

Study of Pulmonary Function Tests (Spirometry and Diffusion Lung Capacity of Carbon Monoxide) in Non-Smoker Diabetic Patients at a Tertiary Care Hospital

Ammlan Mishra¹, Manoranjan Dash², Smrutirekha Swain³, Sabita Maharana^{4*}

¹Assistant Professor, Department of Pulmonary Medicine, IMS & SUM Hospital, Bhubaneswar, Odisha, India

²Professor, Department of Pulmonary Medicine, SCB Medical College, Cuttack, India

³Assistant Professor, Department of Pulmonary Medicine, SCB Medical College, Cuttack, India

⁴Assistant Professor, Department of Community Medicine, IMS & SUM Hospital, Bhubaneswar, Odisha, India

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Corresponding Author: Dr Sabita Maharana

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Abstract:

Introduction: Diabetes Mellitus is a heterogeneous metabolic disorder characterized by impaired glycemic control leading to pulmonary complications.

Aim: To record, compare and correlate the spirometry and diffusion test in non-smoker type 2 diabetes patients as well as in non-smoker non-diabetics.

Materials and Methods: Non-smoker diabetes patients satisfying the inclusion criteria, age and sex matched non-smoker non diabetes volunteers were selected randomly for data collection. Clinical, laboratory examination, spirometry and DLCO were performed and outcomes were measured.

Results: The measured values of FEV1 had a mean of 2.10 ± 0.62 , FVC 2.35 ± 0.76 , and PEF 4.74 ± 1.71 among diabetes patients which were lesser than nondiabetics. FEV1/FVC ratio was higher (89.96 ± 8.50) than the non-diabetics. The mean measured DLCO among diabetes patients was lesser i.e. (20.012 ± 6.59) in comparison to non-diabetic group i.e. (23.91 ± 5.84). The mean FVC, FEV and DLCO values in patients who had >10yr duration of diabetes was lowest. A significant negative correlation exists between FVC (Spearman's $r = -0.677$; P value <0.001) with the HBA1C which means if HBA1C increase the FVC, FEV1 & DLCO decreases. But a significant positive correlation observed between FEV1/FVC with HBA1C.

Conclusion: Our study concludes that, the pulmonary function test parameters (Spirometry & DLCO) in general were consistently lower in the diabetic group when compared to the non-diabetic group.

Keywords: Diabetes Mellitus Type2, Spirometry, DLCO, Pulmonary function test, Nonsmoker.

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Introduction

Diabetes is the most common metabolic disorder which is on an increasing trend globally. According to the International Diabetes Federation, diabetes affects at least 285 million people worldwide, and that number is expected to reach 438 million by the year 2030, with two-thirds of all diabetes cases occurring in low- to middle-income countries. [1]

Diabetes Mellitus is a heterogeneous metabolic disorder characterized by common features of chronic hyperglycemia with disturbance of carbohydrate, fat and protein metabolism. Many organ systems are the targets in diabetes like cardiovascular system, eyes, kidney and nervous system. The possibility that the lung is also a target organ for diabetic complications was first suggested by Schuyler et al in 1976. [2]

The mechanism by which impaired glycemic control may lead to a reduction in lung functions is uncertain, though it has been suggested that the increased systemic inflammation associated with diabetes [3] may result in pulmonary inflammation [4] as well, and hence, it can cause air way damage. [5] Moreover, secondary reduction in the antioxidant defence of lung & increased susceptibility to environmental oxidative insults results in the subsequent loss of lung function [6] and ultimately, lung damage.

It has been demonstrated that pulmonary complications in diabetes mellitus are due to a thickening of the walls of alveoli, alveolar capillaries and pulmonary arterioles, and these changes cause pulmonary dysfunction. [7,8] Diabetes mellitus can cause pulmonary complications due to collagen and elastin changes,

as well as micro-angiopathy. [9] Furthermore, pulmonary function impairment and lung dysfunction in diabetic patients is secondary, due to immune function impairment. [10] Hyperglycemia has been shown to lead to interstitial fibrosis and alveolar capillary microangiopathy; which is associated reduction in forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), lung diffusing capacity (DLCO) and lung elastic recoil. Diabetes is associated with a modest impairment in pulmonary function in a restrictive pattern (Van den Borst et al). [11]

Very few studies are there on pulmonary functions of Type 2 Diabetic patients with controversial results. So, the present study will be focused on the assessment of pulmonary functions like spirometry and DLCO in non-smoker Type 2 Diabetic patients with following objectives:-

Primary Objective: To record the spirometry and diffusion test in non-smoker type 2 diabetes patients as well as in non-smoker non-diabetics.

Secondary Objective: 1. To compare the spirometry and diffusion capacity between non-smokers type-2 diabetes patients and non-smokers non-diabetics.

2. To correlate the findings with duration of diabetes, & glycemic control.

Materials and Methods

The study was a Comparative Cross-sectional Study. It was conducted from September 2019-September 2020 for a period of 1 year in department of Pulmonary Medicine and department of Endocrinology, S.C.B. Medical College & Hospital, Cuttack. The patients coming to OPD and indoor patients of department of Endocrinology diagnosed with diabetes of any duration were taken as cases and age and sex matched non-diabetic non-smoker volunteers from Medicine department of SCB Medical College taken as controls.

All willing participants of age > 18 years and < 65 years of both genders were included in this study. Present or past smokers, patient having any respiratory conditions and individuals with unacceptable spirometry techniques were excluded from the study.

Data was collected from a total of 100 patients. 50 Non- smoker diabetes patients/cases satisfying the

inclusion criteria coming to OPD and IPD of department of Endocrinology and 50 age and sex matched non-smoker non diabetes volunteers/controls from Medicine department of SCB Medical College & Hospital were selected randomly through convenient sampling.

The participants were administered with patient information sheet and were thoroughly counselled regarding the research. After obtaining the informed written consent from the patient or legal guardian of the patient (those unable to give consent due to sickness), a face to face interview was carried out using the proforma to collect information. Contact numbers of the patients were kept for the tracking purpose. Digital Chest X ray was done in Radiology department to rule out any underlying lung disease. Clinical examination was done along with all the routine blood investigation. Spirometry and DLCO were conducted in the department of Pulmonary Medicine.

Statistical Analysis: The predesigned, pretested questionnaire was coded with the help of Guide to ensure quality of the scientific research. The coded data were entered in the statistical software SPSS (version 21). Different statistical tests were done in the process like:- a) Chi-square test b) Student's independent t test c) ANOVA test d) Correlation test. For all analyses, the statistical significance was fixed at 5% level (p value)

Ethical approval: The study protocol was approved by institutional ethical committee, SCB Medical College and Hospital bearing letter no.- IEC-207/dt 26.08.2020

Results:

Mean age with standard deviation of the diabetes patients was 46.30 ± 9.96 . Equal number of males and females were present among diabetics. Anthropometric measurements i.e. the mean weight, BMI, waist circumference found be 64.92 ± 14.778 kg, 25.46 ± 6.40 kg/m² and 92.94 ± 11.32 respectively in cases were higher than controls. This difference found in the anthropometric parameters from the control group was statistically significant. Both the Systolic blood pressure and diastolic blood pressure were higher in comparison to the controls (Table 1).

Table 1: Baseline parameters among the groups studied (N=100)

Parameters	TYPE 2 DIABETICS (Mean \pm SD)	NONDIABETICS (Mean \pm SD)	t statistic	P value	95 % CI
Age	46.30 \pm 9.96	49.04 \pm 9.06	1.439	0.153	-6.518- 1.904
Weight	64.92 \pm 14.778	57.24 \pm 12.439	2.811	0.006	2.259-13.101
Height	160.64 \pm 9.16	156.48 \pm 9.34	2.247	0.063	0.486-7.833
BMI	25.46 \pm 6.40	23.27 \pm 4.27	2.002	0.048	0.019-4.342
Waist circumference	92.94 \pm 11.32	87.02 \pm 5.70	3.303	0.001	2.364-9.483

SBP	140.18±25.49	126.50 ±33.271	2.308	0.023	1.917-25.443
DBP	83.36 ± 12.53	80.22± 13.00	1.229	0.222	-1.929-8.209

The spirometric finding in Type 2 DM was found that, the measured values of FEV1 had a mean at 2.10 ± 0.62 , FVC 2.35 ± 0.76 , and PEFR 4.74 ± 1.71 . The values were lesser than the control group. The measured mean FEV1/FVC ratio was higher (89.96 ± 8.50) than the control group. The % Predicted values of FEV1 (88.92 ± 17.35), FVC (78.10 ± 15.89), PEFR (71.10 ± 19.21), was lower

compared to the mean values of non-diabetics. The mean percentage predicted FEV1/FVC of 113.92 ± 12.88 among diabetic cases which was higher than control group. The difference found in mean measured values and Percentage of Predicted values of FEV1, FVC, FEV1/FVC, and PEFR between two groups was statistically significant. (Table 1,2,3)

Table 2: Comparison of PFT (measured) among two groups studied

Parameters	TYPE 2 DIABETICS (Mean ±SD)	NONDIABETICS (Mean ±SD)	t statistic	P value	95% CI
FEV1	2.10 ± 0.62	2.38 ± 0.473	-2.542	0.013	-0.50 - -0.06
FVC	2.35 ± 0.76	2.77 ± 0.47	-3.299	0.001	-0.67 - -0.16
FEV1/FVC	89.96 ± 8.50	86.79 ± 6.95	2.043	0.044	0.09- 6.25
PEFR	4.74 ± 1.71	6.15 ± 1.05	-4.931	0.000	-1.97- -0.84
FEF27-75%	2.73 ± 1.01	2.95 ± 0.84	-1.187	0.238	-0.59- 0.14
DLCO	20.012 ± 6.59	23.91 ± 5.84	-3.132	0.002	-6.37 - -1.43

Table 3: Differences in PFT (% predicted) between two groups studied

Parameters	TYPE 2 DIABETICS (Mean ±SD)	NONDIABETICS (Mean ±SD)	t statistic	P value	95 % CI
FEV1	88.92 ± 17.35	101.52 ± 7.37	-4.724	0.000	-0.17 - - 7.30
FVC	78.10 ± 15.89	93.16 ± 9.37	-5.771	0.000	-20.23 - - 9.88
FEV1/FVC	113.92 ± 12.88	109.50 ± 8.13	2.051	0.043	0.14 - 8.69
PEFR	71.10 ± 19.21	83.18 ± 5.79	-4.257	0.000	-17.71 - - 6.44
FEF27-75%	98.72 ± 28.88	92.82 ± 16.31	1.258	0.211	-3.40 -15.20
DLCO	74.42 ± 16.79	88.76 ± 8.45	-5.393	0.000	-19.61 - -9.06

The mean measured DLCO among diabetes patients was lesser i.e. (20.012 ± 6.59) in comparison to non-diabetic group i.e. (23.91 ± 5.84). Also the mean % predicted values of DLCO (74.42 ± 16.79) was lower compared to the mean values of non-diabetics. The difference found in mean measured and % Predicted values of DLCO between two groups was statistically significant. In our study it was found that 46% had reduced FVC, 16% had reduced FEV1, 100% had normal or increased FEV1/FVC and 46% had reduced DLCO. According to severity of reduction in DLCO, most i.e. 13 (26%) patients had mild reduction, 8(16%)

had moderate and 2(4%) had severe reduction in DLCO.

A significant negative correlation exists between FVC (Spearman's $r = -0.677$; P value <0.001) with the HBA1C which means if HBA1C increase the FVC, FEV1 & DLCO decreases. But a significant positive correlation observed between FEV1/FVC with HBA1C. In poorly controlled diabetic patients, 76.2% had reduced DLCO (<80) i.e restrictive lung function. The association of DLCO reduction with glycemic control was statistically significant. (P <0.001) (Table 4)

Table 4: Correlation of PFT with HBA1C

Parameters	Mean ± SD	Correlation coefficient (r^2)	P value
FVC	78.10 ± 15.89	-0.677	0.000
FEV1	88.92 ± 17.35	-0.432	0.002
FEV1/FVC	113.92 ± 12.88	+0.429	0.002
PEFR	71.10 ± 19.21	-0.116	0.421
FEF2775	98.72 ± 28.88	-0.125	0.388
DLCO	74.42 ± 16.79	-0.625	0.000

The mean FVC, FEV and DLCO values in patients who had >10 yr duration of diabetes was lowest, i.e. with increase in duration of diabetes there was decrease in lung function. Association of pulmonary function tests and duration of diabetes in 3 different groups (10 years) was obtained by Analysis of Variance (ANOVA) test and found to be statistically significant. (Table 5)

Table 5: Association of Pulmonary Function Tests with Duration of Diabetes

Variables	Pulmonary Function Tests (% Predicted) (Mean \pm SD)			
	FVC	FEV1	FEV1/FVC	DLCO
Diabetic Duration in years				
< 5	85.10 \pm 12.07	94.63 \pm 15.13	111.87 \pm 12.05	82.97 \pm 10.97
5-10	82.20 \pm 10.10	90.60 \pm 14.36	108.60 \pm 8.26	76.80 \pm 12.15
>10	62.73 \pm 13.73	76.93 \pm 17.21	119.80 \pm 14.28	56.53 \pm 13.93

Discussion

In this study, 100 participants were studied of which 50, had type 2 diabetes mellitus (cases) and 50 without diabetes (controls). The mean age in the groups were 46.30 ± 9.96 and 49.04 ± 9.06 for type2 diabetics and nondiabetic controls respectively. In Mori Hiroshi et al [12] study, the mean age among type 2 DM was 57.9 years, which was higher than our study may be due to the fact that patients aged >60 years, were not included in our study.

The BMI of type 2 diabetics showed mean \pm SD of 25.46 ± 6.40 kg/m² and non-diabetic showed mean \pm SD of 23.27 ± 4.27 kg/m². BMI was significantly higher in Type 2 DM with $P = < 0.05$. In this study BMI was within the obesity range among the diabetic which is similar to study done by Klein et al. [13]

Our study found the mean FVC measured (2.35 ± 0.76) and % predicted (78.10 ± 15.89) was significantly lower compared to the control group. In a study done by Davis A Wendy et al, it was found that there was a decrease in mean FVC values in type 2 diabetics. [14] It was also found that there was a progressive decrease in mean forced vital capacity value is 109 ml/year.[15] Our study also revealed that diabetic patients had lower mean measured FEV1 (2.10 ± 0.62), % predicted (88.92 ± 17.35) and measured PEFR (4.74 ± 1.71), % predicted (71.10 ± 19.21) compared to non-diabetics, which was statistically significant. Our study was also similar to study by Meo SA et al, Asanuma Y et al, Verma et al, & Davis et al. [14,16-18] It was observed that there was increased mean measured (89.96 ± 8.50), %predicted (113.92 ± 12.88) FEV1/FVC ratio. The increased FEV1/FVC % suggested that the impairment of pulmonary functions in type 2 diabetics was primarily restrictive in nature. Our study was concordant with study by Robert E Walter et al, Bhuvaneswari et al, Sreeja et al & Aparna et al. [15,19-21]

In our study, the mean DLCO (20.012 ± 6.59), % predicted (74.42 ± 16.79) among diabetes patient was lower in comparison to non-diabetic patients. We found restriction in lung function was significantly more in diabetic cases. Guvener et al. compared the capacity of gas exchange in patients with type 2 diabetes mellitus (DM) and healthy controls. They found decreased alveolar gas

exchange capacity in diabetic patients compared with healthy controls which is similar to our study. [22]

There was a significant negative correlation exists between PFT parameters like FVC, FEV1 and DLCO with HbA1C. It means with increase in the HbA1C level, there is decrease in the FVC, FEV1 & DLCO value. We also found that a positive correlation between FEV1/FVC ratio with HbA1C. So when HbA1c increase, the FEV1/FVC ratio also increased. Our findings were concordant to the findings of the study by Sinha et al & Jamatia et al. [23,24]

In this study, the mean FVC, FEV1 & DLCO found to be significantly lowest in the more than 10 years duration diabetes group. So, with longer duration of diabetes the pulmonary function decreased. FEV1/FVC was highest in more than 10 years duration diabetes group. Our study showed 15(65.2 %) diabetes patients who had restrictive pattern in DLCO also had a longer duration diabetes (>10years). This finding was also statistically significant. This finding was similar to the study done by Davis WA et al & Agarwal A et al [14,25].

Limitation of this study was sample size was less as conducted during COVID period. Smoking was ruled out based on patient's history and there is a question of reliability. HRCT of thorax to rule out ILD and CT Angiography for Pulmonary Vascular diseases were not done. Cardiac disease was ruled out on the basis of history and electrocardiogram. Echocardiography was not done so DCM or Coronary Artery Disease in diabetics was not ruled out confidently.

Conclusion

Our study concludes that, the PFT parameters (Spirometry & DLCO) in general were consistently lower in the diabetic group when compared to the non-diabetic group. The PFT parameters i.e., FVC, FEV1, PEFR, FEV1/FVC & DLCO showed statistically significant difference in diabetic group compared to the non-diabetics. The pattern of spirometric parameters in diabetic group suggested a prevalence of restrictive pattern in lung functions. All these points to a conclusion that diabetes mellitus causes decrement in lung functions in the form of restriction which is more common in

patients with longer duration of Type 2 Diabetes Mellitus and with uncontrolled glycaemic status.

Conflict of Interest-Nil

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