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Original article

Assessment of lung functions in asymptomatic female diabetic patients of more than 5 years duration

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ABSTRACT

Background: Abnormal pulmonary function test (PFT) is one of the complications associated with diabetes mellitus (DM). Nevertheless, the association between DM and PFT has been poorly characterized. Therefore, the present study was conducted to assess lung function in women with asymptomatic diabetes more than 5 years duration.

Methods: This prospective study included patients (aged >18 years) with diabetes >5 years normal chest x-ray and 2D ECHO-ejection fraction >40%. Data related to demographics and laboratory parameters including blood sugar level, HbA1c, fasting lipid profile were investigated. For the assessment of lung function FEV1, FVC, and FEV1 /FVC% of all the patients were measured.

Results: Out of 60 patients, 31.67% were from age group of 41-50 years. The majority of patients (81.67%) had duration of diabetes between 6 and 10 years. The parameters (age, BMI, and lipid profile) being the major determinant of the spirometric values were comparable in this study. Patients with HbA1c ≥7.5 had significantly reduced FEV1/FVC ratio compared to patients with HbA1c <7.5 (P<0.05). Poor glycemic control was correlated with FEV1/FVC and there was strong inverse correlation between HbA1c and FEV1/ FVC ratio (regression coefficient, -2.197).

Conclusions: Impairment of FEV1/FVC was found to be associated with poor glycemic control in women with diabetes more than 5 years suggests wide usability of PFTs in patients with poor glycemic control can be useful to prevent further lung damage.

Keywords: Lung damage, FEV1/FVC, Spirometry, Poor glycemic control

Introduction:

Diabetes mellitus (DM) is a rapidly growing non-communicable disease. Global incidence of DM estimated to be 463 million in 2019 and projected to reach 700 million by 2045.[1] n India, around 30 million people have diagnosed with diabetes and prevalence is higher in urban population.[2] The complications associated with DM give rise to macro vascular and micro vascular damages which mainly affects eyes, kidneys, heart, blood vessels, nerves and also lungs.[3] Diabetes mellitus affects the respiratory system by producing various functional and organic impairments leading to abnormal pulmonary function tests (PFTs).[4]

The association between type 1 DM (T1DM) and lung function abnormalities has been reported in previous studies showing pathological conditions are responsible for lung damage.[5] However, impairment of lung function is due to collagen and elastin change which further alter the systemic microangiopathy in patients with DM. Another theory suggested that increased nonenzymatic glycation of proteins and peptides of the extracellular matrix at high circulating glucose levels may play a vital role in impairment of pulmonary functions in patients with DM.[6]

Force vital capacity (FVC), forced expiratory volume in first second (FEV1), and FEV1/FVC are parameters usually evaluated for the assessment of lung function.[7] Patients with high levels of blood glucose and HbA1c are associated with a significant reduction in FVC values.[8] Other researchers also observed that patients with T1DM have low predicted FVC value.[9] Along with FVC, significant reduction in spirometric values of FEV1 in patients with high blood sugar level was also reported.[10] Few studies have reported an inverse correlation between patients with HbA1c>10% and FEV1.[9, 11] The pulmonary complications associated with DM have been poorly characterized. Very few Indian studies have assessed the pulmonary functions in patients with either T1DM or T2DM. This study will add value to the literature. Therefore, the present study was conducted to assess lung function in women with asymptomatic diabetes more than 5 years duration.

Methodology:

This was a prospective study conducted at Dr. D. Y. Patil hospital and research centre between July 2013 and September 2015. Patients were drawn from general medicine wards, General Outpatient Department and the diabetic clinics. The study was approved by Institutional Ethics Committee and study procedure was in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all study patients before enrolment.

Patients of age >18 years, with diabetes mellitus more than 5 years, normal chest x-ray and 2D ECHO-ejection fraction >40% were included in this study. Patients who are smokers, 2D ECHO suggestive of high pulmonary artery pressure due to other diseases and ejection fraction less than 40%, and who are exposed to occupational hazards causing respiratory disease were excluded.

General data including name, age, sex, BMI, and duration of diabetes of patient was collected. Detail history regarding complaints of respiratory system noted. History of symptoms (cough, fever, hemoptysis etc.) was noted. History of occupational exposure and any significant past history were noted. 2D echo for EF and any significant changes was also done. Chest X-ray for any lung pathology was done. Laboratory parameters including blood sugar level, HbA1c, fasting lipid profile were investigated. Fundoscopic examination was carried out by the ophthalmologist with the help of ophthalmoscope. For the assessment of lung function FEV1, FVC, and FEV1 /FVC% of all the patients were measured. All of these tests were done by spirometric method by using a digital Spirometer (COSMED).

Statistical analysis

Data were analyzed using Statistical Package for The Social Sciences (SPSS) software, version 18.0. Qualitative data were presented as number and percentages, while quantitative data was presented as mean (standard deviation [SD]). A P-value<0.05 was considered statistically significant.

Results:

A total of 60 patients were included in this study. Of these, 8 (13.33%) patients were from age group of ≤40 years, 19 (31.67%) patients were from age group of 41-50 years, 17 (28.33%) patients were from age group of 51-60 years. The majority of patients (81.67%) had duration of diabetes between 6 and 10 years (Table 1). The mean FEV1 and FVC were comparable between patients with HbA1c <7.5% and ≥7.5% (P>0.05). However, patients with HbA1c ≥7.5 had significantly reduced FEV1/FVC ratio compared to patients with HbA1c <7.5 (P<0.05) (Table 2).

According to BMI group, there was no significant difference between mean FEV1, FVC and FEV1/FVC level. The mean FEV1, FVC and FEV1/FVC level were comparable between abnormal and normal 2D ECHO findings (Table 3). There was no significant correlation observed between lipid profiles (cholesterol, triglyceride, HDL, and LDL) and LFTs (FEV1, FVC, and FEV1/FVC) (Table 4). Also, regression analysis showed that no significant impact of FEV1 and FVC on age, duration of disease, HbA1c and BMI. There was strong inverse correlation between HbA1c and FEV1/ FVC ratio (regression coefficient, -2.197) (Table 5).

Table 1: Demographics characteristics

Characteristics	Total (N=60)
Age (years)	
≤40	8 (13.33)
41-50	19 (31.67)
51-60	17 (28.33)
>60	16 (26.67)
Duration of diabetes (years)	
6-10	49 (81.67)
>10	11 (18.33)
Fundus	
PDR	1 (1.67)
NPDR	2 (3.33)
Hypertensive retinopathy	2 (3.33)
Normal	55 (91.67)

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Data shown as n (%). NPDR, non-proliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy

Table 2: Comparison of spirometric values according to glycemic control

Spirometric values	HbA1c <7.5 (n=41)	HbA1c ≥7.5 (n-19)	P value
FEV1 (L)	2.45 (0.36)	2.28 (0.51)	>0.05
FVC (L)	2.79 (0.43)	2.59 (0.49)	>0.05
FEV1/FVC (%)	84.76 (2.91)	82.32 (4.33)	<0.05
Data shown as n (%). FEV1, forced expiratory volume in first second; FVC, forced vital capacity.			

Table 3: Comparison of FEV1, FVC and FEV1/FVC according to BMI and 2D ECHO finding

Parameters	FEV1 (L)	FVC (L)	FEV1/FVC (%)
BMI			
18.50-24.99 (n=29)	2.47 (0.39)	2.79 (0.42)	84.14 (2.94)
25.00-29.99 (n=20)	2.34 (0.39)	2.69 (0.49)	84.80 (3.45)
≥30 (n=11)	2.32 (0.50)	2.69 (0.49)	82.09 (4.78)
P value	>0.05	>0.05	>0.05
2D echo finding			
Abnormal (n=14)	2.48 (0.39)	2.80 (0.42)	83.93 (2.92)
Normal (n=46)	2.80 (0.42)	2.71 (0.47)	84.00 (2.78)
P value	>0.05	>0.05	>0.05
Data shown as mean (SD). BMI, body mass index; FEV1, forced expiratory volume in first second; FVC, forced vital capacity.			

Table 4: Correlation between spirometric values and lipid profile

Parameter 1	**Parameter 2**	**Coefficient correlation**	**P value**
Cholesterol (mg/dL)	FEV1 (L)	-0.05	>0.05
	FVC (L)	-0.04	>0.05
	FEV1/FVC (%)	0.24	>0.05
Triglyceride (mg/dL)	FEV1 (L)	0.002	>0.05
	FVC (L)	0.03	>0.05
	FEV1/FVC (%)	-0.14	>0.05
HDL (mg/dL)	FEV1 (L)	0.20	>0.05
	FVC (L)	0.16	>0.05
	FEV1/FVC (%)	0.10	>0.05
LDL (mg/dL)	FEV1 (L)	0.25	>0.05
	FVC (L)	0.23	>0.05
	FEV1/FVC (%)	0.19	>0.05
FEV1, forced expiratory volume in first second; FVC, forced vital capacity; HDL, high density lipoprotein; LDL, low density lipoprotein.			

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Table 5: Regression analysis

Variable 1	Variable 2	Regression Coefficient	P Value
Age (years)	FEV1 (L)	-0.004521	>0.05
	FVC(L)	-0.004557	>0.05
	FEV1/FVC (%)	0.01993	>0.05
Duration (years)	FEV1 (L)	0.00283	>0.05
	FVC(L)	0.00189	>0.05
	FEV1/FVC (%)	-0.0626	>0.05
HbA1c (%)	FEV1 (L)	-0.2107	>0.05
	FVC(L)	-0.2359	>0.05
	FEV1/FVC (%)	-2.197	>0.05
BMI (kg/m^2)	FEV1 (L)	-0.01129	>0.05
	FVC(L)	-0.00871	>0.05
	FEV1/FVC (%)	-0.06778	>0.05
BMI, body mass index; FEV1, forced expiratory volume in first second; FVC, forced vital capacity; HbA1c, glycated hemoglobin.			

Discussion:

Complications associated with DM are challenging health problems. Diabetes is not associated with any lung impairment and therefore periodic screening for lung diseases is not so common. However, connective tissues and microvascular circulations present in the lungs may be responsible for lung impairment in patients with DM.[12, 13] There is an association between increased levels of systemic inflammatory mediators and inflammatory markers and DM, which alters the lung protein, resulted into pulmonary function abnormalities.[14] Another study has reported deleterious effects of DM on respiratory system including reduced lung volumes, total lung capacity, elastic recoil of the lung, and diffusing capacity of the lung for carbon monoxide.[4]

The present study conducted to assess the lung function in asymptomatic women who had diabetes more than 5 years duration. The key findings suggest that prevalence of diabetic retinopathy was 5%. The parameters (age, BMI, and lipid profile) being the major determinant of the spirometric values were comparable in this study. However, poor glycemic control was significantly correlated with FEV1/FVC and there was strong inverse correlation between HbA1c and FEV1/ FVC ratio.

The incidence of DM has been increased in India and prevalence is even higher among women of age group 55-59 years.[15] An Indian study conducted at urban slum of Pune city reported high prevalence (35%) of type 2 diabetes in women of age group 51-60 years.[16] However, in the present study, the prevalence of DM was higher in women of age group 41-50 years (31.67%).

Several studies have reported strong relationship between poor glycemic control and reduction in FVC and FEV1.[17-19] A cross sectional study carried out to evaluate relationship between spirometric values and HbA1c in 60 male patients with and without T1DM.[18] They found significantly lower mean predicted value of FEV1 and FVC ($p<0.001$) while FEV1/ FVC% was comparatively lower but not statistically significant. They also hypothesized that reduction in lung function parameters are mainly due to poor glycemic control. Likewise, Aparna A. demonstrated a comparative analysis of PFTs in T2DM patients and healthy patients, observed significant reduction in PFTs (FVC, FEV1, PEFR) in patients with T2DM compared to normal healthy individuals. While ratio of FEV1/FVC was significantly higher in patients with diabetes compared to normal healthy individuals.[19] Conversely, the present study did not show any significant association between PFTs (FEV1 and FVC) and diabetes. However, FEV1/FVC was significantly reduced in patients with diabetes. This impairment of lung function could be due to biochemical alterations caused by chronic hyperglycemia in connective tissues of lungs especially collagen and elastin. Furthermore it was noted that, non-enzymatic glycosylation of protein is affected by diabetic microangiopathy.[10] In current study, we found that poor glycemic

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control affects the FEV1/ FVC ratio. A study done by Okyay et al. reported a reverse association between HbA1c and mean FEV1 (P=0.034, r=-0.383) and FVC (P=0.007, r=-0.471).[20] Whereas, positive correlation was observed with HbA1c and FEV1/ FVC ratio (P=0.018, r=0.424). The poor glycemic control may alter the pulmonary functions in patients with T2DM []. In this regard, a cross sectional study conducted in 495 patients with T2DM reported similar results, where significant reduction in FEV1 (difference -75.4 ml; 95%CI: (-92.2, -58.6); P <0.0001) and FVC (difference -121.2 ml; 95%CI: (-134.1, 108.4); p< 0.0001) values were found to be associated in patients with inadequate glucose control than those with adequate glucose control.[14] A progressive reduction in FEV1/FVC is directly proportional with increasing blood sugar levels. Likewise, poor glycemic control causes early obstructive abnormality.[21,22]

A Japanese study evaluated a strong correlation between glycemic status and impaired lung function. This health screening program reported that HbA1c is inversely proportional to lung function, increase HbA1c associated with reduction in FEV1 and FVC, in both men and women.[11] In the present study, inverse relationship between HbA1c and FEV1/FVC ratio was observed.

A recent study done by Agarwal et al. reported significant decrement in the LFTs in patients with diabetes. A significant impact of duration of diabetes on FEV1/FVC values was also noted. However, Spirometric values of FVC, FEV1, FEV1/FVC ratio were significantly reduced in patients with T2DM.[23] Poor glycemic control is associated with increased complications. As lung is a major target organ involved in chronic diseases like diabetes, patients with asymptomatic diabetes have higher chances of having diabetic pnuemopathy as a risk factor.[4] Hence a regular assessment of pulmonary function is needed in these patients. But still more studies are needed to recognize the early derangement of pulmonary function in patients with diabetes.

However, the present study is limited by small sample size with limited time period, and single centre hence larger patient number and long term, multicentre studies will be required to support this findings.

Conclusion

Impairment of some lung functions (FEV1/FVC) was found in women with diabetes, especially due to poor glycemic control. However, judicious use of PFTs in patients with poor glycemic control can be useful to prevent further lung damage and large and multicenter study is required.

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