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To Study Changes in Pulmonary Function Tests in Patients with Type 2 Diabetes Mellitus having Microvascular Complications Compared to the Normal Population

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Explanation: The article consists of the results and observations of the scientific study done at a tertiary care centre which aims to compare the relationship between microvascular complications of type 2 diabetes mellitus (T2DM) and pulmonary function, focusing on diabetic retinopathy and nephropathy. The study emphasizes the significance of spirometry as a simple and reliable tool for identifying early pulmonary complications in diabetes. It advocates strict glycemic control and respiratory muscle-strengthening exercises as part of comprehensive diabetes management to improve patient outcomes.

Abstract: ***Title: To Study Changes in Pulmonary Function Tests in Patients with Type 2 Diabetes Mellitus Having Microvascular Complications Compared to the Normal Population. Aim: This study aims to analyze the impact of microvascular complications (specifically diabetic retinopathy and nephropathy) in individuals with type 2 diabetes mellitus on their pulmonary function parameters compared to the normal population. Objectives: 1) Identify variations in pulmonary function test (PFT) parameters based on the severity of diabetic retinopathy and nephropathy. 2) Establish a correlation between changes in PFT parameters in type 2 diabetes patients and their HbA1c levels at the time of diagnosis. Methods: The study was conducted at Hind Institute of Medical Sciences, Barabanki, over 18 months, involving 122 participants aged 18-60 years. Participants were divided into two groups: Group A: Non-Diabetic Controls, Group B: Type 2 Diabetic Patients with Microvascular Complications (diabetic retinopathy and/or nephropathy). Assessments included: a) Spirometry to measure PFT parameters. b) Ophthalmic examination to assess diabetic retinopathy c) Urinary albumin assessment to evaluate nephropathy d) Routine blood tests including HbA1c levels. Results: The study found a mixed obstructive-restrictive pattern in lung dysfunction among diabetic individuals, attributed to chronic hyperglycemia and non-enzymatic glycosylation of lung collagen. There was a significant bidirectional relationship observed between abnormal lung function and diabetes, with correlations found between diabetes duration, HbA1c levels, and impaired pulmonary function. Severe diabetic nephropathy and retinopathy correlated strongly with reduced spirometry values, predominantly showing a restrictive impairment pattern in type 2 diabetes. Conclusion: Regular spirometry is crucial for early detection of pulmonary complications in diabetes. It serves as an essential, simple, and reliable tool for managing diabetes-related lung impairments. Emphasizing strict glycemic control and incorporating respiratory muscle strengthening exercises may potentially improve lung function in these patients.***

Keywords: Diabetes Mellitus complications, Pulmonary function analysis, Microvascular complications, Spirometry, Respiratory health management.

1. Introduction

Diabetes, a prevalent metabolic disorder, has a significant global impact, characterized by the deterioration of both macrovascular and microvascular systems due to metabolic, hemodynamic, and inflammatory factors [1]. Global public health systems are facing a formidable challenge due to the rising prevalence of diabetes, with predictions indicating a notable increase in the number of affected individuals in the upcoming decades [1, 2]. In addition to having a direct impact on health outcomes, the increase in diabetes incidence is also associated with comorbidities like diabetic retinopathy, nephropathy, neuropathy, and cardiovascular illnesses [2].

Understanding the multifaceted nature of diabetes and its complications requires a comprehensive approach spanning epidemiology, pathophysiology, clinical manifestations, diagnostics, and management strategies. Extensive research efforts, including studies and clinical trials, have contributed to this understanding, resulting in a substantial body of scientific literature [1, 9]. Investigations into the pathogenic mechanisms underlying diabetic complications, such as fibrosis and microvascular diseases, have provided critical insights into metabolic dysregulation and end-organ damage [1, 2].

Moreover, advancements in diagnostic techniques, such as retinal imaging and nerve conduction studies, have enabled early detection and monitoring of diabetic complications, facilitating timely interventions to prevent adverse outcomes. [This introduction provides context for a thorough analysis of the literature on diabetes and its complications, emphasizing important discoveries from pathophysiological understandings, epidemiological studies, clinical manifestations, diagnostic techniques, and therapeutic methods.

By synthesizing evidence from diverse sources, this review aims to provide a holistic understanding of the intricate interplay between diabetes, its complications, and the broader healthcare landscape. Furthermore, by identifying knowledge gaps and areas for future research, this review seeks to inform

healthcare professionals, policymakers, and researchers involved in diabetes care and management.

Complications of Diabetes

The detrimental effects of diabetes on health are compounded by diabetic retinopathy (DR) and diabetic kidney disease (DKD), two outcomes of the illness that have been linked to an increased risk of premature mortality [3]. Globally, people with diabetes are more likely to develop chronic kidney disease (CKD) and end-stage renal disease (ESRD). Despite sporadic reporting, India's total magnitude and pattern of CKD have been documented. DKD prevalence remains notably high across the globe, with diabetes patients having approximately 1.75 times higher odds of developing CKD [4].

The complications of diabetes stem from its effects on both large and small blood vessels, driven by metabolic, hemodynamic, and inflammatory factors. Among these complications, diabetic retinopathy (DR) and diabetic kidney disease (DKD) are prominent, contributing to premature mortality and morbidity globally. DR affects approximately one-third of diabetic individuals and poses a significant risk of vision impairment if left untreated. On the other hand, diabetes patients have almost double the risk of developing chronic kidney disease (CKD) as non-diabetic individuals do. DKD, which is defined by kidney impairment in individuals with diabetes, has become a significant health concern [5,6].

Diabetic Nephropathy (DN)

Renal damage that is directly linked to extended exposure to high blood sugar levels is known as diabetic nephropathy (DN), a dangerous consequence of diabetes mellitus. Its hallmark features include albuminuria (excessive protein in the urine) and/or reduced estimated glomerular filtration rate (eGFR) in individuals with diabetes [10].

In Type 1 diabetes mellitus (T1DM), the onset of DN typically occurs beyond the initial decade of the disease; however, its incidence rises significantly between 10 and 20 years post-diagnosis [5]. Conversely, in Type 2 diabetes mellitus (T2DM), DN exhibits greater clinical heterogeneity among different ethnic groups, with variations in the timing and severity of presentation [4].

The pathogenesis of DN is complex and multifactorial, with hyperglycemia playing a central role in driving renal injury [6, 10]. Extended exposure to elevated glucose levels triggers the activation of many pathways, including as the hexosamine pathway flow, the polyol pathway, the production of advanced glycation end products (AGEs), and protein kinase C (PKC). [10]. These biochemical processes contribute to oxidative stress, inflammation, and fibrosis within the renal microvasculature, ultimately leading to structural and functional abnormalities characteristic of DN [5, 10].

Moreover, the renin-angiotensin-aldosterone system (RAAS) activation and dysregulation of vascular endothelial growth factor (VEGF) signaling further exacerbate renal damage in DN [5, 6]. Additionally, genetic predisposition, epigenetic modifications, and environmental factors such as hypertension, dyslipidemia, and smoking influence the development and progression of DN. To mitigate the evolution of diabetic neuropathic pain (DN) and lower the morbidity and mortality associated with it in diabetics, it is imperative to comprehend the complex interactions among these pathogenic pathways and design tailored therapeutic approaches.

Diabetic Retinopathy

Diabetic retinopathy (DR) is a recognized complication associated with diabetes, characterized by various changes in the retina such as microaneurysms, hemorrhages, and the formation of new blood vessels, often leading to blindness [7]. Globally, around one-third of individuals with diabetes develop DR, with a significant proportion progressing to sight-threatening DR (STDR) [8]. Delayed presentation of STDR, especially in rural areas due to limited access to eye care services, presents challenges for restoring vision and may result in permanent blindness [8]. Timely screening is essential for early detection and intervention to preserve vision. Risk factors for DR include high blood sugar levels, hypertension, abnormal lipid levels, duration of diabetes, ethnicity, pregnancy, adolescence, and previous cataract surgery.

DR has been associated with reduced signalling of insulin receptors in the retina, leading to nerve cell degeneration [7]. Experimental studies suggest that diabetes impacts the entire sensory part of the retina, causing faster death of nerve cells and changes in the metabolism of cells supporting nerve cells [8]. This indicates that DR could be a form of sensory nerve damage affecting the tissue of the retina, similar to peripheral nerve damage in diabetes. Understanding the interaction between nerve and blood vessel elements in the development of DR may lead to the development of new treatments to protect nerves. Regular screening using fundus photography is widely practiced worldwide, aiding in the timely detection of DR and its integration into comprehensive diabetes management [6].

Diabetes and Respiratory Conditions

Diabetic Pulmonary Diseases: Emerging evidence suggests a potential association between diabetes mellitus (DM) and interstitial pulmonary fibrosis (IPF), with age and lifestyle-related factors, including DM, possibly contributing to the risk of IPF development [11]. Furthermore, the higher prevalence of gastroesophageal reflux disease (GERD) in DM patients may exacerbate the risk of IPF due to its association with micro-aspiration [13]. Studies show that diabetic individuals with poorly regulated blood sugar have a rapid deterioration in lung function and microvascular problems, which thickens the pulmonary capillary basal lamina and reduces capillary blood volume [12]. Pulmonary autonomic neuropathy associated with DM also affects ventilation control, leading to impaired responses to hypoxia and an increased susceptibility to lung infections. Moreover, DM-related deficits in muscle metabolism contribute to reduced respiratory muscle strength and endurance [12].

A restrictive ventilatory defect pattern seen in pulmonary function testing indicates a connection between diabetes and a reduction in lung function [11]. Studies indicate a more rapid decline in forced expiratory volume in 1 second (FEV1) among DM patients compared to non-smoking healthy individuals [16]. Decreases in FEV1, forced vital capacity (FVC), and dynamic lung compliance are consistently

reported in DM patients, potentially attributable to peripheral airway obstruction [15]. Meta-analyses and comparative studies consistently demonstrate impaired pulmonary function in DM patients is characterized by decreased FEV1, FVC, and lung diffusing capacity for carbon monoxide (DLCO), independent of hemoglobin A1c levels, body mass index, smoking status, or length of diabetes [17][18].

Integrated Healthcare Strategies

The interconnections between diabetes and respiratory diseases underscore the importance of integrated healthcare strategies. Tailored therapeutic approaches that address both metabolic control and respiratory function may be necessary for diabetic patients with concurrent respiratory conditions. People with diabetes may experience better patient outcomes, fewer complications, and an overall higher quality of life if they adopt this integrated viewpoint [19, 20].

In conclusion, diabetes remains a formidable global health crisis with far-reaching implications for individuals and healthcare systems worldwide. Its impact extends beyond metabolic disturbances to encompass various organ systems, including the kidneys, eyes, and lungs. Understanding the complex interplay between diabetes and its associated complications is vital for developing effective prevention and treatment strategies. By adopting a comprehensive approach to diabetes management, including early detection, targeted interventions, and integrated healthcare strategies, we can strive to mitigate the burden of this pervasive disease and improve outcomes for affected individuals.

Aim and Objectives

Aim:

To analyse the relationship between microvascular complications in patients with type 2 diabetes mellitus and their pulmonary function parameters.

Objectives:

1) To determine changes in PFT parameters with the severity of diabetic retinopathy and nephropathy.
2) To correlate PFT changes in patients with type 2 diabetes mellitus with their HbA1c levels on presentation.

2. Materials and Methods

Materials

a) Study Site: The research was conducted at Hind Institute of Medical Sciences, Department of Medicine, Safedabad, Barabanki, Uttar Pradesh.
b) Study Design: This study followed a cross-sectional, comparative analytical design.
c) Study Group: Participants were divided into two groups: Group A (Control - Non-Diabetic) and Group B (Diabetic with Nephropathy/Retinopathy or both).
d) Sample Size: A total of 122 individuals participated in the study, with 61 participants in each group, including both sexes.

Inclusion Criteria:

1) Patients aged between 18 to 60 years regardless of gender.
2) Patients diagnosed having Type 2 Diabetes Mellitus (DM) with Diabetic Nephropathy.
3) Patients diagnosed having Type 2 DM with Diabetic Retinopathy or both.

Exclusion Criteria:

1) History of smoking.
2) Acute or chronic respiratory disease (including severe COVID-19 infection requiring hospital admission).
3) History of occupational exposure affecting lung function.
4) History of preexisting cardiovascular disease.
5) Neuromuscular, cardiovascular, or end-stage kidney disease.
6) Physical disabilities such as kyphoscoliosis, pectus excavatum, and pectus carinatum that may affect lung function.
7) Patients contraindicated for spirometry, including those with recent myocardial infarction, pneumothorax, hemoptysis of unknown origin, recent eye, thorax, or abdominal surgery, and patients with a proliferative type of diabetic retinopathy.
8) Use of drugs causing pulmonary fibrosis.
9) Obesity (BMI > 30).

Methods:

This cross-sectional study was conducted in the Department of General Medicine at HIMS, Barabanki, UP, India, enrolling a total of 122 participants aged 18-60 years. Participants were divided into two groups based on diabetic status: Group A (Non-Diabetic Control, n=61) and Group B (Diabetic, n=61), each group comprising both male and female individuals (Group A: 39 males, 22 females; Group B: 40 males, 21 females). Eligible participants had no history of respiratory disease and were stratified by the presence or absence of diabetic retinopathy (DR) or diabetic nephropathy (DN).

Ethical Considerations

Ethical approval was obtained from the institutional review board, departmental ethics committee, and the Institutional Human Ethics Committee (IHEC). Informed consent was secured from each participant before enrollment in the study.

Data Collection and Procedures

Participants underwent spirometry to evaluate pulmonary function, utilizing the Spirovit Schiller SP-1 pneumotech flow sensor and SEMA PC software. Chest X-rays were performed to exclude any pre-existing pulmonary conditions. The estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI formula, and chronic kidney disease (CKD) status was determined based on criteria including albuminuria levels and eGFR values.

A pre-tested, standardized proforma was employed to document medical history, clinical findings, and laboratory results. All participants received a thorough physical examination and diagnostic work-up, which included chest X-rays, 2D echocardiography (if indicated), fundoscopy, complete blood count, renal function tests, urine analysis, fasting and postprandial blood glucose measurements, electrocardiogram (ECG), and HbA1c for glycemic control assessment.

Pulmonary Function Testing
Diabetic participants underwent pulmonary function testing three times with medications administered prior, at intervals of 15 minutes, and the best result was recorded. Parameters assessed included forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), peak expiratory flow rate (PEFR), and the FEV1/FVC ratio. Basic spirometric measurements, including FVC and the FEV1/FVC ratio, were obtained using a respirometer to categorize patterns of lung function as normal, restrictive, or obstructive.

Ophthalmic Examination
All participants underwent a comprehensive ophthalmologic examination to assess the severity of diabetic retinopathy (DR). The evaluation included intraocular pressure measurements, visual acuity assessment, slit-lamp examination of the anterior segment, and dilated fundus examination. The severity of DR was graded based on established criteria, allowing correlation with pulmonary function changes.

Diabetic Nephropathy Assessment
Diabetic nephropathy severity was classified based on microalbuminuria levels and correlated with pulmonary function test outcomes. The staging of DR and DN was analyzed against pulmonary function parameters to assess the association between diabetic microvascular complications and lung function.

Statistical Analysis

Sample Size Calculation:
$Z_{1-\alpha/2}$ = Critical value of standard normal variate for the corresponding to (α) level of significance.
(At α=5%, z_α =1.96 & at α =1%, z_α=2.58)
$Z_{1-\beta}$ = desired power (critical value of normal dist^n α+ β)
(For a power of 80%, β is20% z_β=0.84)
X_1 = mean of group 1, x_2 = mean of group 2
σ1 = standard deviation of group 1
σ2 = standard deviation of group 2

$$n = \frac{(1.96+0.84)^2 \times [(0.49)^2 + (0.50)^2]}{(2.45 - 2.70)^2} = 61.47$$

n=61 in each group
So total sample size is 122.

Data Collection
The process of gathering patient data involved conducting thorough interviews to gather comprehensive information regarding major co-morbidities, significant medical histories, and occupational backgrounds. Additionally, patients underwent meticulous physical examinations, covering both general health and specific systemic conditions. Vital lung function parameters, including Forced Expiratory Volume in 1 second (FEV1), Forced Vital Capacity (FVC), and the FEV1/FVC ratio, were measured using a spirometer. Further diagnostic assessments, such as Respiratory Function Tests (RFT), Electrocardiography (ECG), Complete Blood Count (CBC), and Haemoglobin A1c (HbA1c) evaluations, were also performed as indicated.

Data Management and Analysis
Collected data was meticulously organized into an Excel spreadsheet and subjected to analysis using either Epiinfo 3.5.4 or SPSS software (version 26.1). The findings were presented in the form of percentages within each group or as mean values accompanied by their respective standard deviations (±SD), unless stated otherwise. Various statistical methodologies, including the t-test for mean comparison, Fisher's Exact test, ANOVA, and Chi-square analysis, were utilized as appropriate. Significance levels were determined by assessing the p-values, with values below 0.05 considered statistically significant for the parameters under evaluation.

3. Results

In this analysis, 122 cases were assessed, dividing patients into two groups: 61 diabetic (Group A) and 61 non-diabetic (Group B) controls. Group A was further divided based on diabetic complications, including retinopathy and nephropathy. Gender distribution showed slight differences, with a male predominance in both groups (63.93% in controls and 65.57% in diabetics). Within the diabetic group, subcategories were: 19.67% with no complications, 31.14% with retinopathy, 36.06% with nephropathy, and 13.11% with both conditions.

Table 1: Demographic characteristics of Non Diabetic & Diabetic

Variables			Non- Diabetic (NDM), n=61	Diabetic (DM), n=61	Diabetic without Retino & Nephropathy (DWRN)	Diabetic Retinopathy (DMR)	Diabetic Nephropathy (DMN)	Diabetic Retino + Nephropathy (DMRN)	P value
Age Years	18-30	M	7 (11.47%)	3 (4.91%)	3 (4.91%)	0	0	0	0.069
		F	4 (6.55%)	1 (1.63%)	1 (1.63%)	0	0	0	
	31-45	M	13 (21.31%)	9 (14.75%)	2 (3.27%)	3 (4.91%)	3 (4.91%)	1 (3.27%)	0.05
		F	8 (13.11%)	4 (6.55%)	1 (1.63%)	2 (3.27%)	1 (1.63%)	0	
	46-60	M	19 (31.14%)	28 (45.90%)	2 (3.27%)	10 (16.39%)	12 (19.67%)	4 (6.55%)	0.05
		F	10 (16.39%)	16 (26.22%)	3 (4.91%)	4 (6.55%)	6 (9.83%)	3 (4.91%)	
	Total	M	39	40	7 (11.47%)	13 (21.31%)	15 (24.59%)	5 (8.19%)	0.05
		F	22	21	5 (8.19%)	6 (9.83%)	7 (11.47%)	3 (6.55%)	
Gender	Male		39 (63.93%)	40 (65.57%)	7 (11.47%)	13(21.31%)	15 (24.59%)	5 (8.19%)	0.05
	Female		22 (36.06%)	21 (34.42%)	5 (8.19)	6 (9.83%)	7 (11.47%%)	3 (6.55%)	0.05
Total			61	61	12 (19.67%)	19 (31.14%)	22 (36.06%)	8 (13.11%)	

Analysis of the demographic data (Table 1) revealed age-related trends, with a higher prevalence of complications in older age groups. Among diabetic males, the mean age was 47.88 ± 8.76 years, and among females, it was 45.63 ± 9.41 years. Significant differences (p=0.05) were observed

between diabetic subgroups in terms of age distribution and gender.

Table 2: Spirometry Parameters in cases and controls (Group-A & Group -B)

Spirometry Parameters	Case (Diabetic, mean ±SD), n=61	Control (non-diabetic, mean± SD), n=61	Difference, mean	P value (Paired sample t-test)
FVC	104.76±12.51	118.74±13.51	12.27	≤ 0.001
FEV1	102.34±11.43	112.32±14.98	9.56	≤ 0.001
FEV1%	96.98±8.76	104.41±9.12	6.88	≤ 0.001
PEFR	101.45±16.31	116.66±14.11	15.44	≤ 0.001
FEF25-75	73.88±18.76	98.34±15.36	24.86	≤ 0.001

Pulmonary function tests (PFTs) indicated a significant decrease in all spirometry measures among diabetics compared to non-diabetics (Table 2). The FEF25-75 showed the greatest reduction, followed by PEFR, FVC, FEV1, and FEV1%, with differences averaging 13.54%. Subgroup analysis revealed that diabetics with both retinopathy and nephropathy had the lowest spirometry values, suggesting that the cumulative effect of these complications may impact pulmonary function.

Table 3: Illustrates the comparison of correlation strengths between microvascular complications of diabetes and associated nephropathy, retinopathy, or both, with spirometry parameters

Spirometry Parameters		Retinopathy	Nephropathy	Nephro + Retinopathy	Number of Complications	Diabetic W/O Retino & Nephropathy	P value
FVC	Pearson Correlation	-0.329	-0.269	-0.243	-0.356	-0.432	0.05
	Sig. (2 Tailed)	0.020	0.065	0.083	0.013	0.018	
FEV1	Pearson Correlation	-0.456	-0.331	-0.298	-0.457	-0.531	0.49
	Sig. (2 Tailed)	0.003	0.034	0.047	0.003	0.002	
FEV1%	Pearson Correlation	-0.223	-0.123	-0.099	-0.192	-0.298	0.05
	Sig. (2 Tailed)	0.143	0.447	0.612	0.187	0.123	
PEFR	Pearson Correlation	-0.357	-0.498	-0.501	-0.522	-0.302	0.05
	Sig. (2 Tailed)	0.008	0.004	0.002	0.001	0.009	
PEF 25-75	Pearson Correlation	-0.469	-0.554	-0.789	-0.471	-0.412	0.05
	Sig. (2 Tailed)	0.003	0.032	0.046	0.002	0.002	

The correlation analysis in Table 3 demonstrated an inverse relationship between spirometry parameters and microvascular complications. Pearson correlations were highest for PEFR in retinopathy, nephropathy, and combined complications ($p<0.05$), highlighting the significant impact of these diabetic complications on respiratory performance.

Table 4: Comparison of pulmonary function tests among Duration of Diabetes in Diabetic Subjects

Variables (PFT)	Duration of Diabetes in Years (n=61)				Total	P value
	0-5 (11)	6-10 (16)	11-15 (25)	≥15 (9)		
FVC/PRED	3.16±1.12	3.28±1.14	3.54±1.32	2.43±0.96	3.17±1.63	0.20
FVC/ MEASURED	2.44±0.68	2.07±0.43	2.17±0.13	1.43±0.56	2.19±0.77	0.05
FVC/ PRED%	80.88±21.89	65.54±18.67	63.94±22.83	64.11±21.56	72.87±16.66	0.05
FEV1/PRED	2.32±0.69	2.09±0.72	1.84±0.22	1.21±0.31	2.13±0.14	0.069
FEV1/MEASURED	1.89±0.53	1.65±0.41	1.62±0.37	1.16±0.54	1.56±0.31	0.02
FEV1/PRED%	85.32±21.74	78.98±20.17	76.48±21.53	74.22±19.77	81.63± 18.92	0.045
FEV1/FVC	81.66±22.88	82.98±19.59	85.43±23.61	90.22±21.56	83.74± 23.88	0.05
FEV1/FVC MEASURED	78.99±11.76	76.34±9.47	75.87±10.74	74.63±9.22	77.32±11.96	0.05
FEV1/FVC PRED%	97.64±20.88	98.34±23.53	101.53±21.61	104.61±19.65	98.69±21.87	0.05

Moreover, the duration of diabetes correlated inversely with spirometry performance (Table 4), where patients with a longer duration of diabetes (≥15 years) exhibited reduced FVC, FEV1, and FEV1/FVC ratios. Overall, 81.96% of diabetic patients had been diagnosed for more than five years, showing a significant link between diabetes duration and decline in pulmonary metrics. This analysis underscores the importance of monitoring lung function as an integral part of managing diabetes, especially in patients with advanced disease or multiple complications.

4. Discussion

In our study, we observed that lung function in patients with diabetes mellitus (DM) shows significant compromise when compared to control groups, corroborating findings from numerous studies. Although much existing literature emphasizes restrictive patterns in pulmonary function impairment among DM patients, our study identified a mixed obstructive–restrictive pattern. Contrastingly, a few studies report negligible differences in pulmonary function test (PFT) parameters between diabetic and non-diabetic groups, suggesting variability in lung function impact among individuals. Further research may elucidate the underlying mechanisms behind this involvement [14].

One plausible mechanism is non-enzymatic glycosylation of chest wall and lung proteins, which increases collagen resistance to proteolysis, leading to collagen accumulation in pulmonary connective tissue. Non-enzymatically

glycosylated collagen in DM patients resists pepsin and collagenase digestion, potentially explaining the restrictive lung changes due to chronic hyperglycemia's impact on lung collagen and parenchyma flexibility.

Some studies suggest impaired lung function may precede DM diagnosis, indicating potential shared pathophysiology. Research among Asian populations also found declines in spirometric parameters in T2DM, particularly with prolonged disease duration. Autopsy studies in DM patients report thickened alveolar walls and small vessels, which could underlie ventilatory restriction [18,19].

Our study sample included 61 T2DM patients from a Medical College Diabetic Clinic, matched with control groups by age, sex, and height. Given the physical demands of spirometry, only healthy, non-smoking individuals without significant cardiac or pulmonary conditions participated. The average age of study participants was 47.42 ± 10.63 years, with comparable mean ages between male and female participants. Spirometric values showed statistically significant decreases in diabetic patients compared to controls, with FEF25–75 demonstrating the greatest reduction (mean drop of 24.84%; T2DM cases: 73.56 ± 29.19%, controls: 98.40 ± 14.45%), followed by FVC (12.96), FEV1 (8.90), FEV1% (6.28), and PEFR (15.44). The mean decline in spirometric values across groups was 13.54%.

Correlation analyses revealed a negative association between the extent of spirometric derangement and both diabetes duration and HbA1C levels. All spirometric parameters showed decline with prolonged diabetes duration and higher HbA1C, with glycemic control correlating more closely to these declines than disease duration alone. Additionally, a significant relationship was identified between pulmonary function impairment and microvascular complications, with more pronounced reductions in spirometric values among patients with retinopathy or multiple complications. Most participants had a disease history of more than ten years and poor glycemic control (68% with HbA1C >7%).

Our findings align with previous longitudinal and cross-sectional studies indicating spirometric function declines averaging 10% over time in DM patients, with annual decreases in FVC, FEV1, and other measures [15]. This trend suggests that DM accelerates lung aging through glycosylation effects on connective tissue and small airway obstruction. For example, studies on the Framingham Offspring Cohort and meta-analyses reinforce these correlations, showing links between glycemic control and pulmonary function even after adjusting for variables like BMI and smoking [12].

In contrast, several studies found no significant differences in pulmonary function between T2DM and controls. Variations in sample size, disease duration, glycemic control, racial diversity, and age distribution may explain these discrepancies. Importantly, spirometry was performed following ATS guidelines, ensuring test accuracy [20]. The observed reductions in FVC and FEV1% indicate restrictive dysfunction, while decreased FEF25–75 suggests early small airway obstruction, consistent with a "mixed ventilatory dysfunction" pattern. Advanced glycosylated end products (AGEs) are thought to underlie these changes, causing both restrictive and obstructive pulmonary effects through connective tissue modification and inflammatory responses [20].

In terms of demographic specifics, 45% of our T2DM population were male, predominantly aged over 50 years, with mean postprandial blood glucose (PPBS) of 151.6 ± 23.8 mg/dL and fasting blood glucose (FBS) of 114.8 ± 17.5 mg/dL. Disease duration in the cohort was frequently under ten years, yet demonstrated steady progression over time. Spirometric parameters showed an average decline of 9.5% per year, with higher downregulation observed in individuals with diabetic retinopathy, especially at Grade 4 severity, compared to those with nephropathy alone.

Microvascular complications were prevalent, with diabetic nephropathy affecting 36.1% and retinopathy impacting 31.1% of patients. In 67.2% of cases, only one microvascular complication was present, while 13.1% exhibited dual complications. Among the observed impairments, restrictive dysfunction dominated, affecting 77% of patients, while obstructive patterns were rare, observed in only 5% of patients. The restrictive component appears linked to nonenzymatic glycation in the lung's collagen and elastin, yielding reduced pulmonary compliance [18].

Further, weak downstream correlations were noted between diabetes duration, HbA1C, and specific PFT parameters, with marked derangements in the subgroup affected by diabetic retinopathy compared to nephropathy. Given that DM-related systemic inflammation may exacerbate lung dysfunction over time, our findings align with studies linking microvascular complications with restrictive and obstructive patterns. Overall, our study reinforces the hypothesis that prolonged DM and poor glycemic control substantially impair lung mechanics in a clinically significant but sub-clinical manner.

5. Conclusion

In our study, we evaluated 122 patients aged 18 to 60 years, comprising both genders, who were divided into two groups: Group A (non-diabetic controls) and Group B (patients with diabetes and associated microvascular complications, including retinopathy, nephropathy, and combined retinopathy-nephropathy). The study was conducted over an 18-month period at HIMS, Barabanki, with 61 participants in each group. Of the total 122 patients, 40 males and 21 females were in Group B, while 39 males and 22 females were in Group A. The average age of male diabetic participants in Group B was 47.88 ± 8.76 years (range 29–60 years), and for female diabetic subjects, it was 45.63 ± 9.41 years (range 28–60 years). The mean weight of males was 64.78 ± 10.54 kg (range 48–85 kg), while the mean weight for females was 59.34 ± 8.69 kg (range 43–78 kg).

In our study, we found a significant correlation between the duration of diabetes and the deterioration of pulmonary function. Pulmonary function tests (PFTs) showed considerable decline as the duration of the illness increased. The average duration of diabetes in the study population was 6.9 ± 4.74 years, with FVC and FEV1 significantly reduced in nearly 80% of the patients. When compared to expected

values, both male and female FVC and FEV1 were markedly lower, with statistically significant differences.

We also observed a strong correlation between HbA1c levels and PFT parameters (FVC, FEV1, and FEV1/FVC). The results showed that microvascular complications, particularly diabetic retinopathy, had a significant impact on pulmonary function. Diabetic nephropathy was less strongly correlated with lung function, but it still contributed to the decline in PFTs. Diabetic nephropathy was the most common microvascular complication, affecting 36.06% of participants, followed by diabetic retinopathy in 31.15% and combined retinopathy and nephropathy in 13.11%. Only 19.67% of participants had no microvascular complications, while 67.21% had a single microvascular complication, and 13.11% had two.

The majority of participants (77%) in our study exhibited restrictive lung patterns, which were the most common pulmonary impairment in type 2 diabetes. In contrast, only 5% of patients showed an obstructive pattern. 18% of the study population had normal PFT results. Our study highlights that prolonged, uncontrolled type 2 diabetes is associated with both macrovascular and microvascular complications. The restrictive pulmonary impairment observed in our study, characterized by reduced FVC and FEV1, is likely a result of prolonged hyperglycemia. The longer the duration of diabetes, the more significant the decline in pulmonary function. Regular glucose management and respiratory exercises may help mitigate pulmonary decline in diabetic patients. Spirometry offers a simple, reliable, and non-invasive method for early detection of diabetes-related pulmonary impairment, and it can serve as a tool for preventive care.

6. Limitations

The study's limitations include a small sample size of 122 patients, limiting generalizability, and its cross-sectional design, which restricts establishing causality. Additionally, while smokers were excluded, other confounding factors such as physical activity, socioeconomic status, and comorbidities may have influenced the results. Lastly, being a single-center study, the findings may not be applicable to other settings with different patient populations or healthcare practices. Further research with a larger, more diverse sample, and longitudinal design is needed to confirm and expand upon these findings.

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