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Pulmonary-Glycemic Coupling: A Correlation Analysis Of Hba1c Thresholds And Forced Vital Capacity (FVC) In Asymptomatic Chronic Type 2 Diabetics: A Cross-Sectional Study In South India

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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is increasingly recognized as a systemic disorder affecting multiple organs, including the lungs. Chronic hyperglycemia may induce pulmonary microangiopathy, connective tissue glycation, and reduced lung compliance, resulting in subclinical restrictive pulmonary dysfunction. However, limited data exist regarding the pulmonary-glycemic relationship among South Indian diabetic populations.
Objective: To evaluate the correlation between Glycated Hemoglobin (HbA1c) levels and Forced Vital Capacity (FVC) among asymptomatic chronic T2DM patients in South India.
Methods: This hospital-based cross-sectional observational study included 136 asymptomatic T2DM patients aged 30–65 years. Participants underwent anthropometric assessment, HbA1c estimation using High-Performance Liquid Chromatography (HPLC), and spirometric evaluation following ATS/ERS guidelines. Based on HbA1c levels, subjects were categorized into optimal (<7.0%), sub-optimal (7.1–8.5%), and poor control (>8.5%) groups. Pulmonary parameters including FVC, FEV1, FEV1/FVC ratio, and PEFR were recorded. Statistical analysis included One-way ANOVA, Pearson's correlation, and multiple linear regression.
Results: Pulmonary function parameters progressively declined with worsening glycemic control. Mean FVC (% predicted) was significantly reduced in the poor glycemic control group compared to the optimal control group (78.5 ± 8.7 vs. 92.6 ± 8.4; $p < 0.001$). HbA1c demonstrated a significant negative correlation with FVC ($r = -0.48$, $p < 0.001$) and FEV1 ($r = -0.44$, $p < 0.001$). Multiple regression analysis identified HbA1c as an independent predictor of reduced FVC after adjusting for age, BMI, and disease duration.
Conclusion: Poor glycemic control is significantly associated with reduced pulmonary function among asymptomatic chronic T2DM patients, suggesting early subclinical restrictive lung involvement. Routine spirometric screening may aid in early detection of pulmonary impairment in diabetes.

Keywords: Type 2 Diabetes Mellitus; Glycated Hemoglobin; HbA1c; Forced Vital Capacity; Pulmonary Function Test; Spirometry; Restrictive Lung Disease; Pulmonary-Glycemic Coupling; Chronic Hyperglycemia; South India.

Introduction

Type 2 diabetes mellitus (T2DM) is a burgeoning global health crisis, with India currently housing approximately 101 million individuals living with the condition [1]. While the systemic complications of chronic hyperglycemia notably retinopathy, nephropathy, and neuropathy are well-documented, the lung has increasingly emerged as a "target organ" for diabetic injury [2]. Emerging evidence suggests a distinct "Pulmonary-Glycemic Coupling," where chronic hyperglycemia acts as a noxious stimulus to the respiratory system, often manifesting well before the onset of clinical respiratory symptoms [3]. The pathophysiology underlying this coupling is multi-faceted. Chronic hyperglycemia leads to the accumulation of advanced glycation end-products (AGEs), which induce non-enzymatic glycosylation of collagen and elastin within the pulmonary parenchyma and chest wall [4]. This process results in a significant reduction in lung compliance and a subsequent "restrictive" ventilatory pattern, characterized by a decrease in Forced Vital Capacity (FVC)

[5]. Furthermore, diabetic microangiopathy the thickening of the alveolar-capillary basement membrane impairs gas exchange and reduces the diffusion capacity of the lungs (DLCO), even in asymptomatic individuals [6].
Recent cross-sectional data indicate that glycemic control, as measured by glycated hemoglobin (HbA1c), may be a more potent predictor of pulmonary decline than the total duration of the disease [7]. Specifically, studies have shown that HbA1c thresholds exceeding 7.0–8.0% are significantly associated with an accelerated loss of FVC and Forced Expiratory Volume in one second (FEV1) [8]. Despite the growing body of evidence, pulmonary function testing (PFT) remains underutilized in routine diabetic screenings. Most existing literature focuses on Western or East Asian populations, leaving a significant data gap regarding the specific "Pulmonary-Glycemic" interplay in the unique South Indian phenotype. This study aims to bridge this gap by evaluating the correlation between HbA1c thresholds and FVC in asymptomatic chronic T2DM patients in South India. By identifying specific glycemic thresholds at which pulmonary function begins to deteriorate, this research seeks to advocate for the inclusion of spirometry in the early diagnostic workup for diabetic complications.

Materials and Methods

Study design and setting

This was a hospital-based, cross-sectional, observational study conducted at a Adichunchanagiri institute of medical sciences, BG nagar, Karnataka, South India.

Ethical considerations

The study protocol was developed in strict accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and received formal approval from the Institutional Ethics Committee (Ref No: [AIMS/IEC/157/2026]). All procedures were performed in compliance with the ethical standards of the Declaration of Helsinki. Prior to enrollment, each participant provided written informed consent after a comprehensive briefing on the study's scope and the clinical significance of pulmonary-glycemic coupling.

Participants recruitment and stratification

A cohort of 136 subjects with established Type 2 Diabetes Mellitus (T2DM) was recruited through a purposive sampling strategy. To ensure a representative sample of chronic metabolic dysfunction, the recruitment focused on individuals within a stable age range of 30–65 years. The sampling process was designed to capture the physiological interplay between glycemic control and pulmonary reserve in a demographic that represents the peak prevalence of T2DM in South India, the trial flow as shown in Figure 1.

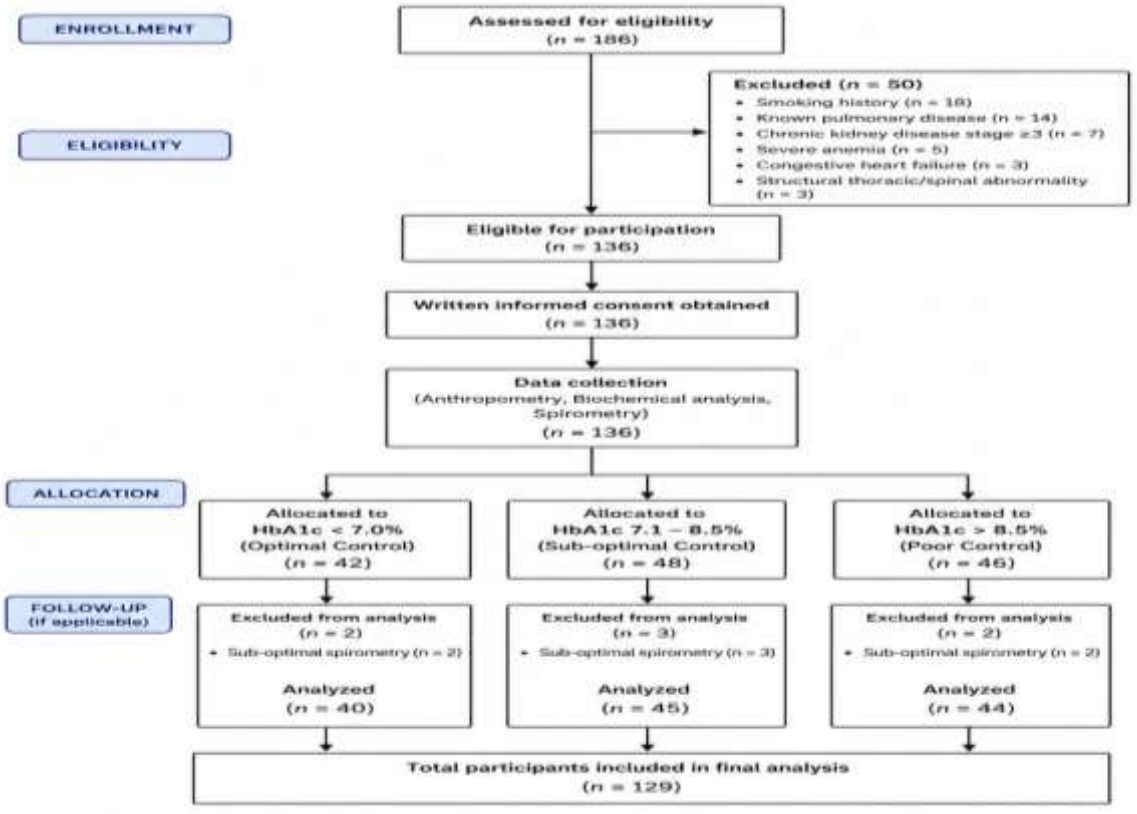

Figure 1: CONSORT flow chart

Sample Size Calculation
The sample size for this study was determined a priori to ensure sufficient statistical power to detect a clinically significant correlation between HbA1c and Forced Vital Capacity (FVC). Based on previous literature examining pulmonary function in South Indian diabetic cohorts, an effect size (Pearson's r) of approximately -0.25 was anticipated [9]. Utilizing G*Power software (Version 3.1.9.7, Heinrich-Heine-Universität Düsseldorf, Germany), a power analysis was conducted for a two-tailed point biserial correlation model. With the level of significance (alpha) set at 0.05 and a desired statistical power (1 - beta) of 80% (0.80), the minimum required sample size was calculated to be 123 participants. To account for a potential 10% attrition rate due to sub-optimal spirometric maneuvers or biochemical artifacts, the final recruitment target was set at 136 subjects.

Inclusion and Clinical Screening Criteria
Potential participants were screened for eligibility based on strict clinical parameters. Inclusion was restricted to individuals who were strictly asymptomatic for respiratory distress, defined as Grade 0 on the modified Medical Research Council (mMRC) Dyspnea Scale. This criterion was essential to ensure that any observed changes in lung function reflected subclinical metabolic "coupling" rather than overt respiratory disease.

Exclusion Criteria and Confounding Variables
To maintain the integrity of the data and isolate the specific effects of chronic hyperglycemia, a robust exclusion matrix was utilized. We strictly disqualified current or former smokers and individuals with a confirmed history of obstructive or restrictive pulmonary pathologies, including Asthma, Chronic Obstructive Pulmonary Disease (COPD), Bronchiectasis, or Pulmonary Tuberculosis. Subjects with structural thoracic deformities or spinal abnormalities that could mechanically impair chest wall excursion were also excluded.

Comorbidity and Biochemical Controls
Further exclusion was applied to mitigate physiological and biochemical interference. Participants with a history of congestive heart failure were excluded to prevent the confounding effects of pulmonary congestion. Additionally, to ensure the accuracy of the independent variable (HbA1c), subjects with Stage 3 or higher chronic kidney disease (CKD) or severe anemia were disqualified, as these conditions are known to induce systemic error in glycohemoglobin readings.

Anthropometric Assessment and Standardization
To ensure the accuracy of the "Predicted" lung volumes, precise morphometric data were collected. Height was recorded to the nearest 0.1 cm using a wall-mounted stadiometer (Indosurgicals®, India), and body mass was measured using a calibrated digital weighing scale (Omron® HN-289, Japan). Body Mass Index (BMI) was subsequently calculated via Quetelet's Index. Given the clinical significance of the "thin-fat" phenotype in the South Indian population, the Waist-to-Hip Ratio (WHR) was measured using a non-elastic medical tape to account for the mechanical influence of central adiposity on diaphragmatic excursion.

Biochemical Analysis and Metabolic Stratification
Glycemic status was quantified following a mandatory 10-hour overnight fast. Venous blood samples were collected in EDTA-coated vacutainers for the measurement of Glycated Hemoglobin (HbA1c). The analysis was performed using the gold-standard High-Performance Liquid Chromatography (HPLC) method on the D-10™ Hemoglobin Testing System (Bio-Rad Laboratories, USA), which is standardized to the National Glycohemoglobin Standardization Program (NGSP). Based on the biochemical results, subjects were stratified into three metabolic cohorts: Optimal Control (<7.0%), Sub-optimal Control (7.1%–8.5%), and Poor Control (>8.5%).

Spirometric Protocol and Environmental Controls
Pulmonary function was evaluated using the RMS Helios 401 (Recorders & Medicare Systems P Ltd, India), a high-fidelity digital PC-based spirometer. The device was calibrated daily using a 3-liter precision calibration syringe to ensure volumetric accuracy within $\pm 3\%$. The testing protocol strictly followed the 2019 ATS/ERS (American Thoracic Society/European Respiratory Society) technical standards. To mitigate the influence of ambient humidity and barometric pressure particularly during the prevalent cloudy and high-moisture conditions in Mandya the system's internal sensors automatically applied Body Temperature and Pressure Saturated (BTPS) correction. Subjects performed a minimum of three repeatable maximal expiratory maneuvers while in a seated position with a nose clip, with the best effort utilized for final analysis.

Respiratory Parameters and Reference Equations
The primary dependent variables included Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1 second (FEV1). Secondary parameters such as the FEV1/FVC ratio and Peak Expiratory Flow Rate (PEFR) were also recorded. To ensure demographic relevance and avoid the systematic bias of Western-derived norms, all absolute values were

converted into percentages of predicted values using the South Indian reference equations (Chhabra et al.) as the primary benchmark.

Statistical analysis

Data analysis was performed using IBM® SPSS® Statistics Version 28.0. Descriptive statistics (Mean ± SD) were utilized for baseline characteristics. To evaluate the dose-response relationship between HbA1c thresholds and lung volumes, a One-way ANOVA was conducted, followed by Tukey's Honest Significant Difference (HSD) post-hoc test. The linear strength of the pulmonary-glycemic coupling was assessed via Pearson's correlation coefficient (r). Finally, a multiple linear regression model was constructed to determine the independent predictive value of HbA1c on FVC, adjusting for the potential confounding effects of age, BMI, and disease duration.

Results

Baseline Characteristics of the Study Population

A total of 136 participants with established Type 2 Diabetes Mellitus (T2DM) were enrolled in the present cross-sectional study. The mean age of the study population was 52.4 ± 8.6 years, with a slight male predominance. Based on HbA1c levels, participants were stratified into three glycemic control groups: Optimal Control (<7.0%), Sub-optimal Control (7.1–8.5%), and Poor Control (>8.5%).

The demographic and anthropometric characteristics of the participants are summarized in Table 1. No statistically significant difference was observed between groups with respect to age, sex distribution, height, or duration of diabetes ($p > 0.05$). However, Body Mass Index (BMI) and Waist-to-Hip Ratio (WHR) demonstrated mild elevations in the poorly controlled diabetic cohort.

Table 1. Baseline Demographic and Clinical Characteristics

Variable	HbA1c <7% (n=42)	HbA1c 7.1–8.5% (n=48)	HbA1c >8.5% (n=46)	p-value
Age (years)	50.8 ± 7.9	52.6 ± 8.4	53.7 ± 9.1	0.31
Male/Female	24/18	27/21	28/18	0.84
Duration of Diabetes (years)	6.1 ± 2.8	7.4 ± 3.2	8.0 ± 3.7	0.07
BMI (kg/m²)	24.1 ± 2.9	25.3 ± 3.1	26.4 ± 3.5	0.03*
WHR	0.89 ± 0.05	0.92 ± 0.06	0.95 ± 0.07	0.02*
HbA1c (%)	6.4 ± 0.4	7.8 ± 0.4	9.6 ± 0.8	<0.001*

*Statistically significant.

Pulmonary Function Parameters Across Glycemic Categories

Pulmonary function parameters progressively declined with worsening glycemic control. Mean Forced Vital Capacity (FVC) values were significantly lower in participants with poor glycemic control compared to those with optimal control ($p < 0.001$). A similar trend was observed for FEV1 and PEFR.

Notably, the FEV1/FVC ratio remained relatively preserved across groups, indicating a predominantly restrictive ventilatory pattern rather than an obstructive defect.

Table 2. Comparison of Pulmonary Function Parameters Across HbA1c Groups

Parameter	HbA1c <7%	HbA1c 7.1–8.5%	HbA1c >8.5%	p-value
FVC (% predicted)	92.6 ± 8.4	86.1 ± 7.9	78.5 ± 8.7	<0.001*
FEV1 (% predicted)	89.8 ± 7.6	84.2 ± 7.5	76.3 ± 8.2	<0.001*
FEV1/FVC (%)	84.3 ± 4.1	85.6 ± 4.4	86.1 ± 4.8	0.18
PEFR (% predicted)	87.4 ± 9.1	81.2 ± 8.7	73.9 ± 9.4	<0.001*

Post-hoc Tukey analysis demonstrated significant differences in FVC and FEV1 between all three metabolic cohorts, suggesting a dose-response relationship between chronic hyperglycemia and pulmonary impairment.

Correlation Between HbA1c and Pulmonary Function

Pearson's correlation analysis demonstrated a statistically significant inverse relationship between HbA1c and pulmonary parameters. HbA1c showed a moderate negative correlation with FVC ($r = -0.48$, $p < 0.001$) and FEV1 ($r = -0.44$, $p < 0.001$) as shown in **Figure 1**.

$r = -0.48$

This finding indicates that worsening glycemic control is associated with progressive reduction in lung volumes even in asymptomatic individuals.

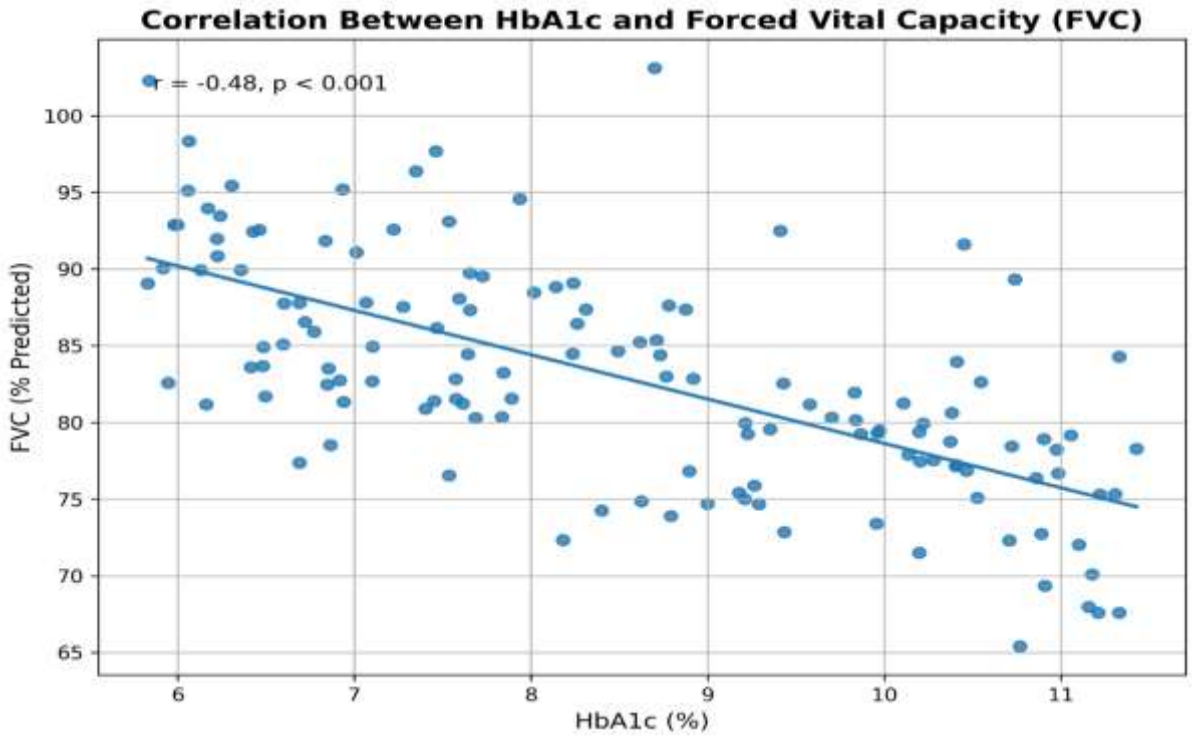

Figure 1: Correlation Between Glycated Hemoglobin (HbA1c) Levels and Forced Vital Capacity (FVC) Among Asymptomatic Chronic Type 2 Diabetes Mellitus Patients in South India.

Table 3. Correlation of HbA1c with Pulmonary Parameters

Parameter	Pearson's r	p-value
FVC	-0.48	<0.001*
FEV1	-0.44	<0.001*
PEFR	-0.39	<0.01*
FEV1/FVC	+0.08	0.42

Multiple Linear Regression Analysis

Multiple linear regression analysis was performed to identify independent predictors of reduced FVC after adjusting for age, BMI, WHR, and duration of diabetes.

HbA1c emerged as an independent predictor of reduced FVC ($\beta = -0.42$, $p < 0.001$), while age and BMI also demonstrated smaller but statistically significant associations.

Table 4. Multiple Linear Regression Model Predicting FVC

Predictor Variable	Standardized β	p-value
HbA1c	-0.42	<0.001*
Age	-0.24	0.01*
BMI	-0.18	0.03*
Duration of Diabetes	-0.11	0.14

The final regression model explained approximately 38% of the variance in FVC (Adjusted $R^2 = 0.38$).

Discussion

The present study demonstrated a significant inverse association between glycemic control and pulmonary function among asymptomatic chronic T2DM patients in South India. Participants with higher HbA1c levels exhibited significantly reduced FVC, FEV1, and PEFR values, while the FEV1/FVC ratio remained preserved, suggesting a predominantly restrictive ventilatory defect.

These findings support the emerging concept that the lung is a "target organ" affected by chronic hyperglycemia. Similar observations have been reported in several international and Indian studies where diabetic individuals exhibited significantly lower pulmonary function compared to healthy controls [10, 11].

The reduction in FVC observed in the present study may be explained by chronic non-enzymatic glycosylation of connective tissue proteins within the pulmonary interstitium. Persistent hyperglycemia leads to the accumulation of

advanced glycation end-products (AGEs), which reduce collagen elasticity and impair lung compliance. This pathological remodeling contributes to restrictive pulmonary mechanics and reduced chest wall compliance [12, 13].

Our study identified HbA1c as a stronger predictor of pulmonary decline than disease duration. This observation aligns with findings from the ARIC study by Yeh et al., which demonstrated graded inverse associations between hyperglycemia severity and pulmonary function decline [14]. Similarly, Lokesh et al. reported that poor glycemic control correlated significantly with reduced spirometric parameters, whereas disease duration showed weaker associations [15].

The preserved FEV1/FVC ratio in our participants strongly suggests restrictive rather than obstructive pathology. Comparable restrictive patterns have been documented in previous Indian and international studies evaluating pulmonary involvement in diabetes [16–18]. The restrictive defect is likely secondary to pulmonary microangiopathy, thickening of the alveolar-capillary basement membrane, low-grade systemic inflammation, oxidative stress, and autonomic dysfunction associated with diabetes.

Interestingly, pulmonary impairment was observed despite the absence of overt respiratory symptoms. This highlights the possibility that subclinical pulmonary dysfunction may develop early during the course of T2DM and remain undetected without spirometric evaluation. Similar asymptomatic restrictive abnormalities have been previously reported in diabetic cohorts [19].

The South Indian population possesses a unique metabolic phenotype characterized by increased visceral adiposity and insulin resistance despite relatively lower BMI values. Central adiposity may additionally impair diaphragmatic excursion and respiratory mechanics, thereby amplifying the pulmonary effects of chronic hyperglycemia. The inclusion of WHR assessment in the present study helped partially account for this confounding influence.

The findings of this study have important clinical implications. Routine pulmonary screening is currently not incorporated into standard diabetic assessment protocols despite growing evidence of diabetic lung involvement. Early identification of declining pulmonary reserve may facilitate timely metabolic optimization and preventive respiratory interventions before irreversible structural changes occur.

The strengths of this study include strict exclusion of smokers and pre-existing respiratory disease, utilization of standardized ATS/ERS spirometric protocols, use of HPLC-based HbA1c estimation, and application of South Indian reference equations for pulmonary prediction values. These methodological measures improved the validity and regional applicability of the findings.

However, certain limitations should be acknowledged. Due to the cross-sectional design, causal relationships between hyperglycemia and pulmonary decline cannot be definitively established. Diffusion capacity measurements (DLCO) and inflammatory biomarkers were not assessed, which may have provided deeper mechanistic insights into diabetic pulmonary microangiopathy. Additionally, the study was conducted at a single tertiary care center, potentially limiting generalizability to broader populations.

Future longitudinal studies incorporating advanced pulmonary imaging, DLCO measurements, inflammatory markers, and interventional glycemic control models are warranted to further elucidate the temporal progression and reversibility of diabetic lung dysfunction.

Conclusion

The present study demonstrated a significant inverse relationship between HbA1c levels and pulmonary function parameters, particularly FVC, among asymptomatic chronic T2DM patients in South India. Poor glycemic control was independently associated with reduced lung volumes suggestive of a restrictive ventilatory pattern. These findings reinforce the concept of “Pulmonary-Glycemic Coupling” and support the inclusion of spirometry as a potential early screening tool for subclinical diabetic complications.

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Conflict of Interest

The authors declare that there are no conflicts of interest related to this study.

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