, Schnohr P, Jensen G. Copenhagen city heart study: Longitudinal analysis of ventilatory capacity in diabetic and nondiabetic adults. Eur Respir J 2002;20:1406-12.
13. Lawlor DA, Ebrahim S, Smith GD. Associations of measures of lung function with insulin resistance and Type 2 diabetes: Findings from the British women's heart and health study. Diabetologia 2004;47:195-203.
14. Sinha S, Guleria R, Misra A, Pandey RM, Yadav R, Tiwari S. Pulmonary functions in patients with Type 2 diabetes mellitus and correlation with anthropometry and microvascular complications. Indian J Med Res 2004;119:66-71.
15. Agarwal V, Gupta B, Dev P, Kumar Y, Ahmad N, Gupta KK, *et al*. Deterioration of lung functions in Type II diabetic subjects from Northern India. Indian J Physiol Pharmacol 2009;53:189-91.
16. van den Borst B, Gosker HR, Zeegers MP, Schols AM. Pulmonary function in diabetes: A metaanalysis. Chest 2010;138:393-406.
17. Sreeja CK, Elizabeth S, Kesavachandran C, Shashidhar S. Pulmonary function in patients with diabetes mellitus. Indian J Phyciol Pharmacol 2003;47:122-31.
18. Agarwal AS, Fuladi AB, Mishra G, Tayade BO.

Spirometry and diffusion studies in patients with Type-2 diabetes mellitus and their association with microvascular complications. Indian J Chest Dis Allied Sci 2010;52:213-6.
19. Asanuma Y, Fujiya S, Ide H, Agishi Y. Characteristics of pulmonary function in patients with diabetes mellitus. Diabetes Res Clin Pract 1985;1:95-101.
20. Sandler M. Is the lung a "target organ" in diabetes mellitus? Arch Intern Med 1990;150:1385-8.
21. Verma S, Goni M, Kudyar RP. Assessment of pulmonary functions in patients with diabetes mellitus. JK Sci 2009;11:71-4.
22. Kaur S, Agarwal N. Pulmonary function tests in Type 2 diabetes mellitus. Arch Med Health Sci 2016;4:35-9.
23. Davis WA, Knuiman M, Kendall P, Grange V, Davis TM, Fremantle Diabetes Study. Glycemic exposure is associated with reduced pulmonary function in Type 2 diabetes: The fremantle diabetes study. Diabetes Care 2004;27:752-7.
24. Meo SA, Al Drees AM, Ahmed J, Ahmed Shah SF, Al-Regaiey K, Husain A, *et al*. Effect of duration of disease on ventilatory function in an ethnic Saudi group of diabetic patients. J Diabetes Sci Technol 2007;1:711-7.
25. Shah SH, Sonawane P, Nahar P, Vaidya S, Salvi S. Pulmonary function tests in Type 2 diabetes mellitus and their association with glycemic control and duration of the disease. Lung India 2013;30:108-12.
26. Matsubara T, Hara F. The pulmonary function and histopathological studies of the lung in diabetes mellitus. Nihon Ika Daigaku Zasshi 1991;58:528-36.
27. Mori H, Okubo M, Okamura M, Yamane K, Kado S, Egusa G, *et al.* Abnormalities of pulmonary function in patients with non-insulin-dependent diabetes mellitus. Intern Med 1992;31:189-93.