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Pulmonary Function Tests and Diffusion Capacity in Type 2 Diabetes and Their Possible Correlation with Proteinuria

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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 proteinuria is not studied more.*

Aims And Objectives- *To compare pulmonary function tests (PFT) and diffusion capacity for carbom monoxide (DLCO) in type 2 diabetes mellitus with control group and to evaluate possible correlation of PFTs and DLCO with proteinuria.*

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 patients with diabetic nephropathy.*

Conclusions- *Our study concludes that lung functions in type2 diabetes mellitus was impaired and there was restrictive pattern of respiratory abnormality. The mean reduction in FEV1, FVC and DLCO was more in diabetes as compared to their matched controls and these lung functions were further reduced in patient with diabetic nephropathy. Duration of diabetes did not influence on pulmonary functions.*

Key Words: *Diabetes mellitus, Pulmonary function Test, proteinuria, nephropathy, Microvascular Complications*

INTRODUCTION

According to World Health Organization (WHO), Diabetes Mellitus (DM) is a metabolic disorder of multiple aetiology which is characterized by chronic hyperglycemia with disturbances of carbohydrate, protein and fat metabolism, resulting from defects in insulin secretion or insulin action or both.[1] India is called Diabetic Capital of World. Other two top countries after India are China and U.S.[2] Diabetes is more prevalent in age group of 40 to 59 years. 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.[3] A previous study had been described an association between diabetic nephropathy and alteration of lung function in type 1 diabetes.[4] Many studies has been demonstrated similar microangiopathy background responsible for development of pulmonary and other late complications in diabetes.[4],[5] There are only few studies about the influence of proteinuria over pulmonary functions and diffusion capacity in type 2 diabetes mellitus. Therefore, it is important to study pulmonary functions and diffusion capacity in patients having diabetes mellitus and to evaluate possible correlation with albumin excrertion rate. So with this background we planned this study to see the changes in pulmonary functions and diffusion capacity for carbon monoxide in diabetic subjects.

MATERIAL AND 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 proteinuria- Type 2 diabetes mellitus with normoalbuminemia (n=30) and type 2 diabetes mellitus with proteinuria (n=30). Inclusion Criteria was type 2 diabetes mellitus patients of 40 to 70 years. Exclusion Criteria: patient not fulfilling above mentioned criteria, patient having microalbuminuria due to other causes eg. UTI, CHF, pregnancy etc, 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. Proteinuria was determined by measuring 24 hours urinary protein excretion rate. An albumin excretion rate between 0-30mg/day is called normoalbuminuria, between 30-300mg/day-microalbuminuria and >300mg/day is macroalbuminuria. Albumin excretion ≥30mg in 24 hour urine sample collection was defined diabetic nephropathy. 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 diffusion capacity for carbon monoxide (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 <4sec. (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 (70.53±16.46) had lower mean value for FEV1, FVC and DLCO than control group

(79.53±10.71) . Statistically, the difference between both groups was significant.(p<0.001) (Table 2) The prevalence of reduced pulmonary function tests was more in diabetes and further increased in diabetes with proteinuria. We divided our sixty cases into two groups on the basis of 24 hours urinary protein loss. Thirty cases of type 2 diabetes mellitus with normoalbuminuria (<30mg) and another thirty cases of type 2 diabetes mellitus with proteinuria (>30mg). It is observed that all the parameters of pulmonary function in type 2 diabetes mellitus with proteinuria. On group comparison, mean difference between these groups was statistically significant for FEV_1, FVC and DLCO respectively *(p<0.05*).(Table 3) It was more interesting in our study that pulmonary functions and diffusion capacity were deteriorating on increasing porteinuria and there was significant difference in the FEV1, FVC and DLCO in different categories of proteinuria. *(p<0.05*).(Table 4) 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.(p>0.05) (Table 5) The present study observed significantly restrictive pattern in diabetic patients which was further more prevalent in diabetic patients with nephropathy. The association of diabetic nephropathy with respiratory pattern was significant (p=0.0001). (Table 6)

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/m2)	26.36±3.9	27.21±2.99	0.18

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

PFTs (in 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 PFT with proteinuria among the cases

Parameters (in litres)	Urinary protein<30(mg/24hrs) (Normoalbuminuria) (n=30)	Urinary protein ≥30(mg/24hrs) (Albuminuria) (n=30)	p-value
FEV1	79.00±12.47	68.67±18.81	0.01
FVC	81.30±16.53	71.73±18.79	0.04
DLCO	96.67±10.85	85.37±13.38	0.0001

Table-4: Comparison of PFT with degree of proteinuria among the cases

Proteinuria (mg/24hrs)	No. (%)	PFTs (Mean±SD)		
		FEV1	FVC	DLCO
<30(Normoalbuninuria)	30 (50.0)	79.00±12.47	81.30±16.53	96.67±10.85
30-300(Microalbuminuria)	17 (28.3)	74.00±19.50	75.06±19.58	89.94±12.69
>300(Macroalbuminuria)	13 (21.7)	61.69±15.99	67.38±17.51	79.38±12.23
p-value		0.006	0.06	0.0001

Table-5: Comparison of pulmonary function tests according to duration of diabetes

PFTs (in litres)	Duration of diabetes		
	<10 years (n=35)	≥10 years (n=25)	p-value
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-6: Comparison of respiratory pattern with proteinuria among the cases

Respiratory pattern	Proteinuria (mg/24hrs)						Ch-square	p-value
	<30 (n=30)		30-300(n=17)		>300 (n=13)			
	No.	%	No.	%	No.	%		
Normal	20	66.67	6	35.3	1	7.7	14.32	0.006
Restrictive	10	33.3	11	64.7	12	92.3		
Obstructive	0	0.0	0	0.0	0	0.0		

DISCUSSION

Our study observed significantly reduced FEV1, FVC and DLCO in diabetic patients as compared to their matched control. The impairment of pulmonary functions and diffusion capacity was more pronounced in cases with diabetic nephropathy. An Indian study showed that the microalbuminuria and retinopathy in type-2 DM patients was correlated with reduced diffusing capacity.[6] The findings of our study were accordance with some previous studies which demonstrated that impairment of pulmonary functions was more on advancing of stages of proteinuria.[7] The Restrictive pattern or low vital capacity in type 2 DM found in our study was also with many prospective and cross sectional studies.[8], [9], [10], [11], [12], [13]

The Diabetes Control and Complications Trial (DCCT) demonstrated a strong relationship between diabetic retinopathy and elevated albumin excretion.[14] The EURODLAB study showed that diabetic retinopathy, in association with increased blood pressure, is an important independent risk factor for diabetic nephropathy progression.[7] chronic complications of lung and kidney in diabetes have similar frequency and severity which might be due to an identical etiopathogenesis.[15]

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.[9] 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.[16] After that many studies have been done for pulmonary functions in diabetic patients with variable results. Thickness of glomerular capillaries causes impaired selectivity for proteins and an increase in proteinuria. In the kidney, thickness of glomerular capillaries causes impaired selectivity for proteins and an increase in albumin excretion rate. All these support the importance of an etio-pathologic mechanism in the development of diabetic microvascular complications.[17], [18] Many previous studies have also observed a significant correlation between DLCO and the grade of albuminuria.[17], [19], [20] Our study showed that dysfunction of pulmonary functions and diffusion capacity was more with progression of proteinuria.

CONCLUSION

Our study showed impaired pulmonary functions and diffusion capacity in type 2 diabetes mellitus. The impairment of pulmonary functions and diffusion capacity was more with increasing degree of proteinuria. Majority of diabetic patient had restrictive pulmonary functions, and it was more prevalent in diabetic patient with nephropathy. Duration of disease has no effect on pulmonary functions and diffusion capacity.

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.

REFERENCES

1. Ali MO, Begum S, Ali .T and Ferdousi .S, FVC, FEV1, and FEV1/FVC% in type 2 diabetes and their relationships with duration of the disease, *J. Bangladesh Soc Physiol.,4(2),* 2009 Dec, 81- 87
2. WHO Diabetes programme, 2011 Jan, Fact sheet no. 312
3. Chance WW, Rhee C, Yilmaz C, et al. Diminished alveolar microvascular reserves in type 2 diabetes reflect systemic microangiopathy. Diabetes Care. 2008;31:1596–1601
4. Orasanu G, Plutzky J: The pathologic continuum of diabetic vascular disease. *J Am Coll Cardiol* 2009, 53(5 Suppl)**:**S35-S42
5. Aronson D: Hyperglycemia and the pathobiology of diabetic complications. *Adv Cardiol* 2008, 45:1-16
6. A.S. Agarwal, A.B. Fuladi, G. Mishra and B.O. Tayade. Spirometry and Diffusion Studies in Patients with Type-2 Diabetes Mellitus and Their Association with Microvascular Complications.[Indian J Chest Dis Allied Sci 2010;52:213-216
7. Shafiee G**,** Khamseh ME, Rezaei N**,** Aghili R**,** Malek M. Alteration of pulmonary function in diabetic nephropathy. *Journal of Diabetes & Metabolic Disorders* 2013, 12:15
8. Davis WA, Knuiman M, Kendall P, Grange V, Davis TM. Glycemic exposure is associated with reduced pulmonary function in type 2 diabetes, the fremantle diabetes study. Diabetes Care 2004;27:752-7
9. 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
10. Lange P, Groth S, Kastrup J, Mortensen J, Appleyard M, Nyboe J, et al. Diabetes mellitus, plasma glucose and lung function in a cross sectional population study. Eur Respir J 1989;2:14-9
11. Barrett-Conor E, Frette C. NIDDM, impaired glucose tolerance, and pulmonary function in older adults. Diabetes Care 1996;19:1441-4
12. Davis TM, Knuiman M, Kendall P, Vu H, Davis WA. Reduced pulmonary function and its association in type 2 diabetes: The fremantle diabetes study. Diabetes Res Clin Pract 2000;50:153-9
13. Anandhalakshmi S, Manikandan S, Ganeshkumar P, Ramachandran C. Alveolar Gas Exchange and Pulmonary Functions in Patients with Type II Diabetes Mellitus. J Clin Diagn Res. Sep 2013; 7(9): 1874–1877
14. Molitch ME, Steffes MW, Cleary PA, Nathan DM: Baseline analysis of renal

function in the Diabetes Control and Complications Trial. The Diabetes Control and Complications Trial Research Group [corrected]. *Kidney Int* 1993, 43:668-674

15. Ljubic S, Roglic G, Mesic R, Pavlic-Renar I, Metelko Z. Trends in pulmonary functions in type 1 diabetic patients with nephropathy. Diabetologia croatica 33-4, 2004
16. Borst BB, Gosker H R , Zeegers M P , Annemie M W J. Pulmonary Function in Diabetes –A Metaanalysis. Chest 2010;138(2):393-406
17. Marvisi M, Bartolini L, del Borrello P, Brianti M, Marani G, Guariglia A, Cuomo A**:** Pulmonary function in non-insulin-dependent diabetes mellitus. *Respiration* 2001, 68**:**268-272
18. Girach A, Manner D, Porta M: Diabetic microvascular complications: can patients at risk be identified? A review.*Int J Clin Pract* 2006, 60:1471-1483
19. Ljubic S, Metelko Z, Car N, Roglic G, Drazic Z. Reduction of diffusion capacity for carbon monoxide in diabetic patients. Chest 1998;114:1033-5
20. 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