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Research Article

To study the effect of glycemic control and duration of disease on pulmonary function tests and diffusion capacity in type 2 diabetes mellitus

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ABSTRACT

Background: Type 2 diabetes mellitus is known to cause serious progressive macro and micro vascular complications leading to end organ damage like retinopathy, nephropathy and neuropathy. Pulmonary complications due to collagen and elastin changes as well as microangiopathy has also been demonstrated in type 2 diabetes mellitus but prevalence in most of population is unknown and its possible correlation with duration of disease and degree of glycemic control is not studied more in our population. Aims and objectives: To compare Pulmonary Function Tests (PFT) in type 2 diabetes mellitus with control group and to evaluate possible correlation of PFT with status of sugar control and duration of disease.
Methods: Consecutively consenting 120 subjects who satisfied the inclusion criteria were recruited over one year duration. These 120 subjects are categorised into two i.e. healthy volunteers recruited as controls (n=60) and type 2 diabetic patients (n=60).
Results: Both group compared and studied with each other. Diabetic patients showed a significant reduction in Forced Expiratory Volume in one second (FEV1), Forced Vital Capacity (FVC) and pulmonary diffusion capacity for carbon monoxide (DLCO) relative to their matched controls and these values were further reduced in diabetic patients with uncontrolled glycemic status.
Conclusion: Our study concluded that lung functions in type2 diabetes mellitus are impaired with restrictive pattern of respiratory abnormality. Duration of diabetes did not influence on pulmonary function and diffusion capacity.

Keywords: Diabetes mellitus, Pulmonary function test, Spirometry, Glycemic control, Glycosylated haemoglobin, Microvascular complications

INTRODUCTION

Diabetes mellitus is a public health problem in developing and developed world. There is an alarming increase in the incidence and prevalence of diabetes mellitus particularly in Asian Indians. According to WHO India will be world diabetic capital in 2025.[1] Diabetes mellitus is associated with widespread hormonal, metabolic, and microvascular abnormalities, as well as with disturbances of the function of many organ systems. The macroangiopathic and microangiopathic complications affect eyes, kidneys, nerves, cardiovascular system and respiratory system. The biochemical and structural change in basement membrane proteins of different body organ systems are the mainstay for development of diabetic complications. Chronic hyperglycaemia causes non-enzymatic glycosylation of

proteins such as collagen, elastin etc. which leads to thickening of basement membrane and microangiopathy. Microangiopathy in alveoli may restrict lung volumes and capacities.[2] Lung function is an independent risk factor for cardiovascular, pulmonary, and all -cause mortality in diabetes.[3] Therefore, it is important to study pulmonary functions in patients having diabetes mellitus and to evaluate possible correlation with status of sugar and duration of disease. Besides this, alteration in diffusion capacity has not been studied extensively in Indian population. So with this background we planned this study to see the changes in pulmonary functions and diffusion capacity for carbon monoxide in diabetic subjects.

METHODS

The present study was conducted in department of medicine in collaboration with department of pulmonary medicine and department of ophthalmology, King George Medical University, Lucknow between Augest 2011 and July 2012 after taking ethical committee clearance.

Sixty Patients having type 2 diabetes mellitus attending diabetes OPD and medical OPD of Gandhi Memorial and associated hospitals were selected. Those sixty patients were divided into two groups on the basis of glycemic status- thirty cases of type 2 diabetes mellitus with control glycemic status (HbA_{1C} <7) and another thirty cases of type 2 diabetes mellitus with uncontrolled glycemic status (HbA_{1C} >7).

Inclusion criteria was type 2 diabetes mellitus patients of 40 to 70 years with at least 5 years history of diabetes.

Exclusion criteria: Patient not fulfilling above mentioned criteria, Patients with lung disease, Smokers with regular smoking of one year or more, neuromuscular disease, malignancy, major abdominal/chest surgery and gross anatomical abnormalities of vertebral thoracic cage were excluded from the study. Informed written consent was taken from all subjects.

Spirometry was performed according to American Thoracic Society / European Respiratory Society (ATS/ERS guidelines) in a quiet room in sitting position by the trained personnel. The following parameters - Forced Vital Capacity (FVC) in liters, Forced Expiratory Volume in 1 second (FEV1), FEV1 /FVC in percentage (%) of all patients and controls were performed by using PK MORGAN SPIRO 232 drum based spirometry in sitting position and at room temperature from 10am to 2pm for three times at every 15 minutes interval and best of the three was taken as final value.

The DLCO was measured by using single breath technique based on the joint statement of ATS and the European Respiratory Society with acceptable test criteria including (i) Spiratory vital capacity of >85% of largest vital capacity in <4 sec. (ii) A stable calculated breath hold for 10 ± 2 sec with no evidence of leaks or valsalva. (iii) Expiration in 4 sec with appropriate clearance of died space gas and proper sampling/analysis of alveolar gas.

Statistical analysis

The results are presented in mean ± SD and percentages. The Chi-square test was used to compare the dichotomous/categorical variables. The one way analysis of variance followed by Tukey's multiple comparison tests was used to compare the continuous variables among the groups and unpaired t-test was used to compare between the groups.

The P value <0.05 was considered significant. All the analysis was carried out using SPSS 16.0 version (Chicago, Inc., USA).

RESULTS

The different risk factors like age, gender and BMI were correlated with reduced pulmonary function tests (FEV1 and FVC and DLCO all <80% of predicted values) among all subjects (n=120). No significant associations were found. (P >0.05) (Table 1).

On comparison of mean pulmonary function test parameters revealed that cases had lower mean value for FEV1, FVC and DLCO than control group. Statistically, the difference between both groups was significant (P <0.001) (Table 2).

The prevalence of reduced pulmonary function tests was found more in case group as compared to control group. We divided our sixty cases into two groups on the basis of glycemic status - Thirty cases of type 2 diabetes mellitus with control glycemic status (HbA_{1C} <7) and another thirty cases of type 2 diabetes mellitus with uncontrolled glycemic status (HbA_{1C} >7). It is observed that all the parameters of pulmonary function in type 2 diabetes mellitus with uncontrolled glycemic status had lower mean than type 2 diabetes mellitus with control glycemic status. On group comparison, mean difference between these groups was statistically significant for FEV_1, FVC and DLCO respectively (P <0.05) (Table 3).

To find any association of duration of disease with pulmonary functions and diffusion capacity, cases were divided and compared. The comparison of pulmonary functions and diffusion capacity of diabetic patients with duration >10 years and <10 years was not found significant difference (P >0.05) (Table 4).

The present study observed significantly restrictive pattern in diabetic patients which was further more prevalent in uncontrolled diabetes (HbA_{1C} >7). The association between glycemic status with respiratory pattern was significant (P = 0.0001) (Table 5).

Table 1: Demographic characteristics of the cases and controls.

Characteristics	Controls (n=60)	Cases (n=60)	P value
Mean age in years	50.32 ± 6.51	51.72 ± 5.95	0.22
Gender, no. (%)			
Male	37 (61.7)	33 (55.0)	0.45
Female	23 (38.3)	27 (45.0)	
Mean BMI (kg/m$^{2)}$	26.36 ± 3.9	27.21 ± 2.99	0.18

Table 2: Comparison of pulmonary function tests between cases and controls.

PFTs (litres)	Controls (n=60)	Cases (n=60)	P value
FEV1	79.53 ± 10.71	70.53 ± 16.46	0.001
FVC	88.37 ± 12.45	75.85 ± 18.75	0.0001
DLCO	99.93 ± 8.32	91.02 ± 13.35	0.0001

Table 3: Comparison of pulmonary function tests between diabetes with and without glycemic control.

PFTs (litres)	Diabetes with glycemic control (HbA_{1C} <7) (n=30)	Diabetes without glycemic control (HbA_{1C} >7) (n=30)	P value
FEV1	79.00 ± 12.47	68.67 ± 18.81	0.01
FVC	81.30 ± 16.53	71.73 ± 18.79	0.02
DLCO	96.67 ± 10.85	85.37 ± 13.38	0.001

Table 4: Comparison of pulmonary function tests according to duration of diabetes.

PFTs (litres)	Duration of diabetes		P value
	<10 years (n=35)	≥10 years (n=25)	
FEV1	73.46 ± 17.08	74.36 ± 16.38	0.83
FVC	79.86 ± 19.71	71.84 ± 14.98	0.09
DLCO	88.23 ± 12.84	94.92 ± 13.33	0.06

Table 5: Comparison of repiratory pattern between diabetes with glycemic status and control.

Pattern	Control (n=60)		HbA_{1C} <7 (n=30)		HbA_{1C} >7 (n=30)		Chi-square	P value
	No.	%	No.	%	No.	%		
Normal	60	100.0	20	66.67	7	23.3	66.50	0.0001
Restrictive	0	0.0	10	33.3	23	76.7		
Obstructive	0	0.0	0	6.7	0	0.0		

Table 6: Comparison of PFT levels with HbA_{1C} and duration of diabetic among the cases.

Parameters	PFT level											
	FEV1				FVC				DLCO			
	Normal		Reduced		Normal		Reduced		Normal		Reduced	
	No.		No.		No.		No.		No.		No.	
HbA_{1C}												
<7	20	66.7	10	33.3	20	66.7	10	33.3	22	73.3	8	26.7
≥7	13	43.3	17	56.7	14	46.7	16	53.3	17	56.7	13	43.3
Chi-square, P value	3.30, 0.06				2.44, 0.11				1.83, 0.17			
Duration of diabetes												
<10 years	22	62.9	13	37.1	24	68.6	11	31.4	24	68.6	11	31.4
≥10 years	11	44.0	14	56.0	10	40.0	15	60.0	15	60.0	10	40.0
Chi-square, P value	2.09, 0.14				4.84, 0.02				0.47, 0.49			

DISCUSSION

Our study had shown significantly reduced FEV1, FVC and DLCO in diabetic patients as compared to their matched control. The findings of our study were accordance with some previous studies.[4-9] The Restrictive pattern or low vital capacity in type 2 DM found in our study was also with many prospective and cross sectional studies.[10,11] The exact pathophysiology for reduced pulmonary functions in diabetics is still not very well understood. Though several mechanism explaining reduced pulmonary functions in diabetes mellitus are microangiopathy of alveolar capillaries and pulmonary arterioles, loss of elastic recoil secondary to collagen glycosylation of lung parenchyma, autonomic neuropathy involving the respiratory muscles and chronic low grade inflammation.[5] The thickening of basement membrane due to microangiopathy, pulmonary blood flow is reduced and redistributed to pulmonary circulation

leading to well ventilated areas into under-perfused. The lung may be target organ for diabetic complications was first suggested in 1976.[12] After that many studies have been done for pulmonary functions in diabetic patients with variable results.

The major consequences of hyperglycemia are excessive non enzymatic glycosylation of various body proteins including haemoglobin, albumin, collagen and elastin. HbA_{1C} % is an indicator of diabetes control. Glycemic goal is to achieve an HbA_{1C} <7%. The level of HbA_{1C} % >7 in patients is called uncontrolled glycemic status. High level of HbA_{1C} % is due to constantly higher level of circulating glucose for 3 months. It can lead to increased non-enzymatic glycosylation of issue proteins including collagen which ultimately will affect PFT if lungs are target organs. The results of our study were similar of studies conducted by Davis et al.,[4] and Mckeevear et al.,[13] they found significantly reduced pulmonary functions (FEV1 and FVC) in diabetes with uncontrolled glycemic status. We divided our cases into two groups on the basis of duration of disease i.e. diabetic patients with duration <10 years and >10 years. We studied and compared PFT of both groups to find any possible correlation but no significant association was found. This result of our study was concordance of studies conducted by Swati H. Shaw et al.,[14] and Pinnar Cellik et al.,[15] It was observed by some studies that DLCO and ratio of DLCO/VA were significantly reduced among the diabetics with poor glycaemic control (HbA_{1C} >7) and there was no significant difference in other pulmonary functions.[16-18] There is increased cross-linkage formation between polypeptides of collagen which leads to thickening, leading to restriction of lung volume and alveolar gas transport, reduced membrane diffusion capacity and pulmonary capillary blood volume.[19-21] The mechanisms postulated to explain the decrease in diffusion capacity include modification of surfactant and its actions and an altered affinity of glycosylated hemoglobin to carbon monoxide.[22,23]

The possible explanation of restrictive type of pulmonary impairment are non-enzymatic glycosylation of pulmonary collagen leading to accumulation of advanced glycosylation and products resulting increased cross-link formation.[24,25] with fibrosis and basal lamina thickening.[26]

There are also many studies showing no correlation between HbA_{1C} and PFTs.[7,27,28] They argued that HbA1c level is an indicator of glycemic control for a short period of 1-2 months and that short duration of hyperglycemia was not adequate to influence PFTs. Some studies showed no significant correlation between PFTs and duration of disease.[28] While some have reported a strong negative correlation of pulmonary tests with duration.[7,8] Further, role of different risk factors like mean age, gender and BMI for reduced pulmonary functions were studied and correlated among all subjects. No significant associations were found (P >0.05).

CONCLUSION

Our study demonstrated the mean reduction in FEV1, FVC and DLCO was significantly more in diabetes as compared to their matched controls and these lung functions were further significantly reduced in diabetes with uncontrolled glycemic status. The reduced pulmonary functions were more prevalent in diabetic patients with uncontrolled glycemic status. Majority of diabetic patient had restrictive pulmonary functions, and it was more prevalent in diabetic patient with uncontrolled glycemic status. Duration of disease has no effect on pulmonary functions. Our study concluded hyperglycemia is major determinant of reduced PFTs and DLCO. Further prospective study with a larger sample size might be needed to determine the associations more clearly. Assessment of the pulmonary functions in type 2 diabetes mellitus are needed accordingly which may be helpful to prevent further respiratory impairments.

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