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Pulmonary Function Abnormalities in Patients with Type 2 Diabetes in Contrast to Healthy Population

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ABSTRACT

Introduction: Diabetes mellitus is a chronic multisystem disease that lungs are also affected .However, there are conflicting evidence about the abnormal pulmonary function in diabetic patients. This study evaluated the difference between pulmonary function tests among patients with type 2 diabetes and healthy adults.

Material and Methods: This present descriptive cross sectional had been studied in Khorasan Razavi province of Iran from November 2016 to May 2017. The patients with type 2 diabetes which were older than 18 years without history of pulmonary diseases, heart failure, smoking, anemia, musculoskeletal, pulmonary or connective tissue disorders were included in the present study. A group of healthy volunteers participated as a control group with similar age, gender, height and weight to the diabetic participants. Both groups underwent spirometry and body box. Pulmonary function tests among study groups were compared.

Results: Total number of 40 diabetic patients as the case group and 40 healthy individuals as control group enrolled in this study. The control group had significantly higher force vital capacity (FVC), forced expiratory volume in 1 second (FEV1) and lower FEV1/FVC (P=0.001, P=0.05 and P=0.001 respectively). Males in diabetic groups had significantly lower FVC and FEV1/FVC (P=0.01 and P=0.003) and diabetic females had significantly higher FVC, FEV1 and lower FEV1/FVC (P=0.001, P=0.05 and P=0.003 respectively). According to the linear regression model, by controlling the effect of gender, diabetes significantly affected both FEV1/FVC and FVC levels.

Conclusion: The present study demonstrated that diabetic patients are more likely to develop abnormal pulmonary function and gender can affect the pulmonary function of the diabetic patients.

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Introduction

Diabetes is a chronic multisystem disease which has considerable global burden and has been reported among common causes of deaths (1). It has been predicted that the prevalence of diabetes would be 9.3% and rising to 10.2% by the end of the next decade (2). Moreover, high income countries are having more diabetic patients than low incomes and 50% of diabetic population are not aware of their disease (2). This endocrine disease characterizes as prolonged hypoglycemic state which is mostly associated with increased oxidative stress and inflammatory status (3). Both micro- and macro-vascular damages are results of diabetes which can occur in most of the body organs including kidneys and cardiovascular system (3). Although the pathologic effect of diabetes on many organs are widely studied, the effect of diabetes on lung tissue and function are not widely studied (4). By considering the vascular abnormalities in diabetes, lung tissue as an organ with complex vascular structure should become affected by vascular changes during diabetes but the extensive physiological reserve of lung will fade out lung damage until pulmonary dysfunction occur (4). Moreover, biochemical impairment mostly including accommodation of glycosylation end products and activation of protein kinase C as well as impaired elastin collagen cross linkage will result in reduced elasticity of connective tissue in lungs (5, 6). Also thickening of basal membrane will lead to reduced impaired diffusion (5, 6). Asthma, chronic obstructive pulmonary disease idiopathic pulmonary fibrosis and pulmonary hypertension are among the common lung diseases among diabetic patients (4). Chronic airway inflammation, airway hyper responsiveness, decreased thoracic compliance and sputum overproduction are considered as underlying causes of such pulmonary disease in diabetic patients (4). However, the pulmonary function of type 2 diabetic patients who did not develop any other disease is not widely studied and the available studies had paradoxical findings (7, 8). While recent studies are highlighting the effect of type 2 diabetes on pulmonary function, an early systematic review on the relation between diabetes mellitus and lung function did not revealed a considerable association (7, 9)(10-13). So, the aim of present study was evaluating the difference between pulmonary functions in healthy population and type 2 diabetic patients without any other underlying diseases.

Material and Methods

The present descriptive cross sectional study took place in Khorasan Razavi province of Iran from November 2016 to May 2017 and was approved by Mashhad University of Medical Sciences ethic committee. Every patient with type 2 diabetes who was referred to Hazrat-e-rasoul clinic in Mashhad enrolled in the present study after filling an informed consent form. Patients who were younger than 18 years and had history of any pulmonary diseases, heart failure, smoking, anemia, musculoskeletal or connective tissue disorders were not included in the study. Also, none of the participants had occupations that are known to cause pulmonary disorders. Each participant was asked to fill a demographic data questionnaire. After performing a pulse oximetry, each patient was asked to take a spirometry test in a body box. Spirometer device from CHEST brand made in USA was used in this design. A group of healthy volunteers participated as a control group with similar age, gender, height and weight to the diabetic participants. The control group also underwent spirometry and body box as same as the diabetic group. The study data was analyzed by SPSS software (version 16) and P value lesser than 0.05 was considered as statistically significant result. The normally distributed variables including the comparison of pulmonary function tests among study groups were analyzed by T-test. Also linear regression test was used for evaluating the relation between pulmonary function tests with age and Body mass index (BMI).

Results

Total number of 40 diabetic patients as the case group and 40 healthy individuals as the control group enrolled in the present study. Demographic data of both case and control groups are summarized in table 1. Among

study groups, the control group had significantly higher force vital capacity (FVC), forced expiratory volume in 1 second (FEV1) and lower FEV1/FVC in contrast to case group (P=0.001, P=0.05 and P=0.001 respectively) (Table 2). When dividing the groups according to their gender, males in diabetic groups had significantly lower FVC and FEV1/FVC (P=0.01 and P=0.003) while diabetic females had significantly higher FVC, FEV1 and lower FEV1/FVC (P=0.001, P=0.05 and P=0.003 respectively) (Table 2).

Table 1. Participant's demographic data according to their groups.

Variables		Case group	Control group
Gender	**Male**	13	13
	Female	27	27
Mean (SD*) of age (year)		57.12(6.93)	56.52(8.07)
Mean (SD) of height (cm)		159(9.38)	161(9.31)
Mean (SD) of weight (kg)		74.75(12.75)	74.02(13.01)
Mean (SD) of BMI (kg/m2)**		29.34(3.8)	28.52(4.82)

* **SD:** standard deviation;
** **BMI:** body mass index

Table 2. Comparison of means of respiratory findings among study participants according to their gender and group.

Variables		Mean(SD)	Difference	P value (T-test)
FVC*	**Case group**	71.02(17.48)	-13.52	0.001
	Control group	84.55(9.00)		
FEV1**	**Case group**	79.15(18.52)	-6.77	0.05
	Control group	85.92(9.43)		
FEV1/FVC	**Case group**	111.72(9.90)	9.92	0.001
	Control group	101.8(10.25)		
TLC***	**Case group**	98.47(24.02)	-9.67	0.063
	Control group	108.15(21.74)		
Male gender				
FVC	**Case group**	76.38(13.56)	-13.46	0.01
	Control group	89.84(10.86)		
FEV1	**Case group**	84.38(15.05)	-3.84	0.47
	Control group	88.23(11.50)		
FEV1/FVC	**Case group**	110.85(10.13)	12.96	0.003
	Control group	98.15(9.47)		
TLC	**Case group**	94.38(16.17)	-6.46	0.27
	Control group	100.85(12.97)		
Female gender				
FVC	**Case group**	68.44(18.77)	-13.55	0.001
	Control group	82.00(6.81)		
FEV1	**Case group**	76.62(19.74)	-8.18	0.05
	Control group	84.81(8.26)		
FEV1/FVC	**Case group**	112.15(9.96)	8.59	0.003
	Control group	103.56(10.32)		
TLC	**Case group**	100.44(27.06)	-11.22	0.115
	Control group	111.67(24.32)		

* **FVC**: force vital capacity;
** **FEV1**: forced expiratory volume in 1 second;
*** **TLC**: total lung capacity.

FEV1/FVC did not have any significant relation with age and BMI among study groups (Table 2). The comparison of means showed a meaningful correlation between FVC among both groups (P=0.003) (Figure 1). However, the comparison of means for FEV1 and total lung capacity (TLC) did not show any meaningful relationship among both groups (P=0.68) (Figure 1). According to the FEV1 and FVC parameters, diabetic group showed significant increase in FEV1/FVC ratio (P=0.001) (Table 3). According to the linear regression model, by controlling the effect of gender, diabetes could significantly affect both FEV1/FVC and FVC (Table 3).

Discussion

Diabetes type 2 is a chronic disease with considerable effect on most of the body systems. The present study demonstrated that diabetic patients will develop some abnormalities in their respiratory functions. Diabetic patients had reduced FVC and increased FEV1/FVC ratio.

Diabetes mellitus as a multisystem disease can affect lung tissue and function. However, the cause and relation between type 2 diabetes and abnormal pulmonary function is not clearly studied. Some studies revealed that individuals with abnormal pulmonary function are more likely to have insulin resistance and diabetes (14-16). While obesity has been considered as a possible risk factor diabetes, it has been also hypothesized that obesity may be a risk factor for development of abnormal pulmonary function (17).

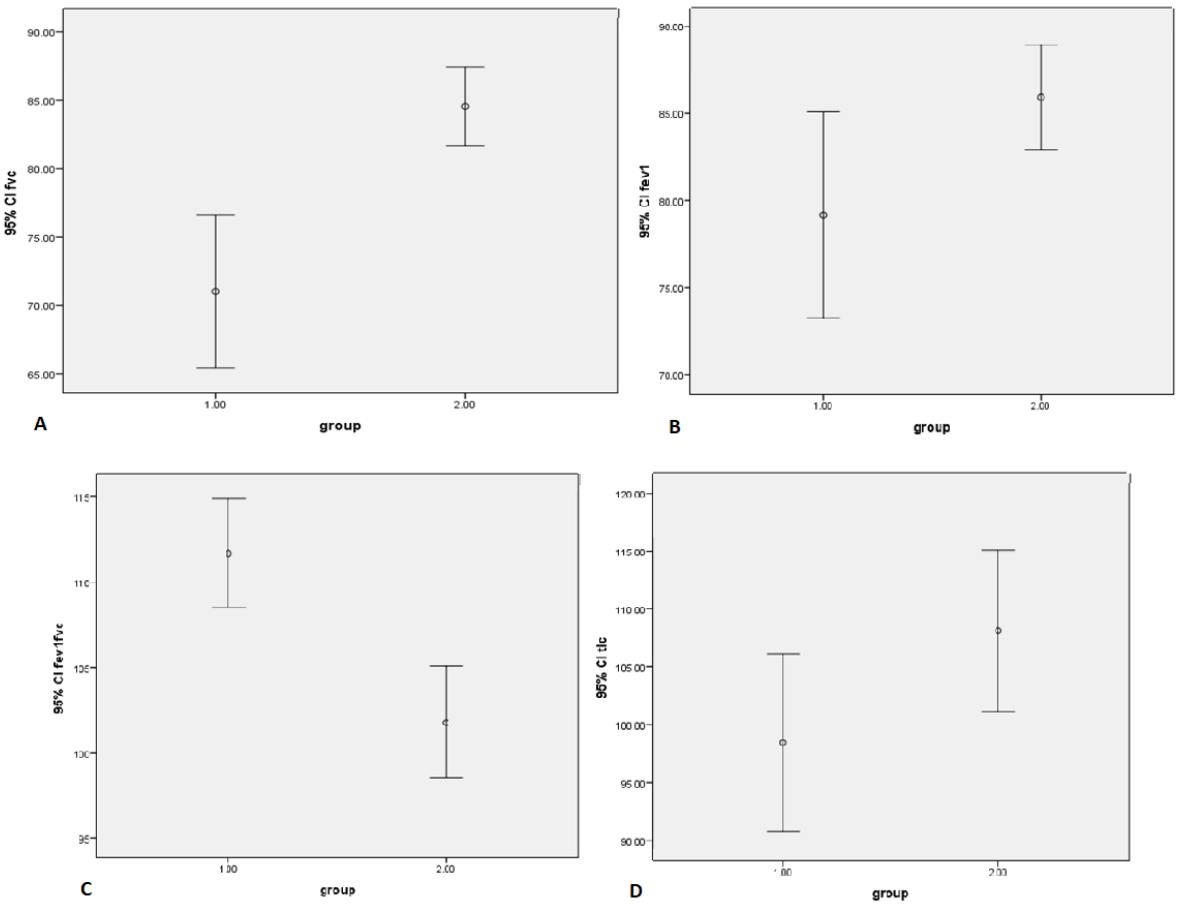

Figure 1. A) Case group had significantly lower mean forced vital capacity (FVC) than control group (P=0.003); B) case group had lower mean FEV1 than control group; C) case group had higher mean FEV1/FVC than control group (P=0.001); D) Case group had lower mean TLC than control group.

Leone et al. study demonstrated that both abnormal lung function and diabetes mellitus are related to abdominal obesity (18). Yeht al. also demonstrated the same finding and proposed that abdominal obesity is a significant factor which can affect development of metabolic syndrome, diabetes mellitus and pulmonary function tests abnormalities (17) While abdominal obesity was not considered in the present study, however, in contrast to such findings about the relation between increased abdominal obesity and development of pulmonary dysfunction, our diabetic patients BMI was not considered as an effective factor on development of abnormal pulmonary function. Regardless of BMI and abdominal obesity, approximately half of type 2 diabetic patients may develop pulmonary function abnormalities which may present as a obstructive restrictive or mix pattern on spirometry (19). Diabetic micro-angiopathy may involve both lung's capillaries and alveolar tissue (20). The effect of this pathological process will manifest itself by reduced diffusion capacity and restriction of lung's volume (20). Both type 1 and type 2 diabetic patients are reported to have reduced Diffusing capacity for carbon monoxide (DLCO) (21, 22). Aparna et al. demonstrated that diabetic patients have reduced FVC and FEV1 levels in contrast to healthy patients[10]. As same as our study, their study demonstrated that FEV1/FVC ratio increases in diabetic patients (10). In both studies, possible confounding factors including smoking, connective tissue disorders and other cardiac or respiratory disease were excluded (10). Similar to Aparna et al. study, we concluded that diabetes type 2 is the most probable cause of pulmonary dysfunction in diabetic patients (10). Kwon et al. study demonstrated similar findings on a larger male population of Korean type 2 diabetic patients (11). According to their study results, both FVC and FEV1 showed significant reduction in those patients who develop diabetes type 2 (11). Our study demonstrated that male patients had reduced FVC levels, however, the FEV1 level was not significantly reduced in our population. Despite of different population size, differences in patient's age could be the other possible reason of this difference. Moreover, some studies demonstrated that laboratory markers of diabetes may also be correlated with pulmonary function. Huang t al. study reported that as same as our study, type 2 diabetes is associated with impaired pulmonary function (9). Their diabetic patients had significantly worsen FEV1, FVC, FEV1/FVC and TLC than healthy subjects and fasting plasma glucose was an independent risk factor for development of abnormal pulmonary function (9). Anandhalak shim et al. evaluated the relation between pulmonary function parameters and hemoglobin A1C level (HbA1c), fasting blood glucose level and the disease duration (12). They demonstrated that disease duration may not affect pulmonary function but the pulmonary function is markedly reduced in diabetic patients (12). Those patients with poor diabetic control had reduced alveolar distribution which was also unrelated to diabetes duration (12). Uz-zaman et al. also reported that those diabetic patients who had HbA1c greater than 7 are more likely to have greater FEV1/FVC ratio (13).

Table 3. Effect of diabetes on FVC and FEV1/FVC.

	FVC*		FEV1**/FVC	
	Regression coefficient, 95% CI	**Pvalue**	**Regression coefficient, 95% CI**	**Pvalue**
Group	13.86 (7.79-19.92)	<0.001	-0.06 (-0.10--0.03)	<0.001
Gender	-8.47 (-15.17--1.77)	0.014	0.05 (0.01-0.09)	0.025
Age	0.016 (-0.419-0.451)	0.942	-0.001 (-0.004-0.001)	0.391
BMI	0.391 (-0.365-1.15)	0.306	0.001 (-0.004-0.005)	0.878

* **FVC:** force vital capacity;
FEV1: forced expiratory volume in 1 second.

The present study did not evaluate the disease duration and HbA1c level, however, we have also demonstrated that diabetic patients have significantly lower FEV1/FVC levels.

Conclusion

The present study demonstrated that diabetic patients are more likely to develop abnormal pulmonary function as reduced FVC and increased FEV1/FVC ratio. While both diabetic male and female diabetic patients may develop decrease in FVC and increased FEV1/FVC, however, reduced FEV1 was significantly seen in male population with type 2 diabetes.

Limitations

Our limitations in this study were the satisfaction of diabetic patients to perform spirometry and the lack of proper cooperation of patients to perform this test successfully.

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