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Does Type 1 Diabetes Affect Pulmonary Function in Children?

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Abstract

Background: Diabetes mellitus type 1 (DM1) is a chronic autoimmune disease associated with micro- and macrovascular complications that may affect multiple organs, especially the kidneys and eyes. Its impact on the pulmonary system and pulmonary function is not clearly studied but is receiving attention in recent studies. In this study, we aimed to investigate the impact of DM1 on pulmonary function among children and young adolescents.

Methods: In this cross-sectional study, children and adolescents with type 1 diabetes mellitus underwent pulmonary function testing (PFT). Respiratory function parameters were compared in well-controlled vs. poorly controlled diabetic children.

Results: Our findings showed that pulmonary function in DM1 patients was generally within normal ranges, with no significant differences based on A1C levels, Diabetic ketoacidosis (DKA) frequency, or diabetes duration. A direct relationship was detected between weight Z-scores and both forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC) indices; however, this association was not statistically significant.

Conclusion: Normal FEV_1 and FVC levels indicate that DM1 does not significantly impair pulmonary function. Further studies with larger sample sizes and longitudinal investigations are suggested. So, we cannot suggest pulmonary function testing as a routine screening test for diabetic children.

Key Words: Child, Diabetic ketoacidosis, Diabetes mellitus, Pulmonary function tests, Type 1.

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1- INTRODUCTION

Diabetes mellitus type 1 (DM1) is a chronic autoimmune disorder that mostly affects children and young adults (1,2). Pathogenesis of DM1 is characterized by the destruction of pancreatic β-cells, resulting in absolute insulin deficiency and chronic hyperglycemia. While the systemic complications of DM1, including nephropathy, neuropathy, and retinopathy, are well-documented, its effect on pulmonary function is under investigation (1). Lungs have a collagen-rich extracellular matrix and a considerable microvascular network, so they can be considered a “target organ” in diabetes-related complications (3). Long-term exposure to high glucose levels may facilitate non-enzymatic glycation of proteins and collagen cross-linking in the alveolar and capillary walls, which may lead to reduced pulmonary compliance and restrictive patterns observed in pulmonary function tests (4, 5). Microangiopathy, a hallmark of diabetes complications, may impair gas exchange by affecting the pulmonary capillary network (6). Pulmonary function assessments, including forced expiratory volume in one second (FEV_1) and forced vital capacity (FVC), serve as non-invasive techniques frequently utilized to evaluate respiratory health (7, 8). This cross-sectional study evaluates lung function in young patients with DM1, addressing the insufficient data regarding its pulmonary effects in this demographic. This study aims to elucidate the relationships between pulmonary function test outcomes and clinical variables, such as hemoglobin A1C levels (HbA1C), duration of diabetes, and incidence of Diabetic ketoacidosis (DKA).

2- MATERIALS AND METHOD

This comparative cross-sectional study involved 56 children and adolescents with DM1 who were admitted to Akbar Children's Hospital, Mashhad University of Medical Sciences, Mashhad, Iran. Stratified random sampling was utilized to enhance generalizability and precision. Participants were categorized according to diabetes duration, HbA1c levels, age, and gender. The inclusion criteria consisted of a confirmed diagnosis of DM1 with a minimum duration of two years (since most hyperglycemia complications need time to evolve) and an age range of 6 to 18 years. Patients with other chronic diseases affecting pulmonary function, such as lung, heart, or chronic kidney disease, and patients without their parents' consent were excluded. Pulmonary function data were collected using spirometry (mechanical model, Pony FX/Digital Flowmeter), and pulmonary function indices, including FEV_1 and FVC, were evaluated and compared across groups categorized by diabetes duration, HbA1c levels, age, and gender. To assess glycemic management, HbA1c was measured. Other variables, including diabetes duration, age, and gender, were obtained from medical records and patient interviews. The patients' weights and heights were recorded on a Beurer digital scale and a Rasai standing height gauge. The review board of Mashhad University of Medical Sciences approved the study under code IR.MUMS.MEDICAL.REC.1401.436, and the children's parents filled out the informed consent form.

2-1. Statistical Analysis

Descriptive analysis was employed for the demographic characteristics of the patients, including mean age, HbA1c levels, diabetes duration, and pulmonary function indices such as FEV_1 and FVC. An independent t-test was used to analyze differences in mean pulmonary function across groups categorized by diabetes duration, HbA1c levels, age, and sex. Additionally, multiple linear regression analysis was conducted to assess the impact of independent variables on pulmonary function indices. Pearson's correlation test evaluated the association

between Z-score and pulmonary function indices.

3- RESULTS

Altogether, 56 patients with DM1 were enrolled, including 31 males and 25 females, aged 6 to 18. Table 1 summarizes pulmonary function indices by patient demographic factors.

Table-1. Demographic and clinical characteristics of patients based on gender.

Feature	Sub groups	Sample size	Age (Years, Mean±SD)	A1C (%, Mean±SD)	Diabetes Duration (Years, Mean±SD)	FEV_1 (% Pred, Mean±SD) Min, Max (%)	FVC (% Pred, Mean±SD) Min, Max (%)	p-value* (FEV_1)	p-value* (FVC)
Gender	Male	31	9.9 ± 2.2	7.9 ±1.3	4.3 ±1.8	93.7 ±17.2 (62, 125)	98.4 ±17.6 (58, 134)	0.286	0.366
	Female	25	11.0 ±2.5	8.3 ±1.5	4.8 ±2.3	88.8 ±16.7 (53,130)	94.1 ±17.5 (69, 149)		

Note: * Independent-t test;
Abbreviations: A1C: Hemoglobin A1C, **FEV_1:** Forced expiratory volume, **Pred:** Predicted, **FVC:** Forced vital capacity, **Min:** Minimum, **Max:** Maximum

Tables 2 and 3 compare pulmonary function indices by gender, diabetes duration, HbA1C levels, DKA frequency, and age range.

Table-2. Comparison of pulmonary function based on gender, diabetes duration, HbA1C levels, and DKA frequency.

Variables	subgroups	Gender	Number	FEV_1 (% Pred, Mean±SD)	FVC (% Pred, Mean±SD)	p-value * (FEV_1)	p-value * (FVC)
Diabetes duration	< 5 years	Male	18	93.6 ± 16.4	97.2 ± 19.1	0.196	0.33
		Female	13	82.5 ± 18.0	90.8 ± 19.7		
	≥ 5 years	Male	13	94.0 ± 18.9	100.2 ± 15.8		
		Female	12	95.7 ± 12.5	97.8 ± 14.7		
A1C Level	< 7.5%	Male	13	97.8 ± 17.1	101.1 ± 17.2	0.569	0.582
		Female	10	87.1 ± 16.7	94.1 ± 16.3		
	≥ 7.5%	Male	18	90.8 ± 17.1	96.5 ± 18.1		
		Female	15	90.0 ± 17.2	94.1 ± 18.9		
DKA frequency	≤ 1 episode	Male	19	95.8 ± 17.0	100.6 ± 15.6	0.268	0.169
		Female	10	90.6 ± 16.1	97.9 ± 16.1		
	≥ 2 episodes	Male	12	90.5 ± 17.6	95 ± 20.6		
		Female	15	87.7 ± 17.5	91.6 ± 19.3		

Note : * Independent-t test;
Abbreviations: FEV_1: Forced expiratory volume, **Pred:** Predicted, **FVC:** Forced vital capacity, **A1C:** Hemoglobin A1C, **DKA:** Diabetic ketoacidosis

Table-3. Comparison of pulmonary function indices based on age range and gender.

Gender	Age range	Number	FEV_1 (% Pred, Mean±SD)	FVC (% Pred, Mean±SD)	p-value* (FEV_1)	p-value * (FVC)
Male	6-10 years	20	92.1 ± 18.2	97.1 ± 20.0	0.482	0.582
	11-18 years	11	96.7 ± 15.5	100.8 ± 12.5		
Female	6-10 years	11	83.1 ± 19.1	92.7 ± 21.0	0.129	0.732
	11-18 years	14	93.4 ± 13.6	95.2 ± 14.9		

Note : * Independent-t test;
Abbreviations: FEV_1: Forced expiratory volume, **Pred:** Predicted, **FVC:** Forced vital capacity

3-1. Comparison of FEV_1/FVC

The ratio of FEV_1/FVC is essential for diagnosing pulmonary conditions. If FEV_1/FVC is below 0.7, obstruction can be considered (10). Using the Multiple Linear Regression test, the FEV_1/FVC ratio results were not associated with clinical variables such as HbA1C levels, DKA frequency, or the duration of diabetes in patients with DM1 ($p > 0.05$). Therefore, pulmonary function is typically preserved in this population regardless of these diabetes-related factors. The mean FEV_1/FVC ratio for male and female patients was 95% with a standard deviation of 7.05 for males and 8.6 for females, suggesting no significant gender differences in pulmonary function indices.

3-2. Comparison of Z-score

The Z-score for weight was calculated for every patient relative to the overall mean. The weight Z-scores within the range of -2 to +2 were classified as "normal," while values outside this range were categorized as "abnormal." The Pearson's correlation test was conducted to investigate a potential relationship between weight Z-scores and pulmonary indices. The results indicated a direct relationship between weight Z-scores and both FEV_1 and FVC indices; however, this association was not statistically significant. The distribution of patients by Z-score category based on gender showed abnormal Z-scores in only two men; however, 25 females and 29 males were within the normal range. The findings showed that most patients are within the normal range, with a smaller proportion classified as abnormal. This distribution suggests that most patients have relatively balanced weights compared to the population means. Table 4 shows the analysis of Z-scores in relation to pulmonary indices.

Table-4. Analysis of pulmonary function test Z-scores in relation to pulmonary indices.

Parameter	Subcategory	Correlation coefficient*	p-value
Correlation with Z-Score	FEV_1 (% Predicted)	0.008	0.952
	FVC (% Predicted)	-0.057	0.674

* Pearson's correlation test

4- DISCUSSION

DM1 is a chronic autoimmune disease resulting in several systemic complications, including DKA, neuropathy, nephropathy, retinopathy, cognitive impairment, atherosclerosis, and cardiovascular diseases (11). The population diagnosed with diabetes is expected to surge to 643 million by 2030 and 783 million by 2045, resulting in adverse effects on the health and financial condition of individuals, families, and nations (2). In the present study, the pulmonary function indices (FEV_1, FVC, FEV_1/FVC) were assessed among DM1 patients aged 6-18, and findings showed preserved pulmonary function in these patients. Demographic and diabetes-associated factors, including age, gender, diabetes duration, HbA1C levels, and DKA frequency, were not associated with FEV_1, FVC, and FEV_1/FVC. Also, the weight distribution of participants was mainly within normal ranges without considerable impact on pulmonary outcomes. Similarly, Benbassat et al. (8) found no significant pulmonary dysfunction in DM1 patients aged 48 ± 13 years using spirometry values. Also, Boulbou et al. (12) found preserved FEV_1/FVC but reduced pulmonary diffusion capacity and decreased total lung capacity (TLC), indicating a restrictive lung pattern in DM1 patients. In 2010, van den Borst et al. (7) showed decreased pulmonary function in DM1 patients associated with a longer duration of DM1. They hypothesized that chronic hyperglycemia can result in structural

changes, including collagen cross-linking in alveolar walls and non-enzymatic glycation of proteins. These changes could lead to restrictive pulmonary patterns. The lack of these findings in the present study may be correlated with its emphasis on younger patients, who probably have not experienced chronic hyperglycemia for a long time. The present study showed no significant relation between HbA1C levels and pulmonary indices. In contrast, a population-based study by Zhang et al. (13) reported a considerable relationship between glycemic control and pulmonary function. Also, Klein et al. (6) found that poor glycemic control leads to reduced pulmonary function. These different results probably arise from variations in demographic characteristics, glycemic management, and type of DM. Additionally, younger DM1 patients, like those included in this study, might receive stricter glucose monitoring, reducing the likelihood of pulmonary complications. The current study showed no significant correlation between diabetes duration and pulmonary function indices; however, longer disease duration contributes to microvascular complications, including in the pulmonary capillary network. Yang, et al. (5) reported that the thickness of the alveolar basal lamina is higher in diabetes patients with longer disease duration, but this thickening of the basal lamina was not statistically correlated with the duration of diabetes. In contrast, Anık et al. (14) demonstrated that pulmonary function decline is associated considerably with diabetes duration in children with DM1. However, Frías et al. (15) detected a subtle reduction in pulmonary function in the pediatric group with DM1 compared to controls, which was not associated with glycemic control and diabetes duration. In this study, the younger patients, with a mean age of about 10 years and a relatively short mean disease duration of around 4.5 years, may account for the absence of significant findings. Minor differences in FEV_1 and FVC measurements were observed between males and females, with males showing slightly higher values. This finding is consistent with physiological norms, as males typically have larger lung volumes than females of the same age (16). However, these differences were not statistically significant, aligning with population studies, such as those by Torén et al. (10), which indicate that similar trends are attributed to anthropometric factors rather than pathological ones. Our study explored the effect of weight Z-scores on pulmonary function indices. However, no significant relationship was detected between weight and pulmonary indices. The weight Z-scores of most patients were within the normal range, indicating balanced weight relative to the population mean. This finding shows that normal weight variations could minimally impact lung function among non-obese pediatric populations. A meta-analysis by Díez-Manglano et al. (17) reported that DM1 is linked to decreased pulmonary function. Still, this association was independent of age, gender, body mass index, geographical region, and smoking. The present study's limitations included a limited sample size, the absence of longitudinal data, and a lack of information on exercise status and lifestyle.

5- CONCLUSION

In the present study, pulmonary function was mainly preserved in pediatric patients with DM1. While this finding is consistent with some previous research, there are discrepancies in the literature indicating that prolonged diabetes duration and poor glycemic control may result in considerable deficits. Therefore, longitudinal studies with larger sample sizes are recommended to consider the long-term effects of DM1 on pulmonary health. Future studies should explore the impacts of environmental and genetic

factors, comorbidities, lifestyle, and exercise status on the incidence of pulmonary conditions in patients with DM1.

6- ABBREVIATIONS

DM1: Diabetes Mellitus Type 1; **FEV_1:** Forced Expiratory Volume in 1 second; **FVC:** Forced Vital Capacity; **HbA1C:** Hemoglobin A1C; **DKA:** Diabetic Ketoacidosis; **PFTs:** Pulmonary Function Tests; **TLC:** Total Lung Capacity.

7- ACKNOWLEDGMENT

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8- CONFLICT OF INTEREST

No conflict of interest.

9- FUNDING

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10- AVAILABILITY OF DATA AND MATERIALS

The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

11- ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This study was performed in line with the principles of the Declaration of Helsinki. The review board of Mashhad University of Medical Sciences approved the study under code IR.MUMS.MEDICAL.REC.1401.436, and the children's parents filled out the informed consent form.

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