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Study of Pulmonary Function Tests in Diabetic Nephropathy

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Abstract

Background: Type 2 diabetes mellitus is a universal public health problem with complications of diabetes on the eyes, kidneys, and nerves well documented, but studies on lung involvement in diabetes are sparse. This study was done to assess pulmonary function tests in patients with diabetic nephropathy and to know the correlation of pulmonary function with duration of diabetes and assess the prevalence of pulmonary hypertension in diabetic nephropathy.

Methodology: This was a cross-sectional study with 50 diabetic patients without nephropathy, 50 diabetic patients with nephropathy, and 50 healthy subjects without diabetes as the control group. Diabetics were age, sex and BMI matched to the control group. Diabetic nephropathy was diagnosed with the presence of diabetes and 24 hours urine protein excretion > 500 mg. Results of pulmonary function tests by spirometry were compared between groups. Pulmonary artery pressure was assessed by 2D ECHO. SPSS 21.0 version for Windows was used for all the statistical analysis. P value less than 0.05 was considered significant.

Results: Mean FEV 1% was 98.12 (+/-10.06), 75.88 (+/- 14.10) and 57.64 (+/- 13.49), mean FVC% was 86.78 (+/-8.77), 69.82 (+/- 13.88) and 53.02 (+/- 13.41) and mean PEF% was 88.62 (+/- 14.47), 59.40 (+/- 18.59) and 48.96 (+/- 20.94) among healthy subjects with no diabetes, diabetes mellitus group with no nephropathy and diabetic nephropathy group respectively. The difference observed between the groups was statistically significant (p value < 0.001). A restrictive pattern of lung function impairment was observed in diabetic patients which were more pronounced in diabetic nephropathy group.

Mean FEV1% was 71.03 (+/- 13.19), 66.74 (+/- 18.34) and 60.29 (+/- 15.25), mean FVC% was 65.66 (+/- 11.06), 60.79 (+/- 18.00) and 56.38 (+/- 16.55) among the participants having diabetes less than 10 years, 10 to 20 years and > 20 years respectively. The difference in mean FEV1%, FVC% with different duration of diabetes was not statistically significant. PAH was present in 3 patients (6%) in diabetes mellitus group without nephropathy and in 20 patients (40%) in diabetes nephropathy individuals, and the observed difference was statistically significant (p < 0.001).

Conclusion: Pulmonary function tests are impaired in diabetics, showing a restrictive pattern, and impairment is more pronounced in diabetics with nephropathy. There is no statistically significant relationship between the duration of diabetes and the derangement of pulmonary functions. Pulmonary hypertension is more common in the diabetic nephropathy group.

Introduction

Diabetes causes microvascular and macrovascular complications which involve organs such as the retina, kidney, nerve, and cardiovascular system, which makes it a major cause for renal failure, stroke, myocardial infarction, blindness, and amputation of limbs. The lungs, although not a classic organ involved in diabetes, may be affected by chronic hyperglycaemia due to its abundant connective tissue and pulmonary capillary network[1]. Pulmonary and other complications of diabetes share a common microangiopathic background, and lungs can be a target organ of diabetic complication[2].

Pulmonary diabetic microangiopathy usually remains clinically under-recognised as a substantial loss of the microvascular bed may not result in dyspnoea or any other clinical symptoms since the lungs have an extensive pulmonary reserve. Pulmonary functions assessment can also be useful in determining the progression of diabetic microangiopathy[3]. The use of spirometry remains a simple, non-invasive diagnostic tool that can provide a warning signal so that patients can take early preventive measures[4].

Derangement of pulmonary functions and pulmonary pressure in diabetics with nephropathy are least studied. Hence, this study was undertaken to study pulmonary functions by spirometry and pulmonary pressure in diabetic nephropathy.

Methodology

This was a cross-sectional observational study done at JSS hospital, Mysuru which included a total of 150 subjects, who were enrolled in our study using purposive sampling methods. Subjects were divided into 3 groups: 50 diabetic

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patients without nephropathy, 50 diabetic patients with overt nephropathy, and 50 healthy non-diabetic individuals. Both males and females with age more than 18 years were included in the study. Individuals with a history of connective tissue disorders or cardiopulmonary problems, history of smoking, end-stage renal disease (GFR < 15 ml/min), and urinary tract infection at the time of urine sample collection were excluded from the study.

Controls were matched according to their age, gender, and body mass index with subjects with diabetes. Diabetics without nephropathy were considered as individuals with a history of diabetes who were taking medications for diabetes and urine (routine test) showing no proteinuria.

Diabetic nephropathy was defined by including all of the following:

i. History of diabetes on medications.

ii. Urine (routine test) showing proteinuria.

iii. 24-hours urine protein estimation > 500 mg per day.

iv. Fundoscopy showing evidence of diabetic retinopathy.

Pulmonary functions were assessed using CONTEC 10 spirometer at room temperature in a sitting position. Subjects were made to undergo pulmonary function tests 3 times at an interval of 5 mins and the best of the three readings was taken. ERS/ATS guidelines for performing spirometry were followed. FVC, FEV1, and PEF were measured. Values were expressed as a percentage of the predicted values according to Knudson's standard predicted values[5,6]. Pulmonary pressure was measured with 2D ECHO by TR jet and calculating RVSP. Pulmonary hypertension was diagnosed if RVSP> 40 mmhg[7].

Statistical analysis

For categorical/binary variables, we used proportions, and for continuous variables, we used interquartile range (IQR), standard deviation, mean, and median. Inferential statistics were done by using fisher exact test/Chi-square test, one-way ANOVA, independent t-test, and person correlation. SPSS 21.0 version for Windows was used for all the statistical analysis. A p-value less than 0.05 was considered significant. Two or more independent proportions were compared using the Chi-square test/Fisher exact test. Comparing means among independent groups versus mutually exclusive groups was done using an independent t test. One-way ANOVA test compared the difference in means between multiple independent groups.

Results

The mean age of the study participants with no diabetes group, diabetes group without nephropathy and diabetic nephropathy group were 58.60 (+/- 10.26), 59.80 (+/- 9.53) and 59.96 (+/- 9.76) respectively. In all three groups, the proportion of males and females were the same and males were more compared to females in each group.

Mean BMI was 25.10 (+/- 3.42), 24.82 (+/- 3.61), and 24.92 (+/- 3.58) among the nil diabetes group, diabetics without nephropathy, and diabetics with nephropathy group respectively.

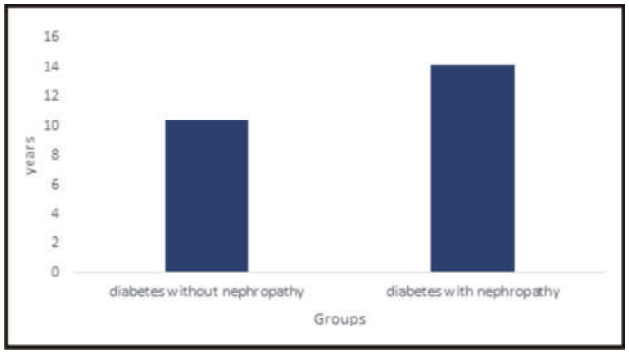

Fig. 1: *Mean duration of diabetes among study groups.*

The mean duration of diabetes mellitus among the diabetics without nephropathy and diabetic nephropathy group were 10.42 (+/- 5.57) and 14.18 (+/- 6.83) respectively. The mean duration of DM among the diabetic nephropathy group was higher than the diabetic group without nephropathy and the difference observed was statistically significant.

Mean FEV 1% was 98.12 (+/- 10.06), 75.88 (+/- 14.10) and 57.64 (+/- 13.49) among no diabetes, diabetes without nephropathy and diabetic nephropathy groups respectively, and the lowest was seen with diabetic nephropathy and the second lowest among diabetics without nephropathy and the difference observed was statistically significant. Mean FVC% was 86.78 (+/- 8.77), 69.82 (+/- 13.88) and 53.02 (+/- 13.41) with no diabetes, diabetes mellitus with no nephropathy and diabetic nephropathy groups respectively, the difference observed was statistically significant. FEV1/FVC was 91.74 (+/- 2.65), 88.88 (+/- 7.06) and 89.48 (+/- 6.08), the difference observed between nil diabetes group and diabetics with nephropathy, was not significant. The mean PEF% was 88.62 (+/- 14.47), 59.40 (+/- 18.59) and 48.96 (+/- 20.94) among nil diabetes group, diabetes without nephropathy and diabetic nephropathy group respectively. The difference observed among three groups was statistically significant.

As FEV1/FVC was more than 70% and FVC reduced, a restrictive pattern of lung functions was observed in diabetics which was more pronounced in diabetic nephropathy group.

Table I: Lung function parameters among the study groups.

Spirometry variables	Group						P value			
	NDM		DM without nephropathy		DN			NDM	DM without nephropathy	NDM
	Mean	SD	Mean	SD	Mean	SD	PValue	DM without nephropathy	DN	DN
FEV1%	98.12	10.06	75.88	14.10	57.64	13.49	<0.0001	<0.0001	<0.0001	<0.0001
FVC %	86.78	8.77	69.82	13.88	53.02	13.41	<0.0001	<0.0001	<0.0001	<0.0001
FEV1/FVC	91.74	2.65	88.88	7.06	89.48	6.08	0.03	0.035	1	0.135
PEF%	88.62	14.47	59.40	18.59	48.96	20.94	<0.0001	<0.0001	0.014	<0.0001

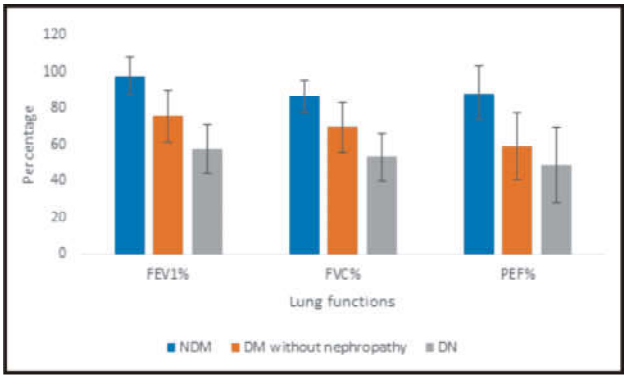

Fig. 1: *Lung functions among study groups.*

Table II: Correlation between lung function tests and duration of DM

		Duration of DM years
FEV1%	Pearson correlation	- .276
	P value	.060
	N	100
FVC%	Pearson correlation	- .245
	P value	.014
	N	100
FEV1/FVC	Pearson correlation	- .005
	P value	.958
	N	100
PEF%	Pearson correlation	- .216
	P value	.051
	N	100

FEV1% showed negative linear relationship with duration of DM in years: i.e, FEV1% decreases with increase in duration of DM.

FVC% showed a negative linear relationship with duration of DM, i.e., FVC% decreases with increase in duration of DM.

FEV1/FVC showed a negative correlation with duration of DM, i.e., FEV1/FVC decreases with increase in duration of DM.

PEF% showed a negative correlation with duration of DM, i.e., PEF% decreases with increase in duration of DM.

FEV1%, FVC%, FEV1/FVC and PEF% with duration of diabetes was not statistically significant (p value > 0.05).

Table III: Prevalence of PAH among study participants.

		Group					
		No DM		Diabetes Mellitus with no nephropathy		Diabetes Nephropathy	
		Count	Column N%	Count	Column N%	Count	Column N%
PAH	No PAH	48	96.0%	47	94.0%	30	60.0%
	PAH	2	4.0%	3	6.0%	20	40.0%

P< 0.0001

PAH was present in 2 subjects with no diabetes (4%), in 3 patients with diabetes with no nephropathy (6%) and in 20 patients with diabetes nephropathy (40%). The prevalence of PAH was highest among diabetic nephropathy and the difference observed between the groups was significant p < 0.0001 using chi square.

Discussion

Globally, diabetes has reached epidemic proportions. More than eight per cent of the world's population suffers from diabetes, which is estimated to be over 350 million people. By 2,035, the number of diabetics is expected to rise to over 550 million. Diabetics are likely to develop CKD in more than 40% of cases, and many will develop ESRD requiring renal replacement therapy[8].

Loss of recoil of lungs due to elastin and collagen changes, autonomic neuropathy of respiratory muscles, chronic inflammation as well as small vessel changes of lung capillaries can cause pulmonary dysfunction. Lung complication and other complications of diabetes share a common microangiopathic background showing the lung can be a target organ of diabetic complications[2].

Measurement of pulmonary functions by spirometry can be a basic screening test for assessing pulmonary dysfunction in diabetics. Hence, in this study, we have measured pulmonary function tests by spirometry to assess the alteration of PFTs in diabetics with and without nephropathy and looked into its correlation with the duration of diabetes.

Studies done by Swati *et al*, Sonali *et al*, Shafiee *et al* and the Framingham heart study by Robert *et al* showed that FEV1, FVC, and PEF by spirometry were reduced significantly in diabetics when compared to normal individuals[2,3,9,10]. In this study we have observed that, the mean FVC% predicted, mean FEV1% predicted, and mean PEF% predicted were significantly less in individuals with diabetes with and without nephropathy in comparison with controls ($P < 0.001$). Shafiee *et al* and He *et al* showed that FVC% predicted, FEV1% predicted, PEF% predicted values, when compared to diabetics without nephropathy and healthy controls, diabetic nephropathy patients showed a significantly lower value ($P < 0.05$)[1,2].

In this study, we observed that pulmonary functions (FVC% predicted, FEV1% predicted, PEF% predicted) were significantly reduced in the diabetics with nephropathy in comparison to diabetics without nephropathy and non-diabetic subjects (p value < 0.001). Shafiee *et al*, He *et al*, and Gilmour 1 *et al* in their respective studies showed a restrictive pattern of lung functions in diabetics with and without nephropathy, changes were more pronounced in the diabetic nephropathy group[1,2,11]. An analysis by Selvaraj *et al* showed a predominant restrictive pattern of lung disease in type 2 diabetics[12]. In this study, we have observed a restrictive pattern of lung functions in diabetics with and without nephropathy patients, significant changes were seen in diabetic nephropathy patients when compared to diabetics without nephropathy and normal healthy individuals (P value < 0.001).

The results of this study showed that type 2 diabetics have a restrictive pattern of lung functions even though they do not seem to have any respiratory symptoms. Spirometry remains a simple and cost-effective and non-invasive diagnostic tool that can be used as an indicator that serves as a warning to patients so they can take early preventive measures.

A study conducted on 106 patients of type 2 diabetes by Mittal *et al* showed that the mean duration of patients with diabetes was 10.18 ± 5.17 years. Diabetes duration and lung functions exhibited a significant negative correlation[3]. A study done by Shah *et al*, who enrolled sixty males with T2 DM and 60 healthy subjects as controls, showed that PFTs were reduced significantly in diabetic patients when compared to healthy subjects. There was no correlation between pulmonary functions and the duration of diabetes[13].

Pande *et al* enrolled 100 type 2 diabetics who came to hospital and 100 healthy individuals from general population. Testing of PFTs revealed a significant decline in PFT parameters in comparison to non-diabetic controls, but a decline in FVC, FEV1, and FEV1% was not significant with diabetes duration[9].

In the present study, it was found that the mean duration of diabetes was 14.18 years among the diabetic nephropathy group and 10.42 years among the diabetics without nephropathy. In this study, it was seen that in diabetics with and without nephropathy, FEV1% predicted, FVC% predicted and PEF% predicted showed a negative correlation with duration of diabetes. As diabetes duration increased, pulmonary functions were reduced. (r-value was negative). But, the correlation of pulmonary functions FEV1% predicted, FVC% predicted, FEV1/FVC, and PEF% predicted with different duration of diabetes was not statistically significant (p value > 0.05).

Mehta *et al* in their study showed that the prevalence of pulmonary HTN in diabetic nephropathy was around 60% and PH increases as the CKD stage increases[14]. This study revealed that pulmonary hypertension was commonly seen in diabetic nephropathy individuals (40%) when compared to diabetics without nephropathy (6%).

Conclusions

Pulmonary functions (FVC, FEV1 and PEF by % predicted values) were significantly lower in diabetic patients with and without nephropathy when compared to the healthy nondiabetic controls which was statistically significant. Diabetes subjects with nephropathy had much lower FEV1 and FVC values compared to diabetics without nephropathy. Restrictive type of pulmonary functions was seen in diabetics and the changes were more pronounced in the diabetic nephropathy group. There was a negative correlation between pulmonary functions and diabetes duration, but the changes observed was not statistically significant. Pulmonary hypertension was more commonly seen in diabetic nephropathy. Alteration in pulmonary functions was evident proving that lung is an organ involved as a part of micro and macrovascular complications in diabetics.

As lung function impairment was more pronounced in diabetic nephropathy patients compared to diabetic patients without nephropathy, strict glycaemic control may help in preventing the progression to diabetic pulmopathy.

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