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Assessment of Spirometric Indices in Patients with Type 2 Diabetes in Imam Hussein Hospital, Shahroud, Iran (2016-2017)

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Abstract

Background: *Diabetes mellitus is the most prevalent metabolic disorder. Previous related studies have shown that, lungs are target organs in diabetic micro-angiopathy. The present study was designed to investigate the spirometric indices in patients with type 2 diabetes referred to the outpatient clinic of Imam Hussein hospital in Shahroud, Iran.*

Methods: *This comparative study included 50 patients with type 2 diabetes and 50 non-diabetic subjects who were matched in terms of weight, age, and sex, and were referred to the Diabetes clinic of Imam Hussein hospital in Shahroud, Iran. MIR SPIROLAB III spirometer was used for spirometric tests to obtain FEV1, FVC, PEFR, and FEF 25-75. Decrease in these indices is determinant of pulmonary complications. Indices were compared between two groups. The relationships between some variables like glycated hemoglobin (HbA1c) and type of their treatment with the severity of spirometric disturbances were also assessed.*

Results: *The average age was equal to 56.3 years old (with SD of 6.3 years) and 58.3 years old (with SD of 6.3 years), respectively in non-diabetic and diabetic group. Comparison of the FEV1, FVC, PEFR, and FEF 25-75 indices between diabetic and non-diabetic groups showed a significant difference (P.V<0.05). No significant difference was found in the FEV1/FVC ratio. According to the Pearson correlation formula, there was a significant association between decreased spirometric indices and increased concentration of Hb A1C (-.630, -.635 and-.374 for FEV1, FVC, and PEFR, respectively). There was no association between decreased concentration of FEV1/FVC and increased HbA1c.*

Conclusions: *The findings of the study revealed that, there was a significant decrease in pulmonary functions in the diabetic group. Impaired pulmonary function can be detected in early stages of diabetes and studying the pulmonary function can be easily preformed. Accordingly, screening lungs function should be carried out regularly, as well as integrating in other routine examinations and screening tests.*

Keywords: Diabetes, Spirometry, Pulmonary disease, Imam Hussein hospital.
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Introduction

Diabetes mellitus is the most prevalent metabolic disorder, and is also a common chronic disease worldwide. It can be presented with different manifestations among all races.[1] According to the WHO, diabetes is a chronic multifactorial metabolic disorder characterized by an impairment in carbohydrate, lipid ,and protein metabolism due to the defects in either insulin production or its decreased function.[2] Type 2 or Non-Insulin-Dependent Diabetes Mellitus (NIDDM) is presented by impaired insulin receptors and insulin resistance. NIDDM is a common type of diabetes, in which there is no aberration in B cells function and develops after the age of 40. During the late decades, several epidemiological studies on the prevalence of type 2 diabetes have been performed in Iran. Studies have shown that, the prevalence of diabetes among>30 people, is between 6.5 to 10.6% (approximately 2.4 million people in the population of Iran in 2010). Moreover, 14.5 to 22.5% of >50 people are affected by the Impaired Glucose Tolerance (IGT).[1] Hyperglycemia is presented by the polyuria, polydipsia and weight loss. Notably, increased appetite and blurred vision have also been documented.

Long-lasting diabetes complications result from macro and micro vascular injuries involving the diabetic retinopathy with the potential risk of blindness, progressive nephropathy with the risk of renal failure, peripheral neuropathy with the risk of diabetic foot ulcer, limb amputation, Charcot joint and autonomic neuropathy inducing the digestive, cardiovascular, urogenital and sexual complications.[3]

A considerable number of studies have introduced the lung as a target organ in diabetic micro-angiopathies. Histopathology results showed the increased thickness and fibrosis of basal membrane. Presence of an abundant amount of connective tissue and an extensive microvascular circulation increase the possibility of lungs involvement in micro-angiopathies and non-enzymatic glycosylation of tissue proteins.[4,5] Normal pulmonary mechanics and its alveolar exchange is influenced by the integrity of connective tissue and pulmonary micro-vascularization. Any perturbation in the system leads to the development of disorders in the Pulmonary Function Tests (PFTs).[6]

On the other hand, diabetes increases the concentration of inflammation mediators and biomarkers. The increase in the inflammatory cytokine, in association with micro-angiopathies can change the proteins in the matrix of pulmonary tissue.[7]

Pulmonary mechanics disorders are divided into obstructive and restrictive disorders. Obstructive pulmonary diseases are characterized by the airway obstruction caused by the constriction of lower airways. In spirometry, the decrease in the exhalation rate results from the obstruction. Consequently, the decrease in Forced Expiratory Volume in 1 second (FEV1) is more than the Forced Vital Capacity (FVC0). Therefore, FEV1/FVC ratio decreases. In the condition, where the FEV1/FVC ratio is lesser than 30% of the normal condition, obstructive pulmonary disease is diagnosed. FEV1/FVC ratio

can also act as a criterion for differential diagnosis between obstructive and restrictive pulmonary diseases. It is now understood that, extra-pulmonary, plural or parenchymal factors can influence on the normal pulmonary stretch and result in the respiratory overload and inadequate oxygenation. The decreased pulmonary capacity (except FEV1/FVC ratio) occurs as a result of the decrease in the total pulmonary capacity.[8] While most of the studies have concluded that, the pattern of spirometric disorders in diabetic patients are similar to the restrictive diseases,[2-12] some of them demonstrated the obstructive pattern.[13] Hence, this study was carried out to assess the spirometric indices (FEV1, FVC, PEFR, FEF 25-75 and FEV1/FVC) in patients with type 2 diabetes referred to Imam Hussein hospital, Shahroud, Iran (2016-2017).

Materials and Methods

This comparative study designed for fulfillment of a MD thesis (with a research code of 180 at Shahroud University of Medical Sciences) included 50 patients with NIDDM referred to the Diabetes clinic of Imam Hussein hospital from 2016 to 2017. In addition, 50 weight -and sex- matched normo-glycemic subjects were included as the control group. Determination of sample size was based on the study by Anandhalakshmi considering the difference between FVC of diabetic and control group (d=0.53) and variance of 2=4σ with confidence level of 5% and power of 80%. Based on these data, the primary sample size was obtained as 22 for each group; but to eliminate the probable errors, it increased to 50 for each group. The control group was selected from the healthy individuals such as patients' accompaniment, patient's relatives, the stuff of Imam Hussein hospital or even the patients needed minor surgeries. An informed consent was taken from all the subjects (research code 180).

Inclusion criteria included previously diagnosed diabetic cases or the patients who were recently diagnosed with diabetes based on the American Diabetes Association criteria (FBS>126). Exclusion criteria (In both diabetic and non-diabetic groups) included history of severe or chronic pulmonary disease, observable abnormalities in vertebral column and rib cage (for example kyphoscoliosis), uncontrolled pulmonary and cardiac disorders, neuro-muscular disorders, malignancies, patients who recently had a major abdominal or thoracic surgery, addiction, any kind of tobacco smoking either currently or in the past, pregnancy and patients with ascites and abdominal tumors.

Spirometry was performed for both groups by a single skilled technician using the MIR SPIROLAB III spirometer. Before preforming spirometry, the information of the patients was written on an identification paper and weight and height were measured and entered into the instrument. All the patients sat on a chair while their soles were on the ground. To remove the pressures from their lungs, they took off any of their tight clothes. After putting the clips on their nose, they took several normal inhalation and exhalation. Then, they took a deep fast breath so that, the whole lungs becomes full of air. After that, they exhaled with all intensity and strength so that, the lungs become empty, and the exhalation lasted for about 6 seconds.

Forced Expiratory Volume in 1 second (FEV1), Forced Vital Capacity (FVC), Forced Expiratory Volume Percentage (FEV1 /FVC), Peak Expiratory Flow Rate (PEFR), and Forced Expiratory Flow (FEF) (25–75%) were used as respiratory indices. These indices can be used as diagnostic criteria in early stages of obstruction in lower respiratory tract.

To prevent any measurement variations, the spirometry was performed between 9 am to 1 pm (before having meal) on all patients. Patients should not have eaten a heavy meal before the test. The test was carried out in the sitting posture and the subjects performed the test 3 times at an interval of 15 minutes. The results of the tests were compared and the best functions were selected and reported. Notably, the test was carried out for all the patients by the same technician.

From the point of view of disease control, the diabetic patients were classified into two groups of patients with greater than 7 and lesser than 7 HbA1c concentration[14] and then they were compared to each other. Based on the type of treatment, the patients were categorized into the group who received insulin and the group who underwent anti-diabetic medication. To analyze the collected data, SPSS software version 20 was used at a significance level of 0.5%. To compare spirometric indices between the diabetic and non-diabetic groups, Independent Samples T-Test was used and to study the association between pulmonary indices and HbA1c, Pearson correlation coefficient was recruited for evaluating the correlation between glycosylated hemoglobin and spirometric indices (FEV1, FVC.PEFR, FEF25-75 and FEV1/FVC).

Results

Totally, 50 diabetic patients and 50 non-diabetic subjects were studied as the diabetic and non-diabetic groups, respectively. In the diabetic group, 50 patients were included with the mean age of 58.3±6.3 years old (median of 59 years old, age range between 43 and 69 years old). In the control group, 50 individuals were involved with the mean age of 56.3±6.3 years old (median of 57 years old, age range between 43 and 68 years old). There were significant differences in the FEV1, FVC, PEFR and FEF25-75 (P< 0.05) between the diabetic and non-diabetic groups. However, there was no significant difference in the FEV1/FVC ratio between the diabetic and non-diabetic groups. (Table1).

Table 1. The association between spirometric indices in diabetic and non-diabetic groups

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Variable	Group	Mean	Standard Deviation	P.V
(Predicted %) FEV1	Diabetic	٨٢/٣	١٥,٢	٠,٠٠٢
	Non-diabetic	٩٠,٤	٩,٤	
(Predicted %) FVC	Diabetic	٨٠,٧	١٤,٦	٠,٠٠
	Non- diabetic	٩٠,٥	٨,٦	
(Predicted %) PEFR	Diabetic	٧٥,٤	١٤,٤	٠,٠٠
	Non- diabetic	٨٦	٦,٨	
(Predicted %) FEF25-75	Diabetic	٧١,٩	١٧,٥	٠,٠٠٢
	Non- diabetic	٨٢,١	١٣,٩	
FEV1/FVC	Diabetic	٨٠,٧	٧,٩	٠,٢٣٠
	Non- diabetic	٨٢,٤	٦,٤	

According to the Pearson correlation coefficient, there was a significant relationship between the decrease in the spirometric indices (FEV1, FVC, PEFR and FEF 25-75) and increased Hb A1C. Though, no significant difference was found between decreased FEV1/FVC and increased Hb A1C. (Table2).

Table 2. The association between spiro-metric indexes and glycosylated hemoglobin

	Variable	FEV1	FVC	PEFR	FEF25-75	FEV1/FVC
HbA1c	and Pearson correlation coefficient	۰٫۶۳۰-	۰٫۶۳۵-	۰٫۳۷٤-	۰٫٦٤۰-	۰٫۲۵۰-
	P.V	۰٫۰۰۰	۰٫۰۰۰	۰٫۰۰۷	۰٫۸۰	۰٫۰۰۰

Table 2.The association between spirometric indices and glycosylated hemoglobin

FEV1, FVC, FEF 25-75 parameters showed significant differences with low HbA1c and HbA1c greater than 7 between two groups. But no significant difference was observed in relation to PEFR parameter and FEV1/FVC ratio between two groups. (Table3)

Table 3. Comparison of spirometric indices between the diabetic groups with HbA1c>=7 and HbA1c<7

Table 3. Comparison of spirometric indexes between the diabetic and non-diabetic groups with HbA1c>=7 and HbA1c<7

Index	HbA1c	Number	Mean	Standard Deviation	P.V
FEV1	۷=<	۳۵	۷۷,۳٤	۱۴/۵۹	۰/۰۰۲
	۷>	۱۵	۹۴/۱۳	۹/۰۰	
FVC	۷=<	۳۵	۷۵/۲۲	۱۲/۵۲	۰/۰۰
	۷>	۱۵	۹۳/۵۳	۱۰/۸۲	
FEV1/FVC	۷=<	۳۵	۷۹/۷۴	۸/۳۶	۰/۱۷۶
	۷>	۱۵	۸۳/۰۶	۶/۴۱	
PEFR	۷=<	۳۵	۷۳/۸۸	۱۳/۲۸	۰/۲۶۱
	۷>	۱۵	۷۸/۹۳	۱۶/۷۲	
FEF25-75	۷=<	۳۵	۶۷/۰۰	۱۶/۷۱	۰/۰۰۲
	۷>	۱۵	۸۳/۵۳	۱۳/۸۰	

There was no significant difference between two treatment types (treatment with insulin and anti-diabetic medication) and the severity of spirometric abnormalities was evident. (Table 4)

Table 4. Comparison between the insulin treatment and anti-diabetic medication group.

Table 4. Comparison between the insulin treatment and anti-diabetic medication group

Index	Treatment Type	Number	Mean	Standard Deviation	P.V
FEV1	anti-diabetic drugs	۳۷	۸۳,۰۰	۱۵/۹۵	۰/۸
	Insulin	۱۳	۸۲/۱۶	۱۳/۴۳	۷
FVC	anti-diabetic	۳۷	۸۱/۸۶	۱۵/۱۳	۰/۳
	Insulin	۱۳	۷۷/۴۶	۱۳/۰۹	۶
FEV1/FVC	anti-diabetic	۳۷	۸۱/۶۹	۶/۵۰	۰/۶
	Insulin	۱۳	۸۰/۴۰	۱۱/۲۸	۲
PEFR	anti-diabetic	۳۷	۷۳/۳۰	۱۵/۳۰	۰/۵
	Insulin	۱۳	۷۶/۱۳	۱۱/۷۹	۵
FEF25-75	anti-diabetic	۳۷	۷۱/۰۷	۱۷/۶۵	۰/۸
	Insulin	۱۳	۷۲/۲۷	۱۷/۸۲	۴

Discussion

The comparison between diabetic and non-diabetic groups showed a significant decrease in the FEV1, FVC, PEFR and FEF25-75 indices in the diabetic patients (P.V<0.05). Though, the FEV1/FVC ratio (decrease in this ratio represents obstructive diseases) did not reveal any significant difference. These results were consistent with the findings of the studies by Malek et al,[3] Abdolazim et al[9] also reported the same significant results in pulmonary parameters without a decrease in the FEV1/FVC ratio. Although, Serikant et al[13] and Sheravia kerti [2] reported a significant decrease in this ratio.

The pathophysiology of the decreased pulmonary function is not completely understood. Normal pulmonary mechanics and gas exchange are influenced by the composition of connective tissue and tiny pulmonary vessels. Accelerating aging process in cross linkage of the cells of connective tissue and the presence of non-enzymatic glycosylation and alteration in surfactant function causes the lung function disorders.[10] Sandler et al studied the lungs by electron-microscope. Microscopic studies revealed thickening of the alveolar epithelium, endothelium capillary, and basal membrane in the diabetic patients. Also, they documented a decrease in the blood flow attributing to the micro-angiopathy.[11] Thorax and lungs are rich in elastin and collagen. The decrease in the flexibility of thorax and pulmonary parenchyma results from non-enzymatic glycosylation of these structures.[9] Our results showed a decrease in the pulmonary parameters in the diabetic group which are compatible with these pathologic findings. Furthermore, similar studies have shown the diabetic poly-neuropathy leading to pulmonary neuro-muscular and consequently a decreased lung capacity.[12]

It can be concluded that, there is an obvious decreased pulmonary function in the diabetic group. Because of no significant change in the FEV1/FVC ratio, this decrease in the capacity is assumed to be alarming. To confirm the extent of danger in relation to the decreased capacity, plethysmography should be performed. In this study, there was a significant association between spirometric indices-related disorders and increased BMI or the type of treatment. According to the mild to moderate association between the decrease in the spirometric indices and the increase in the glycosylated hemoglobin, it can be concluded that, there was a direct association between uncontrolled diabetes and pulmonary function disorder.

Patients lack of awareness about their duration of disease could be considered as the first limitations of this study, so there was no possibility to assess the relationship between the duration of the disease and severity of the spirometrical disturbances. The use of spirometer instead of plethysmograph was the second limitation, as it is able to measure more volume-related indices such as total lung capacity and is also able to confirm the diagnosis of restrictive diseases, highlighting the need for further studies. Considering incompatible results of different studies, further prospective studies with greater sample size are required. In the future studies, the measurement of concentration of glycosylated hemoglobin and spirometric indices should be repeated at particular intervals and they should be compared with each other. So, it can be concluded that, the lung is a target organ in diabetes and hyperglycemia is a potential determinant in the decreased pulmonary function in diabetic patients. Therefore, monitoring the concentration of blood sugar can improve respiratory function. As reported in the study by Aprana et al., decreased lung capacity is an early manifestation of diabetes and can be easily diagnosed by examining the pulmonary function. Therefore, performing the pulmonary function test along with other routine tests and examinations is highly recommended.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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