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Research Paper

The Relationship Between Diabetic Peripheral Neuropathy and Pulmonary Function Tests

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ABSTRACT

Background and Aim: Diabetes mellitus (DM) is a systemic disease with complications in the cardiovascular system, nerves, eyes, and kidneys. The potential targeting of the lung as an organ in diabetes is suggested by the rich pulmonary microvascular circulation and ample connective tissue present. This study aims to assess the relationship between pulmonary function tests and diabetic peripheral neuropathy in patients with type 2 DM.

Materials and Methods: One hundred patients were included in the study. Michigan neuropathy screening instrument (MNSI) was used to evaluate diabetic peripheral neuropathy in all patients. Based on the results of the MNSI, patients were divided into two groups, 50 diabetic subjects without neuropathy and 50 subjects with neuropathy. Also, a flow-sensitive spirometer was used to evaluate the pulmonary function test (PFT) for all subjects. All the pulmonary function parameters were measured as a percentage of predicted value. In addition, according to hemoglobin A1c (HbA1c) level, patients were divided to three groups (group 1≤7%, group 2=7%-9%, group 3≥9%).

Results: No significant difference was observed between the two groups with and without diabetic neuropathy in terms of PFTs, but in subjects with diabetic peripheral neuropathy, a significant reduction of forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) was observed in group 3 (HbA1c>9) compared to groups 1 (HbA1c<7).

Conclusion: This study does not show a significant reduction in pulmonary function in patients with type-2 DM with neuropathy compared to those without neuropathy. However, a significant difference was observed in FVC, FEV1, and forced expiratory flow (FEF)25-75 based on HBA1C level in subjects with neuropathy.

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Introduction

Diabetes mellitus (DM), a systemic disease, triggers secondary pathophysiological alterations in various organ systems. The resulting complications significantly contribute to the disease's morbidity and mortality [1]. These complications, including the heart, kidney, eyes and central nervous systems, are on the rise, posing considerable economic and social burdens. The origin of diabetic complications remains debated, involving both microangiopathic processes and non-enzymatic glycosylation of tissue proteins at elevated glucose levels [1, 2]. Biochemical processes lead to impaired collagen and elastin cross-linkage, reducing the strength and elasticity of connective tissue. Microvascular and macrovascular complications result in the thickening of the basement membrane, endothelium, and epithelium [1, 3, 4]. Common microvascular complications include neuropathy, nephropathy, and retinopathy. Studies suggest that diabetes may impact lung function, with changes in elastic recoil, chronic inflammation, autonomic neuropathy, and microangiopathy of alveolar capillaries contributing to pulmonary dysfunction [5]. Despite this, pulmonary complications in diabetic individuals may be clinically underdiagnosed. Glycemic control reflects long-term glycemic status, correlating with the degree of non-enzymatic glycosylation and microangiopathic complications [6-9]. However, pulmonary complications in the Iranian diabetic population remain inadequately characterized, this study was conducted to assess lung function in type 2 DM.

Material and Methods

This cross-sectional and retrospective study was conducted in the diabetic outpatient department, from August to September 2015 to assess pulmonary function in people with type 2 diabetes.

A total of 130 type 2 DM cases were selected from patients attending the diabetic clinic outpatient department of Qom University of Medical Sciences. Among them, 100 patients were included following inclusion and exclusion criteria, and the two groups were compared, 50 diabetic patients with peripheral neuropathy and 50 without peripheral neuropathy. Age and sex group matched among them. The approval of the Institutional Ethical Committee was obtained from Qom University of Medical Sciences.

The inclusion criteria included a fasting blood glucose level of 126 mg/dL or above (7.0 mmol/L), a non-fasting glucose level of 200 mg/dL or above (11.1 mmol/L), and current use of anti-diabetic medications.

Neuropathy, as defined by the Michigan neuropathy screening instrument (MNSI), involves two distinct evaluations. The first is a 15-item self-administered questionnaire, with abnormal responses summed for scoring. The second entails a lower extremity examination, including inspection, assessment of vibratory sensation, and ankle reflexes, scored based on points assigned for abnormal findings [10].

The exclusion criteria included any condition affecting the lung functions, a history of chronic or recent respiratory infections, gross abnormalities of the vertebral column or thoracic cage, malignancy and cardiopulmonary disease, neuromuscular disease, and those undergoing major chest or abdominal surgeries. All subjects had no history of severe osteoarthritis, connective tissue disorder, autoimmune disease, and renal or hepatic disease.

Spirometry

Subjects' height and weight were measured, and their smoking history (self-reported) was considered. Pulmonary function parameters were assessed using an electronic spirometer (Model-Spirolab class 2), following the standards set by the American Thoracic Society/European Respiratory Society (ATS/ERS) [11]. The pulmonary function report incorporated age, sex, weight, height, and smoking status. Standard spirometric measures included forced expiratory volume in one second (FEV1), forced vital capacity (FVC), forced expiratory flow rates (FEF 25%, FEF 50%, FEF 75%, and FEF 25%-75%), the ratio of FEV1 to FVC (FEV1/FVC), and peak expiratory flow rate (PEFR). These pulmonary function variables were recorded as a percentage of the predicted normal value based on reported height and age [11].

We categorized patients into three groups based on hemoglobin A1c (HBA1c) levels, <7%, between 7 to 9, and >9%, to assess the relationship between diabetes control and spirometric measures.

Statistical analysis

Data were analyzed using SPSS software, version 23. The $P<0.05$ was considered significant.

Results

In this study, pulmonary function tests (PFTs) were performed on diabetic patients in two groups, diabetic people with peripheral neuropathy and diabetic people without peripheral neuropathy to assess the relationship of pulmonary function parameters changes with neuropathy as one of the common microvascular complications of diabetes.

Fifty subjects with peripheral neuropathy compared to 50 subjects without peripheral neuropathy existed. Two groups have been matched according to age, and gender. No statistically significant difference was observed in baseline characteristics (height, body mass index (BMI), and HBA1c) for participants (Table 1). Duration of diabetes was significantly longer in the group with diabetic peripheral neuropathy at 11.86±6.55 vs 8.38±5.09 in the group without neuropathy (P<0.05).

Table 2 presents the pulmonary function parameters of two groups. No statistically significant difference was observed in the PFT parameter (FEV1, FVC, FEV1/FVC, FEF 25-75, and PEFR) among the two groups. This conclusion was also observed after adjusting for age, gender, height, HBA1c and duration of diabetes in a general linear model.

The results of analysis of variance (ANOVA) test between three groups according to HBA1c level showed no significant difference in PFT parameters among them (Table 3). However, in the neuropathic group, the ANOVA test showed a significant difference of FVC, and FEV1 in group 1 (HBA1c <7) compared to group 3 (HBA1c >9). This result was not observed in subjects without diabetic peripheral neuropathy (P>0.05).

Table 1. Basic characteristics of patients in two groups (n=50)

Parameters	Mean±SD		P
	With Neuropathy	Without Neuropathy	
Age (y)	54.36±8.086	51.46±8.343	0.077
BMI (kg/m^2)	29.91±13.343	28.86±17.548	0.254
Height (cm)	160.64±10.915	161.64±10.036	0.497
Weight (kg)	76.74±5.503	75.35±5.178	0.657
Duration of diabetes (y)	11.86±6.55	8.38±5.09	0.007*
FBS (mg/dL)	173.10±79.98	164.82±61.15	0.858
HBA1C	8.76±2.018	8.21±1.835	0.172

*Significant.

Table 2. The relationship between pulmonary function test parameters and diabetic neuropathy (n=50)

Pulmonary Function Tests (% of Predicted)	Mean±SD		P
	With Neuropathy	Without Neuropathy	
FVC (L)	94.02±16.930	92.74±15.257	0.692
FEV1 (L)	99.28±18.069	96.04±15.329	0.336
FEV1/FVC (L)	110.88±7.80	108.94±6.056	0.168
PEF (L)	77.16±19.966	78.06±26.314	0.780
FEF25-75 (L)	98.40±26.653	93.62±28.557	0.229

Abbreviations: FVC: Forced vital capacity; FEV1: Forced expiratory volume in one second; PEF: Peak expiratory flow; FEF25: Forced expiratory flow.

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Table 3. The relationship between pulmonary function tests parameters and HBA1c level in diabetic patients

Pulmonary Function Tests Parameters (% of Predicted)	Mean±SD			P
	HBA1c Level (%)			
	Group-a (<7)	Group-b (7-9)	Group-c (>9)	
FVC (L)	97.10±18.538	93.76±15.542	90.85±15.235	0.40
FEV1 (L)	102.25±18.424	97.47±15.108	95.67±18.204	0.392
FEV1/FVC (L)	110.5±8.382	109.53±6.686	110.70±6.706	0.783
PEF (L)	80.30±19.377	77.87±18.621	76.60±31.339	0.861
FEFE25-75 (L)	102.65±27.921	93.18±21.775	99.07±34.811	0.401

Abbreviations: FVC: Forced vital capacity; FEV1: Forced expiratory volume in one second; PEF: Peak expiratory flow; FEF25: Forced expiratory flow, HBA1c: Hemoglobin A1c.

Table 4. Linear regression model to assess correlation of pft with HbA1c level

Pulmonary Function Tests Parameters (% of Predicted)	Beta	SE	P
FVC (L)	-0.295	3.269	0.041*
FEV1 (L)	-0.337	3.697	0.027*
FEV1/FVC (L)	-0.120	1.626	0.428
PEF (L)	-0.252	4.353	0.120
FEFE25-75 (L)	-0.339	5.488	0.026*

Abbreviations: FVC: Forced vital capacity; FEV1: Forced expiratory volume in one second; PEF: Peak expiratory flow; FEF25: Forced expiratory flow, HBA1c: Hemoglobin A1c, SE: Standard erorr.

*Significant.

Also, the linear regression model showed the relationship between FVC, FEV1 and FEFE25-75 and HBA1c level after adjustment for age, gender, height and duration of diabetes (Table 4).

Discussion

The present study was conducted to investigate the hypothesis that pulmonary function impairment in diabetic people has a similar background with other microvascular complications such as neuropathy. The meta-analysis by Van den Borst et al. showed that diabetes is associated with a modest, albeit statistically significant, impaired pulmonary function in a restrictive pattern [12].

The exact pathophysiology behind reduced lung functions in individuals with diabetes remains unclear, but some reported histopathological changes include basal lamina thickening [4] and fibrosis [13]. The impaired lung function in diabetic patients is thought to be caused by biochemical alterations in lung connective tissue, particularly involving collagen and elastin, as well as microangiopathy induced by chronic hyperglycemia's nonenzymatic glycosylation of proteins [3, 13-15]. Clinically, these changes lead to reduced elastic recoil of the lung, decreased lung volumes, and compromised pulmonary capacity for carbon monoxide diffusion [16]. Structurally, observed thickening of the alveolar epithelial basal lamina and specific nodular fibrosis of the lung are observed [13]. Additionally, one study suggested that autonomic and phrenic neuropathy may contribute to alterations in bronchial reactivity and respiratory muscle function [17].

To our knowledge, a few studies explain the relationship between microvascular complications with pulmonary functions in diabetic' patients, especially in Iranian people. Shafiee et al. demonstrated that individuals with diabetes experienced compromised pulmonary function. Additionally, the advancement of diabetic nephropathy to later stages was linked to a greater decline in pulmonary function [18]. Various clinical studies indicated an inverse correlation between pulmonary function parameters in individuals with diabetes and factors, such as glycemic control, diabetes duration, and its severity. Other potential contributing factors include age, sex, and genetic influences [19].

In one study [20], the authors showed the relationship between glycemic control (HBA1c) and pulmonary function parameters. A decrease in the percent of FEV1, FVC, FEF25-75, PEFR, DL/VA, and diffusing capacity of the lungs for carbon monoxide (DLCO) also an increase in FEV1/FVC% was showed with an increase in the level of HBA1c. Agarwal et al. showed that a significant reduction of diffusion capacity for alveolar volume (%DL/VA) was corrected in diabetic patients with microangiopathies. Also, they found no differences among the three groups for other PFTs [20]. In addition, Sinha et al. [21], in a study showed a negative correlation between DLCO and HBA1c level, and they showed that with deterioration of glycemic control, lung function parameters decreased. They found no difference in other PFTs. Two other studies [20, 21] have observed a correlation between diffusing capacity but spirometric values did not differ in type-2 diabetes patients.

In some studies, it has been shown that in diabetic patients, the pulmonary and other organ systems share a similar microangiopathic background. Previous studies showed that in diabetic people with microvascular complications peak expiratory flow rate is decreased compared to those without microvascular complications [22-25]. In the current study, the results are consistent with the study of Agarwal et al. and Sinha et al. [20, 21]; no statistically significance alteration of PFTs was associated with neuropathy as a microvascular complication but in the study of Shafiee [18], it showed the relationship of pulmonary function impairment with the progression of diabetic nephropathy. Our study showed no relationship between lung function parameters with glycemic control (HBA1c) contrary to the study conducted by Agarwal et al. and Sinha et al. [20, 21].

This study had some limitations, including the use of a small sample size that limited the power of the study to firm the results, not accomplishing diffuse lung capacity for carbon monoxide in subjects of both groups and the detection of peripheral neuropathy only according to the MNSI.

Conclusion

This study does not show a significant reduction in pulmonary function in patients with type-2 DM with neuropathy as compared to those without neuropathy. However, no significant difference was observed in FVC, FEV1, and FEF25-75 based on HBA1C level in subjects with neuropathy.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed about the purpose of the research. They were also assured of the confidentiality of their information. Written consent was obtained from the patients.

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Authors' contributions

All authors participated equally in the design, execution, and writing of all parts of this research.

Conflict of interest

The authors declared no conflict of interest.

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