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CORRELATION OF PULMONARY FUNCTION TESTS IN DIABETES MELLITUS: CASE CONTROL STUDY

Dr. Jai Prakash Gangani[1], Dr. Yadvendra Gupta[2], Dr. Utsav Joshi[3], Dr. Madhvi Sanwelka[4]

[1]Senior resident, Department of General Medicine, AIIMS, Jodhpur
[2]Assistant professor, Department of Medicine, Mahatma Gandhi Medical College, Jaipur.
[3]Assistant Professor, Department of Pathology, SMS Hospital, Jaipur
[4*]Assistant Professor, Department of Pathology, NIMS&R, Jaipur, madhvisanwelka00@gmail.com

***Corresponding Author:** Dr. Madhvi sanwalka
*Assistant Professor, Department of Pathology, NIMS&R, Jaipur, madhvisanwelka00@gmail.com

Abstract

Introduction: Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycaemia. The duration of diabetes and the glycemic control are the important factors that determine the risk of lung involvement in diabetes. The majority of the people with type 2 diabetes are under a chronic glycemic burden which places them at significant risk of such complications. Spirometry is a widely used pulmonary function test, ideally suited to describe the effects of obstruction or restriction of lung function. The present study was undertaken to determine if there is difference between pulmonary functions (FEV_1, FVC and FEV_1/ FVC, PEFR, FEF 25-75%) of patients of type 2 diabetes mellitus and those of healthy controls.

Material and method: This study was case control observational analytical type and done in two years in Department of General Medicine from October 2021 to September 2023 in a tertiary care centre. Sample size taken was 100 subjects (50 cases & 50 controls)

Result: Mean FVC was found to be lower in cases as compared to controls (70.68 $\pm$ 20.42 vs. 91.17 $\pm$ 21.11) & p-value (0.0001) was found to be extremely statistically significant. Mean FEV_1 was found to be lower in cases as compared to controls (73.92 $\pm$ 20.87 vs. 86.03 $\pm$ 15.75) & p-value (0.0015) was found to be very statistically significant. Mean FEV_1/FVC was found to be higher in cases as compared to controls (105.26$\pm$ 10.16 vs. 97.26 $\pm$ 11.98) & p-value (0.0005) was found to be extremely statistically significant. Mean PEFR was found to be lower in cases as compared to controls (64.1 $\pm$ 20.64vs. 83.67 $\pm$ 23.24) & p-value (0.0001) was found to be extremely statistically significant. Mean FEF 25-75% was found to be higher in cases as compared to controls (71.8 $\pm$ 28.06 vs. 68.04 $\pm$ 30.20) & p-value (0.5205) was found to be not statistically significant.

Conclusion: The conclusion drawn from this study is that the type 2 diabetes mellitus being a systemic disease, also affects lungs .This is likely to be a chronic complication of type 2 DM. Spirometry can be used as the screening tool.

Keywords: Lung, Diabetes Mellitus, Spirometry, Glycemic control

Introduction

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. Several distinct types of DM are caused by a complex interaction of genetics and environmental factors. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. With an increasing incidence worldwide, DM will be a leading cause of morbidity and mortality for the foreseeable future.[1]

DM and its complications have become the most important and challenging health problem. Practically every organ system is affected by complications of DM. Attention is usually paid to angiopathy (micro, macro), retinopathy, neuropathy and nephropathy but one of the systems most neglected in DM is the respiratory system, except for recognition of increase in the prevalence of infection like tuberculosis.

The duration of diabetes and the glycemic control are the important factors that determine the risk of lung involvement in diabetes. The majority of the people with type 2 diabetes are under a chronic glycemic burden which places them at significant risk of such complications.[2,3]
Spirometry is a widely used pulmonary function test, ideally suited to describe the effects of obstruction or restriction of lung function. It is a powerful diagnostic tool to assess the early diagnosis of lung damage & its associated structures.

The present study was undertaken to determine if there is difference between pulmonary functions (FEV_1, FVC and FEV_1/ FVC, PEFR, FEF 25-75%) of patients of type 2 diabetes mellitus and those of healthy controls.

Method and material

This study was case control observational analytical type and done in two years in Department of General Medicine from October 2021 to September 2023 in a tertiary care centre. Sample size taken was 100 subjects (50 cases & 50 controls)

Inclusion criteria:-

1. Previously diagnosed cases of type 2 diabetes mellitus, minimum duration of 5 years.
2. Matched healthy Controls.

Exclusion criteria:-

1. History, clinical & radiological evidence of respiratory illness (Pulmonary tuberculosis, COPD, Asthma, Pleural effusion etc).
2. Smokers.
3. History or clinical evidence of cardiac illness (e.g. Coronary Artery Disease, Congestive Cardiac Failure, Hypertensive Heart disease, Valvular Heart disease).
4. History or clinical evidence of cerebrovascular accidents.
5. Pregnant women.
6. Any history of obstructive sleep apnoea (OSA)

A detailed clinical history was recorded regarding duration of diabetes mellitus, smoking, ischemic heart disease, respiratory illness. All patients underwent complete clinical examination and routine relevant investigations to assess diabetic status and complications. Resting 12 lead ECG (electrocardiograms) & chest skiagram (chest x-ray) were done in every patient. Additionally HbA_{1c} estimation was done for diabetic patients. and after that subjects were given an appointment for PFT. All 100 subjects (50 suffering from diabetes mellitus type 2 + 50 non diabetics) were subjected to PFT (pulmonary function tests i.e. spirometry).

The statistical analysis was carried out using Statistical Package for Social Sciences (SPSS Inc., Chicago, IL, version 17.0 for Windows) & Graphpad software. Means were calculated for all quantitative variables and for measures of dispersion standard deviation was calculated. Normality of data were checked by measures of Kolmogorov Smirnov tests of normality. For normally distributed data means were compared using t-test.

Result

Table-1: Distribution of subjects according to age

Groups	**Cases**	**Controls**
Number of subjects (N)	50	50
Age range	40-70 years	40-70 years
40-55 years	26 (52% of cases)	31 (62% of controls)
56-70 years	24 (48% of cases)	19 (38% of controls)

In this study 50 cases & 50 age & sex matched controls were taken in the age range of 40-70 years . Out of the 50 cases 26 (52%) were in 40-55 years age group & 24 (48%) in 56-70 years age group. Out of the 50 controls 31 (62%) were in 40-55 years age group & 19 (38%) in 56-70 years age group. (as represented in table-1)

Table-2: Distribution of subjects according to sex

Group	**Males**	**Females**	**Total**
Cases	25 (50%)	25 (50%)	50 (100%)
Controls	25 (50%)	25(50%)	50 (100%)

In this study out of 50 cases, 25 (50%) were females & 25 (50%) were males. Out of 50 controls, 25 (50%) were females & 25 (50%) were males (table 2)

Table-3: Distribution of subjects according to age & sex

Groups	**Cases**		**Controls**	
	Females	**Males**	**Females**	**Males**
40-55 years	12	14	16	15
56-70 years	13	11	9	10

Out of 26 cases in 40-55 years age group, 12 were females & 14 were males. Out of 24 cases in 56-70 years age group 13 were females & 11 were males. Out of 31 controls in 40-55 years age group 16 were females & 15 were males & out of 19 controls in 56-70 years age group 9 were females & 10 were males. (table 3)

Table-4: Distribution of cases according to duration of diabetes

Groups (in years)	**Cases (N=50)**
5-10 years	30 (60%)
>10 years	20 (40%)

According to the duration of diabetes the cases were divided in 2 groups-In first group there were 30 (60%) cases with duration of diabetes of 5-10 years & in the second group 20 (40%) cases were taken with duration of diabetes more than 10 years.(as represented in table-4)

Table-5: Distribution of cases according to glycemic control

Glycemic control	**Cases (N=50)**
Good (HbA1c < 7)	07 (14%)
Poor (HbA1c > 7)	43 (86%)

According to ADA guidelines for control of diabetes the cases were divided in to 2 groups. First group of 7 (14%) cases having good glycemic control ($HbA_{1C} < 7$) second group of 43 (86%) cases with poor glycemic control ($HbA_{1C} \geq 7$). (as represented in table-5)

Table-6: PFT parameters in subjects

PFT parameters (predicted %)	Cases (N=50)			Controls (N=50)			*p-value*
	Mean	SD	SEM	Mean	SD	SEM	
FVC	70.68	20.42	2.89	91.17	21.11	2.98	0.0001
FEV_1	73.92	20.87	2.95	86.03	15.75	2.23	0.0015
FEV_1 / FVC	105.26	10.16	1.44	97.26	11.98	1.69	0.0005
PEFR	64.1	20.64	2.92	83.67	23.24	3.28	0.0001
FEF 25-75 %	71.8	28.06	3.97	68.04	30.20	4.27	0.5205

Mean FVC was found to be lower in cases as compared to controls (70.68 $\pm$ 20.42 vs. 91.17 $\pm$ 21.11) & p-value (0.0001) was found to be extremely statistically significant.

Mean FEV_1 was found to be lower in cases as compared to controls (73.92 $\pm$ 20.87 vs. 86.03 $\pm$ 15.75) & p-value (0.0015) was found to be very statistically significant.

Mean FEV_1/FVC was found to be higher in cases as compared to controls (105.26$\pm$ 10.16 vs. 97.26 $\pm$ 11.98) & p-value (0.0005) was found to be extremely statistically significant.

Mean PEFR was found to be lower in cases as compared to controls (64.1 $\pm$ 20.64vs. 83.67 $\pm$ 23.24) & p-value (0.0001) was found to be extremely statistically significant.

Mean FEF 25-75% was found to be higher in cases as compared to controls (71.8 $\pm$ 28.06 vs. 68.04 $\pm$ 30.20) & p-value (0.5205) was found to be not statistically significant.

Table-7: PFT parameters in subjects (in 40-55 years age group)

PFT parameters (predicted %)	Cases (N=26)			Controls (N=31)			*p-value*
	Mean	SD	SEM	Mean	SD	SEM	
FVC	76.80	22.12	4.34	93.39	24.04	4.32	0.009
FEV_1	78.73	22.20	4.35	86.40	16.84	3.02	0.1440
FEV_1 / FVC	103.04	8.35	1.64	96.09	12.29	2.21	0.0176
PEFR	69.15	19.80	3.88	84.76	24.09	4.33	0.0108
FEF 25-75 %	73.88	29.37	5.76	63.22	28.01	5.03	0.1672

Mean FEV_1 was found to be lower in cases as compared to controls (78.73 $\pm$ 22.20 vs. 86.40 $\pm$ 16.84) & p-value (0.1440) was found to be not statistically significant.

Mean FEV_1/FVC was found to be higher in cases as compared to controls (103.04 $\pm$ 8.35 vs. 96.09 $\pm$ 12.29) & p-value (0.0176) was found to be statistically significant.

Mean PEFR was found to be lower in cases as compared to controls (69.15 $\pm$ 19.80 vs. 84.76 $\pm$ 24.09)& p-value (0.0108) was found to be statistically significant.

Mean FEF 25-75 % was found to be higher in cases as compared to controls (73.88 $\pm$ 29.37 vs. 63.22 $\pm$ 28.01) & p-value (0.1672) was found to be not statistically significant (table 7)

Table-8: PFT parameters in subjects (in 56-70 years age group)

PFT parameters (predicted %)	Cases (N=24)			Controls (N=19)			*p-value*
	Mean	SD	SEM	Mean	SD	SEM	
FVC	64.05	16.37	3.34	87.53	15.09	3.46	0.0001
FEV_1	68.70	18.38	3.75	85.43	14.21	3.26	0.0022
FEV_1 / FVC	107.67	11.51	2.35	99.18	11.50	2.64	0.0209
PEFR	58.63	20.54	4.19	81.90	22.29	5.11	0.0010
FEF 25-75 %	69.54	27.01	5.51	75.90	32.71	7.50	0.4888

In 56-70 years age group mean values of PFT parameters were compared among the cases & controls. Mean FVC was found to be lower in cases as compared to controls (64.05 +/- 16.37 vs. 87.53 +/- 15.09) & p-value (0.0001) was found to be extremely statistically significant.

Mean FEV_1 was found to be lower in cases as compared to controls (68.70 +/- 18.38 vs. 85.43 +/- 14.21) & p-value (0.0022) was found to be very statistically significant.

Mean FEV_1/FVC was found to be higher in cases as compared to controls (107.67 +/- 11.51 vs. 99.18 +/- 11.50) & p-value (0.0209) was found to be statistically significant.

Mean PEFR was found to be lower in cases as compared to controls(58.63 $\pm$ 20.54 vs. 81.90 $\pm$ 22.29) & p-value (0.0010) was found to be extremely statistically significant.

Mean FEF 25-75 % was found to be lower in cases as compared to controls (69.54 $\pm$ 27.01 vs. 75.90 $\pm$ 32.71) & p-value (0.4888) was found to be not statistically significant. (as represented in table-8)

Discussion

In the present study, the sample size selected was 50 cases & 50 controls. Pinar Celik et al [4] studied 30 non smoking diabetics & divided them in to subgroups & did intergroup comparison without using controls. In the other studies done by Pednekar SJ et al[5], Sinha S et al[6], Meo SA et al[7] cases studied were below 50 with unequal number of controls. Anandhalakshmi S et al[8] selected 30 cases & 30 controls .The above comparison therefore shows that the appropriate number of cases & controls were selected for the present study that will not affect the outcome of study.

In the present study the cases were in the age group between 40-70 years. We further divided the cases & controls both in 2 subgroups. Group-1& group-2 ages between 40-55 years and 56-70 years respectively. We had 26 cases in 40-55 years group & 24 in 56-70 years group. Among controls 31 were in 40-55 years & 19 were in 56-70 years age group. Pinar Celik et al[4] studied 30 non smoking diabetics in the age group of 23-74 years. Meo SA et al[7] conducted study using 32 healthy volunteer male type 2 diabetics in the age group of 24-73 years and 40 matched healthy controls. Elvira Valerio et al[9] studied 73 patients of type 2 diabetes, selected from Fillipino population of 30 years & above compared with 70 non diabetics in 30-75 years age group . Swati H Shah et al[10] conducted the study using 60 male cases & 60 male controls in 40-60 years age group.

the present study out of 50 cases, 25 were females & 25 males. Out of 50 controls, 25 were males & 25 female. In the other studies like Benbassat CA et al[11], Sanjeev Sinha et al[6] & Elvira Valerio et al[9] sex distribution among cases & controls was not even. In some studies like Meo SA et al[7] & Swati Shah et al[10] only male subjects were studies. So in the present study, equal number of males & females were included in the cases & the controls to avoid bias due to sex distribution In the present study cases were divided in 2 groups according to the glycemic control (assessed by HbA_{1C} values). Good glycemic control was found in 7 cases having $HbA_{1C} < 7$ & 43 cases had poor glycemic control having $HbA_{1c} \geq 7$. So in the present study maximum number of cases had poor glycemic control. Similarly

Pinar Celik et al[4] used HbA_{1c}<7.5, Elvira Valerio et al[9] used HbA_{1c}<6.5 & Anandhalakshmi S et al[8] used HbA_{1c}<7 for defining good glycemic control.

In the present study, mean values of FVC & FEV_1 predicted % were significantly lower in cases as compared to controls .While mean FEV_1/FVC predicted % values were significantly higher in cases as compared to controls. These findings suggest a restrictive type of ventilatory abnormality. Jhanwar R et al[12] observed that diabetics showed a restrictive type of ventilatory dysfunction, indicated by significant decline in FVC and FEV_1 with insignificant changes in FEV_1/FVC. Elvira Valerio et al[9] found that FVC & FEV_1 were significantly lower in diabetics as compared to nondiabetics. While FEV_1/FVC predicted % values were similar for both groups. Meo SA et al[7] and Swati H Shah et al[10] found that FVC & FEV_1 were significantly lower in cases as compared to controls. While FEV_1/FVC predicted % values were nonsignificantly high in cases as compared to controls.

On the contrary, Sanjeev Sinha et al[6] observed that FVC & FEV_1 were nonsignificantly low in cases as compared to controls. The author said that the limitation of this study was small number of subjects in each group. Benbassat CA et al[11] found that FVC & FEV_1 values were similar in cases as compared to controls. The author said that limitation of this study was small number of subjects in each group & the differences found in various studies were explained on the basis of bias in selected populations
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In the present study other PFT parameters (PEFR & FEF 25-75%) were also studied. We found significant reduction in PEFR values in cases as compared to controls & non significant changes in FEF 25-75 % values. Swati H Shah et al[10] also found similar changes in PEFR values but significant reduction in FEF 25-75% values were found in cases as compared to controls.

The pattern of abnormal pulmonary function tests observed in our study i.e. low FVC & high FEV1/FVC ratio are suggestive of restrictive type of lung disease. In the present study we compared PFT parameters in both sex groups. Mean FVC, FEV_1, PEFR predicted % values were found to be significantly low in female cases as compared to female controls .While FEV_1/FVC predicted % values were significantly high in female cases as compared to their controls. While comparing in males, FVC predicted % values were found significantly low & FEV_1/FVC values were significantly high in male cases as compared to their controls. Similarly in the study Mahadeva Murthy[13] there was a significant decline only in mean FVC & PEFR predicted % values in female cases as compared to their controls. No significant changes were observed in PFT parameters in male cases as compared to their controls. In the present study PFT parameters were compared in both the age groups. In both the groups FVC & PEFR predicted % were significantly low while FEV_1/FVC ratio was significantly high in cases as compared to their controls. In 56-70 years age group FEV_1 predicted % was also found significantly low in cases as compared to controls.

Conclusion

The conclusion drawn from this study is that the type 2 diabetes mellitus being a systemic disease, also affects lungs . This is likely to be a chronic complication of type 2 DM. We found that the glycemic levels & the duration of type 2 DM are probably not the major determinants of lung pathology and this requires further research. Spirometry can be used as a screening tool among diabetics.

Conflict of interest
None as stated by authors

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