Section: General Medicine

Original Research Article

PULMONARY FUNCTION ASSESSMENT IN TYPE 2 DIABETES MELLITUS: A CROSS-SECTIONAL STUDY OF SPIROMETRY, DIFFUSING CAPACITY, AND BREATH HOLDING TEST

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is increasingly recognised as a systemic disorder with pulmonary manifestations. The lung, with its extensive microvascular network, is susceptible to glycation-mediated injury, microangiopathy, and fibrosis. Pulmonary function tests (PFTs) including spirometry, diffusing capacity for carbon monoxide (DLCO), and breath holding test (BHT) can detect these subclinical changes early. This study aimed to systematically assess these parameters in T2DM patients and correlate findings with disease duration and glycaemic control. **Materials and Methods:** A single-centre, hospital-based, observational cross-sectional study was conducted at the Department of General Medicine, L.N. Medical College & Research Centre, Bhopal. A total of 182 non-smoking T2DM patients aged >35 years with diabetes duration >5 years were enrolled using consecutive sampling. All participants underwent spirometry (ATS/ERS guidelines), single-breath DLCO measurement in sitting and supine positions, and BHT assessment. Correlations were examined with disease duration (5–10, 11–15, >15 years) and glycaemic control stratified by HbA1c (<7%, 7–9%, >9%). **Results:** The mean age was 54.2 years (57.7% male). Spirometric abnormalities were present in 76.9% of patients; restrictive pattern was most common (37.4%). Mean FVC was 95.8±18.4%, FEV1 92.4±19.7%, and FEF25–75 76.8±24.6% predicted. Mean DLCO (sitting) was 82.6±16.8% predicted; 65.9% showed abnormal (negative) delta DLCO. Mean BHT was 28.4±8.6 seconds; 62.6% had reduced BHT. All parameters deteriorated significantly with increasing disease duration and worsening HbA1c ($p<0.001$). HbA1c demonstrated stronger inverse correlations with pulmonary function than disease duration (FEF25–75: r=–0.58 vs r=–0.52; FEV1: r=–0.54 vs r=–0.48). A dose-response relationship was observed with microvascular complication burden (r=–0.60 for FEF25–75 and DLCO supine). **Conclusion:** T2DM is significantly associated with multifaceted pulmonary dysfunction. DLCO is the earliest and most sensitive marker of pulmonary microangiopathy, while FEF25–75 is the most sensitive spirometric index. Glycaemic control is a stronger predictor of pulmonary impairment than disease chronicity. Routine pulmonary function assessment should be integrated into standard diabetic complication screening, particularly in patients with poor glycaemic control or established microvascular complications.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) constitutes 90–95% of all diabetes cases globally and has emerged as one of the leading causes of morbidity and mortality in the 21st century. The International Diabetes Federation (IDF) 2025 Atlas estimates that approximately 11.1% of adults aged 20–79 years are living with diabetes, with projections indicating a 46% rise to 853 million affected individuals by 2050. India, with over 100 million affected individuals, bears a disproportionate burden of this epidemic.

Classical teaching emphasises microvascular complications of T2DM nephropathy, retinopathy,

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and neuropathy along with macrovascular disease. However, growing evidence designates the lung as an additional and often overlooked target organ. The pulmonary parenchyma, with its alveolar-capillary surface area approximating 70–100 m² and a rich microvascular network, is profoundly susceptible to the biochemical consequences of chronic hyperglycaemia.

Multiple pathophysiological mechanisms mediate diabetic pulmonary injury. Non-enzymatic glycation of structural proteins such as collagen and elastin reduces lung compliance and alveolar surface area. Advanced glycation end-products (AGEs) accumulate in the alveolar basement membrane, impairing gas diffusion. Oxidative stress, chronic low-grade inflammation, TGF-β-mediated fibrogenesis, and autonomic neuropathy collectively impair ventilatory function, gas exchange, and respiratory muscle control. These changes manifest as restrictive spirometric defects, reduced DLCO, and decreased BHT even before clinical symptoms emerge.

Despite a growing body of international literature, data from the Indian subcontinent remain limited and heterogeneous, potentially influenced by distinct genetic, dietary, and environmental factors. The present study was therefore designed to comprehensively assess pulmonary function using spirometry, DLCO (including postural delta DLCO as a marker of pulmonary microangiopathy), and BHT in T2DM patients and to correlate findings with disease duration and glycaemic control indexed by HbA1c.

MATERIALS AND METHODS

Study Design and Setting This was a single-centre, hospital-based, observational cross-sectional study conducted over 18 months at the Department of General Medicine, L.N. Medical College & Research Centre and J.K. Hospital, Bhopal, Madhya Pradesh, a tertiary care referral centre. The study was approved by the Institutional Ethics Committee (Ref: LNMC&RC/Dean/2024/Ethics/404, dated 10/05/2024) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

Participants Consecutive sampling was used to enrol 182 patients with previously diagnosed T2DM (as per American Diabetes Association criteria) from the Medicine OPD and IPD. Inclusion criteria: age >35 years and diabetes duration >5 years. Exclusion criteria: active or past smoking, any cardiorespiratory illness (COPD, asthma, pulmonary tuberculosis, pleural effusion, CCF), severe obesity (BMI >35 kg/m²), pregnancy, and inability to perform PFTs. Sample size was calculated using the standard prevalence formula (p=14%, d=5%, Z=1.96), yielding n=182.

Clinical and Biochemical Assessment All participants underwent comprehensive clinical evaluation including anthropometric measurements, blood pressure recording, and assessment for diabetic complications (retinopathy by ophthalmoscopy, neuropathy by clinical examination, nephropathy by 24-hour urinary protein). Fasting blood glucose (FBS), postprandial glucose (PPBS), and glycated haemoglobin (HbA1c) were measured using standardised automated methods. Participants were stratified into three glycaemic control groups: good (<7%), fair (7–9%), and poor (>9%) based on HbA1c.

Pulmonary Function Testing

All PFTs were performed by trained personnel under standardised conditions. Spirometry was performed using a calibrated spirometer following ATS/ERS guidelines. A minimum of three acceptable manoeuvres were recorded, and the best values were used. Parameters measured included FVC, FEV1, FEV1/FVC ratio, PEFR, and FEF25–75, expressed as percentage of age-, sex-, height-, and ethnicity-matched predicted values. Spirometric patterns were classified as normal (FVC ≥80%, FEV1/FVC ≥70%), restrictive (FVC <80%, FEV1/FVC ≥70%), obstructive (FEV1/FVC <70%), or mixed.

DLCO was measured by the single-breath technique (ATS/ERS guidelines) in both sitting and supine positions. Delta DLCO (supine minus sitting DLCO) was calculated; a positive delta indicates normal postural increase in diffusing capacity, while a negative delta indicates pulmonary microvascular impairment. BHT was assessed after normal expiration; the participant performed a maximal inspiration and held breath for as long as possible; the best of two attempts was recorded in seconds. BHT <30 seconds was classified as reduced.

RESULTS

Demographic and Clinical Profile

A total of 182 T2DM patients were enrolled. Males constituted 57.7% (n=105) and females 42.3% (n=77), with a male-to-female ratio of 1.36:1. The predominant age group was 51–60 years (34.0%), followed by 41–50 years (28.0%) and 61–70 years (22.0%). Urban residents comprised 59.3%, and 52.2% had a positive family history of diabetes. The most common diabetes duration was 5–10 years (41.8%), followed by 11–15 years (37.4%) and >15 years (20.8%). Glycaemic control was fair (HbA1c 7–9%) in 48.4%, good (<7%) in 29.7%, and poor (>9%) in 21.9%.

Diabetic retinopathy was the most prevalent microvascular complication (48.9%), followed by neuropathy (42.9%) and nephropathy (39.0%). Overall, 68.1% of patients had at least one microvascular complication; 13.7% had all three simultaneously.

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Table 1: Spirometric parameters and DLCO findings in the study population (n=182)

Parameter	Mean ± SD (% predicted)	Range	p-value
FVC	95.8 ± 18.4	62.0–128.0	<0.001
FEV1	92.4 ± 19.7	58.0–125.0	<0.001
FEV1/FVC ratio	89.2 ± 8.6	70.0–102.0	<0.001
PEFR	88.6 ± 21.3	52.0–118.0	<0.001
FEF25–75	76.8 ± 24.6	42.0–115.0	<0.001
DLCO sitting	82.6 ± 16.8	54.0–106.0	<0.001
DLCO supine	78.4 ± 17.2	48.0–102.0	<0.001
Delta DLCO	–4.2 ± 3.6	–12.0 to +2.0	<0.001
BHT (seconds)	28.4 ± 8.6 sec	12.0–48.0	—

SD: standard deviation; BHT: breath holding test; DLCO: diffusing capacity of the lungs for carbon monoxide; FEF25–75: forced expiratory flow at 25–75% FVC; PEFR: peak expiratory flow rate

Pattern of Spirometric Dysfunction

Spirometric abnormalities were detected in 76.9% of patients. Restrictive pattern was the most frequent (37.4%), followed by obstructive (20.9%) and mixed (18.6%) patterns. Only 23.1% had normal spirometry. DLCO was abnormal (negative delta DLCO) in 65.9% (n=120). BHT was reduced (<30 sec) in 62.6% of patients, with 17.6% showing severely reduced values (<20 sec).

Table 2: Correlation of pulmonary parameters with HbA1c and disease duration

Parameter	Duration r	Duration p	HbA1c r	HbA1c p	Stronger Predictor
FVC	–0.42	<0.001	–0.46	<0.001	HbA1c
FEV1	–0.48	<0.001	–0.54	<0.001	HbA1c
FEF25–75	–0.52	<0.001	–0.58	<0.001	HbA1c
DLCO sitting	–0.44	<0.001	–0.52	<0.001	HbA1c
DLCO supine	–0.46	<0.001	–0.54	<0.001	HbA1c
Delta DLCO	–0.42	<0.001	–0.50	<0.001	HbA1c
BHT (sec)	–0.48	<0.001	–0.52	<0.001	HbA1c

r: Pearson's correlation coefficient; BHT: breath holding test; HbA1c: glycated haemoglobin

Effect of Disease Duration

A significant progressive decline in all pulmonary parameters was observed with increasing disease duration ($p<0.001$ for all). Patients with duration >15 years had the lowest values: FVC 85.6±18.4%, FEV1 82.4±20.6%, DLCO sitting 74.2±18.6%, and BHT 22.6±9.2 seconds, compared to the 5–10 year group (FVC 102.4±15.8%, FEV1 99.8±16.4%, DLCO sitting 88.6±14.2%, BHT 32.4±7.2 seconds). Delta DLCO worsened from –2.8±2.4 (5–10 years) to –5.8±4.2 (>15 years).

Effect of Glycaemic Control

HbA1c emerged as the strongest predictor of pulmonary dysfunction, consistently demonstrating stronger correlations than disease duration across all parameters (Table 2). Patients with poor control (HbA1c >9%) had markedly reduced FEV1 (78.6±20.4%), FEF25–75 (62.8±26.4%), DLCO sitting (72.6±18.8%), and BHT (22.8±9.4 sec) compared to those with good control (HbA1c <7%): FEV1 103.6±15.2%, FEF25–75 92.6±20.4%, DLCO sitting 92.4±12.6%, BHT 34.6±6.8 sec (all $p<0.001$). The delta DLCO deteriorated from –2.2±2.0 (good control) to –6.4±4.6 (poor control), underscoring the role of chronic hyperglycaemia in pulmonary microvascular damage.

Microvascular Complications and Lung Function

Patients with any microvascular complication had significantly worse pulmonary function compared to those without ($p<0.001$ for all parameters). A clear dose-response relationship was observed: patients with all three complications had the worst values (FVC 79.8±19.6%, FEV1 75.4±21.8%, DLCO sitting 70.6±19.8%, BHT 21.4±9.8 sec) versus those with no complications (FVC 105.2±14.8%, FEV1 102.6±15.4%, DLCO sitting 90.8±13.2%, BHT 33.6±6.4 sec). Among individual complications, retinopathy showed the strongest correlation with DLCO impairment (r=–0.50 for DLCO supine), while the total complication count was the strongest overall correlate (r=–0.60 for FEF25–75 and DLCO supine).

Statistical Analysis

Data were entered in Microsoft Excel 2024 and analysed using R software (version 4.4.5). Continuous variables were expressed as mean ± standard deviation. One-way ANOVA or Kruskal-Wallis test was used for inter-group comparisons. Pearson's or Spearman's correlation coefficients were calculated depending on data distribution. Chi-square test was used for categorical variables. Multiple linear regression was performed to identify independent predictors of pulmonary dysfunction. A p-value <0.05 was considered statistically significant.

DISCUSSION

The present study provides comprehensive evidence that T2DM is associated with significant and multidimensional pulmonary dysfunction, detectable through spirometry, DLCO, and BHT. The high

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prevalence of abnormal findings — 76.9% for spirometry, 65.9% for delta DLCO, and 62.6% for BHT — underscores that the lung is a frequently yet silently affected organ in T2DM.

The predominance of a restrictive spirometric pattern (37.4%) is consistent with published literature. Barik et al. (2025) in 143 T2DM patients reported restrictive dysfunction in 56.6%. Skm et al. (2025) found restriction in 39% of their cohort. Kusare et al. (2022) documented restrictive patterns in 30% of 100 diabetic patients. This pattern reflects non-enzymatic glycation of pulmonary connective tissue proteins — primarily collagen and elastin — leading to reduced lung compliance, diminished elastic recoil, and impaired lung expansion. The additional presence of obstructive and mixed patterns in our cohort suggests heterogeneity in pulmonary involvement, encompassing both parenchymal and airway disease. The significant reduction in FEF25–75 (76.8±24.6% predicted), which showed the strongest correlation with HbA1c (r=–0.58) and complication burden (r=–0.60), identifies small airway dysfunction as an early and sensitive manifestation of diabetic pulmonary disease. Sharma et al. (2023) similarly reported FEF25–75 as the most affected spirometric parameter in their hospital-based study of 50 T2DM patients. This likely reflects inflammation, oedema, and connective tissue remodelling in peripheral airways driven by chronic hyperglycaemia.

DLCO, particularly postural delta DLCO, emerged as the earliest indicator of pulmonary microangiopathy. In healthy individuals, DLCO increases in the supine position due to gravitational redistribution of pulmonary blood flow; in diabetic pulmonary microangiopathy, this response is blunted or reversed, resulting in a negative delta DLCO. In our study, 65.9% of patients showed abnormal (negative) delta DLCO, implying widespread subclinical pulmonary microvascular disease. Agarwal et al. (2008) demonstrated a strong negative correlation between %DL/VA and albuminuria (r=–0.975, $p<0.001$) and retinopathy (r=–0.550, $p<0.05$), confirming the parallel microangiopathic processes in renal, retinal, and pulmonary capillary beds. Pawar et al. (2022) specifically validated delta DLCO as a non-invasive predictor of pulmonary microangiopathy in T2DM.

A critical and clinically actionable finding is that HbA1c is a stronger predictor of pulmonary dysfunction than disease duration across all parameters. This finding is corroborated by Vanidassane et al. (2018), who reported strong negative correlations of FEV1 (r=–0.739) and FVC (r=–0.370) with HbA1c. Uz-zaman et al. (2014) showed that patients with HbA1c >7% had the greatest decline in DLCO and spirometric values. These observations collectively suggest that metabolic derangement drives pulmonary injury more potently than chronological disease duration alone, conferring a direct therapeutic implication: optimising glycaemic control may attenuate or delay pulmonary deterioration in T2DM.

The dose-response relationship between cumulative microvascular burden and pulmonary dysfunction is a particularly compelling finding. Patients with all three microvascular complications (retinopathy, neuropathy, nephropathy) showed the worst pulmonary parameters, while those without complications had near-normal values. This graded relationship strongly supports the concept of the lung as an integral component of diabetic systemic microangiopathy. Retinopathy demonstrated the strongest individual association with DLCO impairment, consistent with the shared retinal-pulmonary microvascular pathology.

Our findings align with the biological plausibility of pulmonary involvement: AGE accumulation in the alveolar basement membrane, TGF-β-mediated fibrogenesis, mitochondrial ROS production, endothelial dysfunction, and autonomic neuropathy impairing respiratory muscle control and ventilatory response to hypoxia collectively produce a multifaceted pulmonary phenotype.

This study has several limitations. The cross-sectional design precludes causal inference; a longitudinal study is required to establish directionality. The absence of a non-diabetic control group limits comparative analysis. Body plethysmography (TLC, RV) was not performed, precluding comprehensive restrictive disease assessment. Respiratory muscle strength (MIP/MEP) and comprehensive autonomic function tests were not measured. Potential confounders including indoor air pollution, occupational exposure, and physical activity were not exhaustively assessed.

CONCLUSION

This study confirms that T2DM is significantly and independently associated with multifaceted pulmonary dysfunction affecting ventilation, gas diffusion, and respiratory endurance. Restrictive spirometric pattern is the predominant defect. DLCO — especially postural delta DLCO — is the earliest and most sensitive marker of pulmonary microangiopathy, while FEF25–75 is the most sensitive spirometric index of early airway involvement. Glycaemic control (HbA1c) is a stronger predictor of pulmonary impairment than chronological disease duration, underscoring the centrality of metabolic optimisation. A clear dose-response with microvascular complication burden confirms that the lung should be regarded as a target organ of diabetic microangiopathy.

Routine pulmonary function assessment including spirometry, DLCO, and BHT should be incorporated into standard T2DM evaluation protocols, particularly for patients with poor glycaemic control or established microvascular complications. Early detection offers the window to implement glycaemic optimisation, pulmonary rehabilitation, and lifestyle modification to prevent long-term respiratory morbidity. The null hypothesis is rejected; a

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statistically and clinically significant association exists between T2DM and impaired pulmonary function correlating with disease duration and glycaemic control.

Conflict of Interest

No conflict of interest declared by any author.

Ethical Approval

Approved by the Institutional Ethics Committee, L.N. Medical College & Research Centre (Ref: LNMC&RC/Dean/2024/Ethics/404, dated 10/05/2024). Written informed consent obtained from all participants.

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