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Effect Of Type 2 Diabetes Mellitus on the Pulmonary Functions of the Patient and Their Association with Glycemic Control at Tertiary Care Institute of Northern India

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KEYWORDS

Type 2 diabetes mellitus, pulmonary function tests, glycemic control, HbA1c, spirometry, restrictive pattern

ABSTRACT:

Background: Type 2 diabetes mellitus (T2DM) is a systemic metabolic disorder associated with chronic hyperglycemia that affects multiple organ systems. The lungs, though not classically recognized as a target organ, may exhibit functional impairments due to microvascular damage and non-enzymatic glycation of connective tissue. This study aimed to evaluate the correlation between glycemic control and pulmonary function tests (PFTs) in T2DM patients.

Objectives: To assess pulmonary function parameters in patients with T2DM and to correlate these findings with glycemic control as measured by glycated hemoglobin (HbA1c).

Materials and Methods: A cross-sectional study was conducted involving 100 T2DM patients attending the outpatient department of a tertiary care hospital. Pulmonary function was assessed using spirometry, recording Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 second (FEV_1), FEV_1/FVC ratio, Peak Expiratory Flow Rate (PEFR), and Forced Expiratory Flow 25–75% ($FEF_{25–75}$%). Glycemic control was evaluated through HbA1c levels. Patients were categorized into good (HbA1c ≤7%) and poor (HbA1c >7%) glycemic control groups.

Results: A statistically significant reduction in FVC, FEV_1, PEFR, and $FEF_{25–75}$% was observed in patients with poor glycemic control compared to those with good control ($p < 0.05$). The most common pattern observed was a restrictive ventilatory defect. A negative correlation was found between HbA1c levels and pulmonary function parameters, indicating worsening lung function with increasing glycemic levels.

Conclusion: Pulmonary function is significantly impaired in T2DM patients, especially among those with poor glycemic control. Routine pulmonary function testing may be beneficial in the early detection of subclinical lung involvement in diabetic patients.

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INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder characterized by persistent hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Among its two main forms, Type 2 Diabetes Mellitus (T2DM) accounts for over 90% of diabetes cases globally and is primarily associated with insulin resistance and relative insulin deficiency [1]. India ranks among the top countries with the highest number of diabetic individuals, with prevalence estimates expected to rise significantly due to changing lifestyles, urbanization, and aging populations [2].

Although the classical complications of diabetes involve the microvascular (retinopathy, nephropathy, and neuropathy) and macrovascular (coronary artery disease, stroke, and peripheral arterial disease) systems, emerging evidence suggests that pulmonary dysfunction is a significant yet underrecognized complication of diabetes [3]. The lungs, owing to their vast microvascular network and connective tissue matrix, may become susceptible to chronic hyperglycemia-induced damage through mechanisms such as non-enzymatic glycation of proteins, oxidative stress, and low-grade inflammation [4,5].

Recent studies have demonstrated that diabetic patients, particularly those with poor glycemic control, show reduced values of pulmonary function test (PFT) parameters such as Forced Vital Capacity (FVC), Forced Expiratory Volume in 1 Second (FEV1), and Forced Expiratory Flow rates [6,7]. These alterations are often subtle and may be overlooked during routine clinical care. Notably, the pattern of lung dysfunction in diabetes has been reported to be predominantly restrictive or a mixed restrictive-obstructive type [8].

Glycemic control, typically assessed via glycated hemoglobin (HbA1c), is a critical determinant of long-term complications in diabetes. Evidence suggests that poor glycemic control may accelerate the decline in pulmonary function by perpetuating endothelial dysfunction, capillary basement membrane thickening, and fibrotic changes in the alveolar interstitium [9,10].

Given the increasing burden of diabetes in the Indian population and the potential impact of pulmonary dysfunction on morbidity, especially in older adults, the evaluation of lung function in diabetic patients becomes imperative. However, there is a scarcity of data in the Indian context, particularly exploring the correlation of pulmonary function parameters with glycemic indices such as HbA1c, FBS, and PPBS. Hence, this study aims to evaluate the pulmonary function in T2DM patients and examine its association with glycemic control at a tertiary care institute in Northern India.

MATERIALS AND METHODS

Study Design and Setting

This was a case-control study conducted at the Department of Medicine in collaboration with the Pulmonary Function Testing Laboratory, IIMSR. The study was carried out over a period of 18 months, from March 2023 to October 2024.

Sample Size Calculation

The required sample size was determined using the following formula:

n=(r+1r)σ2(Zβ+Zα/2)2(d)2n = \left(\frac{r + 1}{r} \right) \frac{\sigma^2 (Z_{\beta} + Z_{\alpha/2})^2}{(d)^2}n=(rr+1)(d)2σ2(Zβ+Zα/2)2

Where:

- Zβ=0.842Z_{\beta} = 0.842Zβ=0.842 (Power = 80%)
- Zα/2=1.96Z_{\alpha/2} = 1.96Zα/2=1.96 (Type I error = 5%)
- σ=1.36\sigma = 1.36σ=1.36 (Standard deviation)
- d=0.3d = 0.3d=0.3 (Expected effect size)
- r=1r = 1r=1 (equal group size ratio)

Based on this, the calculated sample size was 60 in each group, with a total of 120 participants.

Study Population

A total of 120 participants were enrolled and categorized into three groups:

- Group A: Type 2 diabetic patients with good glycemic control (HbA1c 6.5%–7%)

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- Group B: Type 2 diabetic patients with poor glycemic control (HbA1c >7%)
- Group C: Non-diabetic healthy controls (HbA1c <6.5%)

Inclusion Criteria

- Cases: Diagnosed cases of Type 2 diabetes mellitus for more than 1 year with HbA1c >6.5%
- Controls: Individuals with no history of diabetes and HbA1c <6.5%

Exclusion Criteria

- History of smoking
- Occupational exposure affecting lung function
- Known neuromuscular diseases (e.g., Myasthenia Gravis, ALS, Multiple Sclerosis)
- Cardiovascular conditions (e.g., ACS, heart failure, cardiomyopathy, valvular heart disease, HOCM)
- End-stage kidney disease
- Physical deformities affecting lung function (e.g., kyphoscoliosis, pectus excavatum or carinatum)
- Obesity (BMI >30 kg/m²)
- Contraindications for spirometry (e.g., recent myocardial infarction, pneumothorax, hemoptysis of unknown cause, recent eye/thoracic/abdominal surgery, acute illness)
- Refusal to provide written informed consent

Data Collection Methodology

Demographic and Clinical Assessment

The following parameters were recorded:

- Age, sex, weight, height, and BMI
- Detailed history including diabetes duration, comorbidities (e.g., hypertension, dyslipidemia), and current medications
- Complete physical examination

Biochemical Investigations

Blood samples were collected under aseptic conditions to evaluate:

- Fasting Blood Glucose (FBS)
- Postprandial Blood Sugar (PPBS)
- Glycated Hemoglobin (HbA1c)
- Lipid profile (Total Cholesterol, HDL, LDL, Triglycerides)
- Renal function tests (Serum Creatinine)

All biochemical analyses were conducted at the Central Laboratory, IIMSR, using standardized protocols and calibrated instruments.

Pulmonary Function Testing (PFT)

Pulmonary function was assessed using a Computerized Spirometer (PulmOne Minibox +) as per the American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines.

The following parameters were measured:

- Forced Vital Capacity (FVC)
- Forced Expiratory Volume in 1 Second (FEV1)
- FEV1/FVC Ratio
- Peak Expiratory Flow Rate (PEFR)
- Forced Expiratory Flow at 25–75% of FVC (FEF25–75%)

Each subject performed a minimum of three acceptable and repeatable efforts. The best values were used for analysis. The results were expressed as absolute values and as percentages of predicted values based on age, sex, and height. All tests were performed by trained personnel using a standardized protocol to minimize observer variability.

Ethical Considerations

The study was conducted in accordance with the ethical standards. Approval was obtained from the Institutional

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Ethics Committee, and written informed consent was acquired from all participants before enrolment.

Statistical Analysis

Data were recorded in Microsoft Excel and analyzed using SPSS version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages.

The statistical methods applied included:

- Mean: Calculated as the sum of all values divided by the number of observations.
- Standard Deviation (SD):

$\sigma = \sqrt{\frac{\sum (X - \bar{X})^2}{n - 1}}$ $\sigma = \sqrt{\frac{\sum (X - \bar{X})^2}{n - 1}}$

- Chi-square (χ^2) test: Used for comparison of categorical variables.
- Analysis of Variance (ANOVA): Used to compare means among more than two groups. The F-ratio was interpreted to assess inter-group variation.

Level of Significance

- $p > 0.05$: Not significant
- $p < 0.05$: Statistically significant
- $p < 0.01$: Highly significant
- $p < 0.001$: Very highly significant

RESULTS AND OBSERVATION;

Table 1: Age-wise Distribution of Glycemic Uncontrolled Cases, Glycemic Controlled Cases, and Controls

AGE	Glycemic Uncontrolled Cases (n=30)		Glycemic controlled Cases(n=30)		CONTROL S (n=60)		P-VALUE
	N	%	N	%	N	%	
40-49	16	53.33%	14	46.67%	39	65.00%	X=3.035 p=0.2193
50-60	14	46.67%	16	53.33%	21	35.00%	
Grand Total	30	100.00 %	30	100.00%	60	100.00 %	
MEAN±S D	48.83±5.40		49.90±6.21		48.77±6.76		F=0.3489 p=0.7062

The age group of 40-49 years comprises 53.33% of the glycemic uncontrolled cases, 46.67% of the glycemic controlled cases, and 65.00% of the control group, whereas the 50-60 years age group includes 46.67%, 53.33%, and 35.00%, respectively. The chi-square test ($X^2=3.035$, $p=0.2193$) indicates no statistically significant association between age distribution and glycemic control status. Additionally, the mean age (±SD) for glycemic uncontrolled cases, glycemic controlled cases, and controls is 48.83±5.40, 49.90±6.21, and 48.77±6.76 years, respectively. The one-way ANOVA test ($F=0.3489$, $p=0.7062$) shows no significant difference in mean age among the three groups, suggesting that age distribution is comparable across all groups.

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Table: 2 Gender-wise Distribution of Glycemic Uncontrolled Cases, Glycemic Controlled Cases, and Controls

GENDER	Glycemic uncontrolled Cases (n=30)		Glycemic controlled Cases(n=30)		CONTROL S (n=60)		P- VALUE
	N	%	N	%	N	%	
FEMALE	18	60.00%	21	70.00%	33	55.00%	
MALE	12	40.00%	9	30.00%	27	45.00%	X=1.875 p=0.3916
Grand Total	30	100.00 %	30	100.00%	60	100.00 %	

Table: 3 Comparison of Glycemic Indices (HbA1c, FBS, and PPBS) Among Glycemic Uncontrolled Cases, Glycemic Controlled Cases, and Controls

GLYCEMI C INDEX	Glycemic uncontrolled Cases (n=30)		Glycemic controlled Cases(n=30)		CONTROLS (n=60)		P- VALUE
	MEAN	SD	MEAN	SD	MEA N	SD	
Hba1c	9.82	1.91	6.72	0.17	5.12	0.48	F=215 p<0.0001 *
FBS	173.97	26.04	120.03	13.99	94.95	8.39	F=247.8 p<0.0001 *
Ppbs	296.9	36.03	214.8	22.27	151.32	22.10	F=310.4 p<0.0001 *

The mean HbA1c levels are significantly higher in Glycemic uncontrolled cases (9.82±1.91) compared to Glycemic controlled cases (6.72±0.17) and controls (5.12±0.48), with a highly significant difference (F=215, p<0.0001*). Similarly, mean FBS is highest in Glycemic uncontrolled cases (173.97±26.04 mg/dL), followed by Glycemic controlled cases (120.03±13.99 mg/dL) and controls (94.95±8.39 mg/dL), with a statistically significant difference (F=247.8, p<0.0001*). PPBS also follows a similar trend, with the

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highest mean in Glycemic uncontrolled cases (296.9±36.03 mg/dL), followed by Glycemic controlled cases (214.8±22.27 mg/dL) and controls (151.32±22.10 mg/dL), showing a highly significant difference (F=310.4, p<0.0001*).

Table: 4 Comparison of Pulmonary Function Test Parameters Among Glycemic Uncontrolled Cases, Glycemic Controlled Cases, and Controls

PULMONARY FUNCTION TEST	Glycemic Uncontrolled Cases (n=30)		Glycemic Controlled Cases(n=30)		CONTROLS (n=60)		P- VALUE
	MEAN	SD	MEAN	SD	MEAN	SD	
Fev1/fvc	81.79	3.17	81.95	2.89	82.11	3.07	F=0.013 p=0.988
Fvc (in L)	1.84	0.41	2.98	0.33	3.35	0.39	F=121.435 p<0.0001*
Fev1 (in L)	2.23	0.37	3.12	0.34	3.39	0.32	F=116.401 p<0.0001*
Fef 25-75 (in L/sec)	1.69	0.70	3.25	0.45	3.59	0.33	F=99.518 p<0.0001*
PeF (in L/sec)	3.83	0.97	5.67	0.41	6.15	0.30	F=66.334 p<0.0001*
Fef (in L/sec)	3.53	0.88	5.11	0.38	5.79	0.30	F=81.194 p<0.0001*
Fef 50 (in L/sec)	2.28	0.84	4.09	0.41	4.66	0.43	F=81.194 p<0.0001*
Fef 75 (in L/sec)	0.64	0.37	1.21	0.34	1.68	0.29	F=155.136 p<0.0001*

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The FEV1/FVC ratio is similar across all groups (81.79±3.17 in uncontrolled, 81.95±2.89 in controlled, and 82.11±3.07 in controls) with no significant difference (F=0.013, p=0.988), suggesting preserved airway function. However, all other PFT parameters, including FVC, FEV1, FEF 25-75, PEF, FEF, FEF 50, and FEF 75, show significantly lower values in Glycemic uncontrolled cases compared to Glycemic controlled cases and controls, with highly significant p-values (p<0.0001). This indicates a marked impairment in lung volumes and expiratory flow rates in Glycemic uncontrolled patients. The progressive reduction in pulmonary function in diabetic patients, particularly those with poor Glycemic control, suggests a possible restrictive pattern and small airway dysfunction, reinforcing the impact of diabetes on pulmonary health

Table: 5 Distribution of Baseline Health Characteristics Among Glycemic Uncontrolled Cases, Glycemic Controlled Cases, and Controls

	Glycemic Uncontrolled Cases (n=30)		Glycemic Controlled Cases(n=30)		CONTRO LS (n=60)		P- VALU E
	N	%	N	%	N	%	
No neurological deficits	30	100.00%	30	100.00%	60	100.00 %	-
No cardiovascular abnormalities	30	100.00%	30	100.00%	60	100.00 %	-
No respiratory distress	30	100.00%	30	100.00%	60	100.00 %	-
Non-smoker/ non-alcohol	30	100.00%	30	100.00%	60	100.00 %	--
NO H/O Cardiovascular/ Respiratory Disease	30	100.00%	30	100.00%	60	100.00 %	

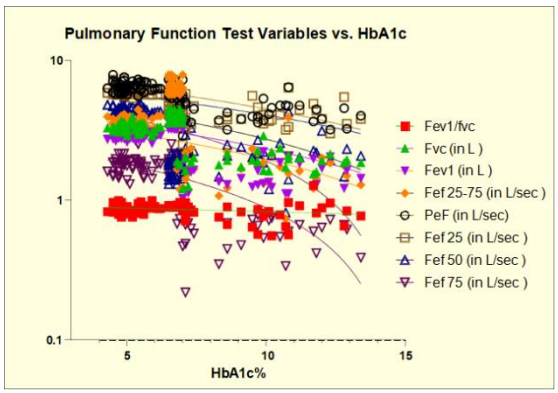

Figure: 1 Graphical representations of Correlation Between HbA1c Levels and Pulmonary Function Test Variables (Pearson Correlation Analysis)

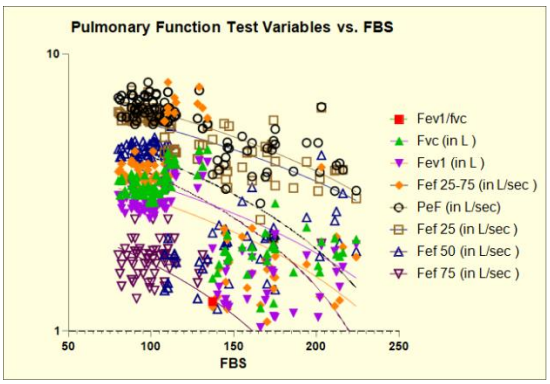

Figure 2: Graphical representations of the Correlation Between Fasting Blood Sugar (FBS) Levels and Pulmonary Function Test Variables (Pearson Correlation Analysis)

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Table: 6 Correlation Between Postprandial Blood Sugar (PPBS) Levels and Pulmonary Function Test Variables (Pearson Correlation Analysis)

		PPBS		
		R	95% CI	p-value
Pulmonary Function Test Variables	Fev1/fvc	-0.2009	-0.3669 to -0.02249	0.2789
	Fvc (in L)	-0.6117	-0.7128 to -0.4857	<0.0001*
	Fev1 (in L)	-0.5889	-0.6948 to -0.4580	<0.0001*
	Fef 25-75 (in L/sec)	-0.3728	-0.5175 to -0.2075	<0.0001*
	PeF (in L/sec)	-0.773	-0.8364 to -0.6893	<0.0001*
	Fef 25 (in L/sec)	-0.741	-0.8124 to -0.6479	<0.0001*
	Fef 50 (in L/sec)	-0.6814	-0.7670 to -0.5720	<0.0001*
	Fef 75 (in L/sec)	-0.7307	-0.8045 to -0.6345	<0.0001*

A strong negative correlation was observed between PPBS and PEF ($r = -0.773$; 95% CI: -0.8364 to -0.6893; $p < 0.0001$), followed closely by FEF 25 ($r = -0.741$), FEF 75 ($r = -0.7307$), and FEF 50 ($r = -0.6814$)—all statistically significant ($p < 0.0001$). This indicates a pronounced decline in small airway function and expiratory airflow with higher postprandial glucose levels. FVC ($r = -0.6117$) and FEV1 ($r = -0.5889$) also showed strong, statistically significant negative correlations ($p < 0.0001$), suggesting that higher PPBS is associated with reduced lung volumes and airflow capacity. A moderate negative correlation was noted with FEF 25–75 ($r = -0.3728$; $p < 0.0001$), reinforcing the impact of elevated blood sugar on small airway performance. In contrast, FEV1/FVC ratio exhibited a weak and statistically non-significant correlation with PPBS ($r = -0.2009$; 95% CI: -0.3669 to -0.02249; $p = 0.2789$). Overall, the findings suggest that elevated postprandial glucose levels are significantly associated with diminished pulmonary function—especially involving the small airways—while the FEV1/FVC ratio remains unaffected

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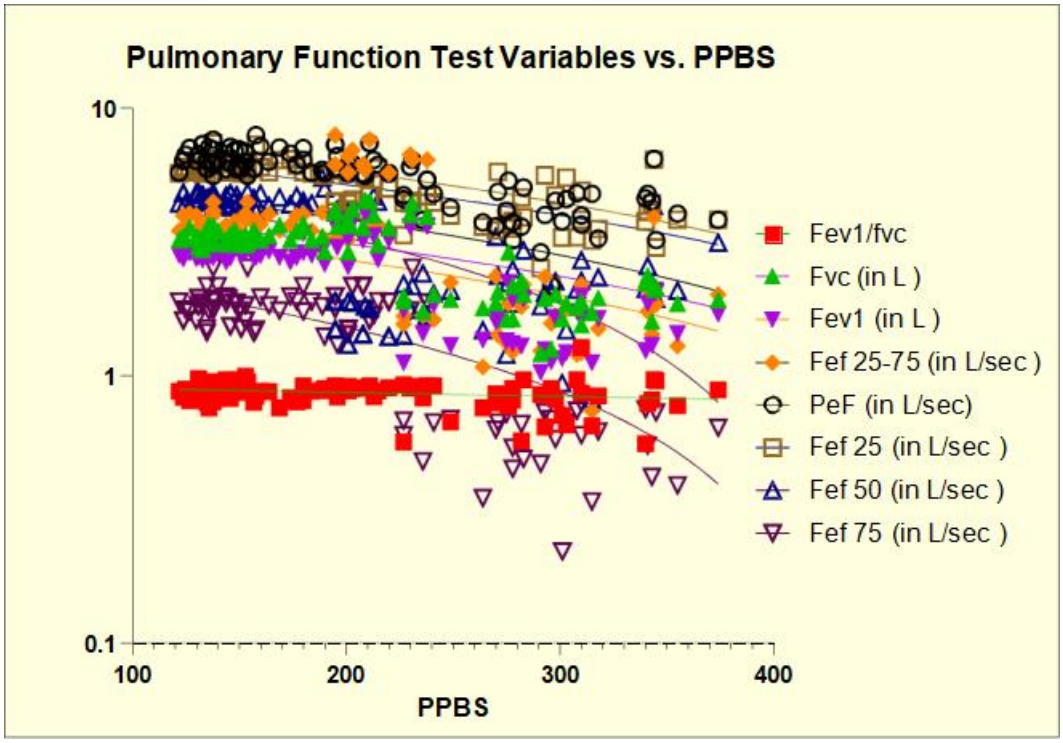

Figure 3: Graphical representation of the Correlation Between Postprandial Blood Sugar (PPBS) Levels and Pulmonary Function Test Variables (Pearson Correlation Analysis)

DISCUSSION

The present study investigated the correlation between glycemic control, as assessed by HbA1c levels, and pulmonary function parameters in patients with type 2 diabetes mellitus (T2DM). Our findings indicate a significant reduction in key pulmonary function test (PFT) parameters—namely Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), Peak Expiratory Flow Rate (PEFR), and forced mid-expiratory flows (FEF25–75%)—in T2DM patients compared to non-diabetic controls. These reductions were more pronounced in individuals with poor glycemic control (HbA1c >7%). However, the FEV_1/FVC ratio remained largely unchanged, suggesting a predominantly restrictive ventilatory defect rather than an obstructive one.

These observations align with existing literature, which supports the hypothesis that diabetes mellitus has a deleterious impact on lung function. Chronic hyperglycemia leads to non-enzymatic glycation of proteins, increased oxidative stress, and microvascular complications, all of which contribute to thickening of the alveolar-capillary basement membrane and loss of lung elasticity [1,2]. These histological alterations may reduce pulmonary compliance and lung volumes, manifesting clinically as reduced FVC and FEV_1.

Davis et al. in the Fremantle Diabetes Study reported significant reductions in FVC and FEV_1 among patients with type 2 diabetes, independent of smoking status, BMI, and other confounding variables [3]. In a meta-analysis by van den Borst et al., similar reductions in lung function were observed across multiple cohorts with diabetes, emphasizing the presence of a restrictive pattern of lung impairment [4].

In our study, the FEV_1/FVC ratio was preserved, indicating that the airflow limitation is not due to obstructive airway disease. This contrasts with conditions such as chronic obstructive pulmonary disease (COPD), where FEV_1 is disproportionately reduced relative to FVC, resulting in a decreased ratio. Our results reinforce the notion that diabetes predominantly affects lung parenchyma and the pulmonary vasculature rather than the airways.

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The mid-expiratory flow rates (FEF25–75%, FEF50%, and FEF75%) were significantly lower in patients with poor glycemic control. These values are sensitive markers of small airway involvement. Their reduction suggests that microvascular damage and early small airway disease may precede overt clinical symptoms, and may serve as early indicators of pulmonary involvement in T2DM [5].

We also observed a negative correlation between HbA1c levels and pulmonary function parameters, implying that poor glycemic control is associated with greater deterioration of lung function. Shah SH demonstrated a similar inverse relationship between lung volumes and glycemic indices, suggesting that chronic hyperglycemia accelerates pulmonary functional decline [6].

The mechanisms underlying this relationship may include:

- Non-enzymatic glycation of lung connective tissue proteins
- Microangiopathy affecting alveolar-capillary units
- Chronic low-grade inflammation and increased oxidative stress
- Autonomic neuropathy, potentially impairing respiratory muscle function [7,8]

Our study strengthens the evidence that the lung should be considered a target organ in diabetes, similar to the kidneys, retina, and peripheral nerves. Given the progressive and often subclinical nature of diabetic pulmonary dysfunction, routine PFT assessment in diabetic patients, especially those with poor glycemic control, may be a useful strategy for early detection and intervention.

Limitations

This was a cross-sectional study, so causal relationships cannot be firmly established. Lung diffusion capacity (DLCO), imaging, or histopathological confirmation of structural changes were not included. Additionally, the study did not assess the impact of duration of diabetes or presence of other microvascular complications. Longitudinal studies are warranted to establish temporal relationships and assess the reversibility of pulmonary changes with improved glycemic control.

CONCLUSION

The present study demonstrates a significant impairment in pulmonary function among patients with type 2 diabetes mellitus, particularly those with poor glycemic control (HbA1c >7%). Spirometric parameters such as FVC, FEV_1, PEFR, and $FEF_{25–75}$% showed a marked decline in patients with elevated HbA1c levels, suggesting a restrictive pattern of pulmonary dysfunction.

These findings indicate that the lungs may be an overlooked target organ in diabetes-related complications. The negative correlation between HbA1c and pulmonary function underscores the importance of stringent glycemic control in preventing or minimizing pulmonary involvement. Early screening of pulmonary function in diabetic patients, even in the absence of respiratory symptoms, may aid in the timely identification of subclinical lung dysfunction and allow for better management and improved quality of life.

Further longitudinal studies with larger sample sizes are recommended to establish causality and to evaluate the potential benefits of pulmonary rehabilitation in diabetic populations.

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