International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 13, No. 10, October 2024 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_13.10.2024.133

ORIGINAL RESEARCH

Comparison of pulmonary functions in patients with diabetes mellitus and healthy individuals: A prospective case-control study

[1]Nitesh Kumar Gupta, [2]Elias Mir, [3]Abdul Ahad Wani, [4]Dr. Sajad

[1]Resident Doctor and MD fellow, [3]Assistant Professor, Department of General Medicine, SKIMS Medical College, Srinagar, JK, India
[2]Assistant Professor, Department of Chest Medicine, SKIMS Medical College, Srinagar, JK, India
[4]Faculty, SKIMS Medical College, JK, India

Corresponding author
Abdul Ahad Wani
Assistant Professor, Department of General Medicine, SKIMS Medical College, Srinagar, JK, India

Received Date: 27 August, 2024 Accepted Date: 30 September, 2024

ABSTRACT

Background: The lung has not been considered routinely as a seat of target organ damage in patients with diabetes mellitus (DM) even though DM has proven detrimental effects on the microvasculature and connective tissue. We intended to compare the lung functions of patients with DM and healthy individuals. **Methods:** This was a single-center, observational, prospective, cross-sectional, case-control study done from July 2021 to June 2023. Spirometery parameters (including forced expiratory volume in first second (FEV1), Forced vital capacity (FVC), and FEV1/FVC ration) of non-smoker patients with Type 2 DM without lung diseases in the age-group of 20-60 years were compared with healthy, never-smoker, non-diabetic individuals.were enrolled as controls. **Results:** A total of 123 DM patients and 129 healthy controls were enrolled.Mean duration of DM andHBA_1C in cases were 7.2850±2.43 years and 7.78±0.63% respectively. The mean FVC, FEV1 were lower in DM as compared to healthy controls [p<0.001]. Patients with DM had a significantly less proportion [p<0.001] with normal spirometery [77 (62.6%) vs 113 (87.6%)] and higher proportion [p<0.001]with restrictive patterns of spirometery [34(27.6%) vs 9 (7.0%)]. FVC and FEV1 values differed significantly in patients with DM duration less than 5 years, 5-10 years and greater than 10 years. FVC, FEV1 and FEV1/FVC values did not differ significantly between cases with HBA_1C < 7% and > 7%. FEV1 [correlation coefficient = -0.88], FVC [correlation coefficient = -0.89] negatively correlated significantly with duration of diabetes but not with age, BMI and HBA_1C levels. **Conclusions:** Patients with DM have more incidence of restrictive pattern on pulmonary function testing than normal healthy controls. The duration of DM negatively impacts the pulmonary function in these patients.

INTRODUCTION

Diabetes mellitus (DM) is a global public health problem in the developing as well as the developed world [1]. DM is a chronic disease affecting 463 million people worldwide over the age of 20 years and is expected to affect 570 million people by 2030 [1]. The metabolic deregulation associated with DM causes secondary patho-physiologic changes in multiple organ systems that impose a tremendous burden on the individual with DM and on the healthcare system [1, 2]. The metabolic deregulation in DM leads to the long-term damage, dysfunction, and failure of organsystems including eyes, kidneys, nerves, heart, and blood vessels [2]. In contrast to organs like eyes and kidneys, the lung has not been considered routinely as a seat of target organ damage [3].

As DM has been proven to have detrimental effects on the microvasculature, it is quite probable that pulmonary functions may be affected in diabetes mellitus [2-10]. Since the pulmonary reserves are larger, the symptoms and disability from DMrelated damage in the lungsmay be delayed [2-10]. Pulmonary functions are generally determined by the strength of respiratory muscles, compliance of the thoracic cavity, airway resistance, and elastic recoil of the lungs. Spirometry is important in the screening, diagnosis, and monitoring of respiratory diseases [11]. The literature on lung functions especially spirometery in patients with DM is scarce and

DOI: 10.69605/ijlbpr_13.10.2024.133

heterogenous [12-23]. We therefore intended to conduct a cross sectional observational study to assess the lung functions using spirometery parametres in DM patients attending our centre.

MATERIALS AND METHODS

Center

The study was conducted at the Department of General Medicine and the Department of Chest Medicine, SKIMS Medical College Hospital, Bemina, Srinagar. The centre is a 250 bedded tertiary care, multi-specialty centre, located in the central district of Srinagar of the Kashmir Valley. The centre attends to approximgtely 1000 patients daily in the out-patients sections of all the clinical departments. The centre also has 24-hour emergency services including operation theatres, intensive care units, blood bank, laboratories and radiological services. Due to its central location and availability of multi-specialty care in the hospital the centre receives referrals from all the 10 districts of Kashmir valley, adjoining districts of Chenab valley and the Pir Panjal region of the Jammu division as well as the Union territory of Ladakh. This region has a population of approximately 10 million.

Design

It was a single-center, observational, prospective, cross-sectional, case-control study done over a period of two years (July 2021 to June 2023). The study was approved by the Institutional Ethics Committee under protocol number IEC/113/2022.

Cases

The patients were enrolled after a written informed consent was obtained. All patients with Type 2 DM in the age-group of 20-60 years who attended the outpatient department (OPD) or were admitted as inpatients at our center and were fit to perform spirometery manure were enrolled in the study. Current or former smokers, patients with previous lung diseases including bronchial asthma and chest deformities, obstructive sleep apnea, those with history of thoracic surgery and those taking medications likely to interfere with spirometery results were excluded from the study.

Controls

Healthy, never-smoker, non-diabetic individuals who attended as outpatients for routine health check-ups or accompanied members of the case group were enrolled in the control group of the study. Current or former smokers and people with history of current or previous chest diseases were excluded from the study.

Assessment

All cases and controls were assessed by a detailed medical history and a comprehensive physical examination, including an assessment of the respiratory, cardiovascular and central nervous systems as well as anthropometric measurements (weight, height, BMI). Cases underwent investigations including blood sugar, HbA1c and chestradiographs. All cases as well as controls underwent a spirometry in which forced expiratory volume in first second (FEV1), Forced vital capacity (FVC), and FEV1/FVC ration were measured. The spirometery was conducted and interpreted following *American Thoracic Society – European Respiratory Society* (ATS-ERS) guidelines [11].

Analysis

The demography, anthropometry, laboratory and spirometery parameters of cases and controls were compared. All the statistical analysis was carried out using the statistical software SPSS. Mean and standard deviation were computed for all continuous variables and comparison was done using t-test. Frequencies were generated for categorical variables and compared using the Chi–squared test and a p – value of < 0.05 was considered as statistically significant. Correlations were assessed using the Spearman Correlation Coefficient.

RESULTS

A total of 123 cases and 129 controls were enrolled over the study period. Males comprised of 46 (37.4%) cases and55 (42.6%) of controls. Mean age of cases was 50.85 ± 4.48 years while those of controls were 51.07 ± 4.35 years. Mean BMI of the cases was 24.77 ± 0.78 kg/m^2 while as mean BMI of controls was 25.71 ± 0.80 kg/m^2.Average duration of diabetes in cases was 7.2850 ± 2.43 years. MeanHBA1C was 7.78% ± 0.63% [Table 1].

The mean values of FVC, FEV1 were lower in cases as compared to controls. Cases had a significantly less proportion with normal spirometery [77 (62.6%) vs 113 (87.6%)]. Similarly patients with diabetes had more frequency of restrictive patterns of spirometery [34(27.6%) vs 9 (7.0%)]. There was no significant difference between the values of FVC, FEV1 and FEV1/FVC between cases with HBA1C less than 7% and more than 7%. However there was statistically significant difference between FVC and FEV1 values in patients with diabetes duration less than 5 years, 5-10 years and greater than 10 years [Table 2].

Similarly there was statistically significant negative correlation between FEV1 and FVC values and duration of diabetes. While there was no statistically significant correlation between FEV1, FVC values with age, BMI and HBA1C levels [Table 3].

DOI: 10.69605/ijlbpr_13.10.2024.133

Table 1: Comparison of demographic characteristics and BMI of cases and controls.

Parameter		Case N=123	Control N=129	P value
Age in years	Mean (SD)	50.85 (4.48)	51.07 (4.35)	0.189
	31-40 Years Number (percent)	1 (0.8%)	6 (4.7%)	0.569
	41-50 Years Number (percent)	59 (48.0%)	66 (51.2%)	0.821
	51-60 Years Number (percent)	63 (51.2%)	57 (44.2%)	0.917
BMI (kg/m^2)	Mean (SD)	24.77(0.78)	25.71(0.80)	0.473
	18.5-22.9 Number (percent)	1 (0.8%)	3 (2.3%)	0.796
	23.0-24.9 Number (percent)	73(59.3%)	76 (58.9%)	0.867
	>25.0-30 Number (percent)	47 (39.8%)	41 (31.8%)	0.639
	>30 Number (percent)	2(1.6%)	9 (7.0%)	0.581
Gender	Male	46 (37.4%)	55 (42.6%)	0.601
	Female	77 (62.6%)	74 (57.4%)	
Duration of diabetes in years	Mean (SD)	7.28 (2.43)		
	<5 years	23 18.7%)		
	5-10 years	83 (67.5%)		
	>10 years	17 (13.8%)		
HbA1C	**Mean ± SD**	7.78±0.63		

Table 2: Comparison of spirometery results in cases and controls

		Cases	Controls	P value
FEV1/FVC Mean (SD)		78.42 (6.38)	79.06 (5.08)	0.422
FVC Mean (SD)		2.32 (0.67)	2.69 (0.58)	**<0.001**
FEV1 Mean (SD)		1.81 (0.52)	2.10(0.49)	**<0.001**
Normal Number (percent)		77 (62.6%)	113 (87.6%)	**<0.001**
Obstructive Number (percent)		6 (4.9%)	3 (2.3%)	0.078
Restrictive Number (percent)		34 (27.6%)	9 (7.0%)	**<0.001**
Mixed Number (percent)		6 (4.9%)	4 (3.1%)	0.079
FEV1/FVC Mean (SD)	**HbA1C </=7%**	78.84 (6.50)	NA	0.606
	HbA1C >7%	78.30 (6.38)	NA	
FVC Mean (SD)	**HbA1C </=7%**	2.47(0.60)	NA	0.147
	HbA1C >7%	2.27(0.68)	NA	
FEV1 Mean (SD)	**HbA1C </=7%**	1.94 (0.44)	NA	0.113
	HbA1 >7%	1.77(0.54)	NA	
FEV1/FVC Mean (SD)	**<5 years**	76.31 (7.34)		0.072
	5-10 years	79.62 (5.48)		
	>10 years	75.40 (7.68)		
FVC Mean (SD)	**<5 years**	3.17(0.50)		**<0.001**
	5-10 years	2.24(0.49)		
	>10 years	1.53(0.29)		
FEV1 Mean (SD)	**<5 years**	2.41(0.28)		**<0.001**
	5-10 years	1.78(0.43)		
	>10 years	1.15(0.26)		

Table 3: Correlation of FVC with age, BMI, HbA1C and duration of diabetes mellitus (in years)

	Spearman Correlation Coefficient	*P* value
Age (Years) *vs* FEV1 (percent of predicted)	-0.09	0.334
BMI (kg/m^2) *vs*FEV1 (percent of predicted)	-0.14	0.129
HbA1C (%) *vs*FEV1 (percent of predicted)	-0.15	0.126
Duration of DM *vs*FEV1 (percent of predicted)	-0.88	***<0.001***
Age (Years) *vs* FVC (percent of predicted)	-0.07	0.334
BMI (kg/m^2) *vs* FVC (percent of predicted)	-0.12	0.188
HbA1C (%) *vs* FVC (percent of predicted)	-0.13	0.181
Duration of DM *vs* FVC (percent of predicted)	-0.89	**<0.001**

DOI: 10.69605/ijlbpr_13.10.2024.133

DISCUSSION

Since DM has proven detrimental effects on the microvasculature and connective tissue, lungs which have an extensive microvascular circulation and abundant connective tissueare susceptible to structural changes induced by chronic hyperglycemia [1-5]. The underlying mechanism for structural lung changesdue to DM includes microangiopathy of alveolar capillaries and pulmonary arterioles, glycosylation of tissue proteins, oxidative stress, neuropathy and myopathy involving respiratory neuro-muscular function [2,3].Due to these structural abnormalities caused by DM, alterations in pulmonary function such as a reduction in the vital capacity, total lung capacity, lung compliance, reduction in airflows and reduced diffusion capacity can be expected [1-10].

Numerous previous studies have shown that DM is associated with impaired lung function [3-10, 11-23]. Our study has shown that patients with DM have restrictive pattern on pulmonary function testing. This is in commensurate with other studies including a meta-analysis by Borst *et al*which showed that DM was associated with a restrictive pattern of pulmonary function [18]. There are studies which favor a causative role of DM in idiopathic pulmonary fibrosis although the evidence is preliminary. Another study from Korea showed that metabolic syndrome increased the odds ratio for restrictive lung disease [5]. Another study showed that breathlessness in combination with restrictive lung disease was found in 9% of the patients with prediabetes, 20% of patients with newly diagnosed diabetes, and 27% of patients with long-term DM [6]. Similarly another study has shown that patients with DM had significant reduction in the carbon monoxide diffusion capacity as compared to non-diabetic population without any significant difference in FVC, FEV1 and FEV1/FVC [8]. All these studies including ours have shown a consistent impact of DM on pulmonary function parameters. It may be possible that early DM may impact diffusion capacity of lungs due to structural derangements at the alveolo-capillary level before leading to frank lung restriction after a certain time period. We have not measured diffusion capacity in our patients due to cost issues.

Our study did not show any significant difference in the proportion of obstructive defects on pulmonary function in patients with DM as compared to normal controls. There is striking heterogeneity in the existing literature on the presence of obstruction in diabetic patients without other obvious cause for the presence of obstruction like smoking and other noxious aerosol exposure or bronchial asthma [12-23]. The heterogeneity in these studies may be due to differences in demography, inclusion and exclusion criteria used in these studies [12-23]. The differences in confounding factors like smoking exposures, residence in high pollution areas with profound aerosol exposures may also lead to conflicting observations [12-23]. DM and bronchial asthma have been shown to be closely related. DM increases the risk of development of bronchial asthma. Poor DM control increases the risk of exacerbations, worsens asthma control and leads to poor quality of life in asthmatics [24].

In our study spirometery values did not differ significantly between case subgroups of HBA1C and age and also did not correlate with BMI. However there was significant difference between the FEV1 and FVC values of patients with DM duration of more than 10 years and the correlation between the duration of DM and spirometery values was also significantly negatively correlated. This is an expected finding as DM adverse effects are dependent on the duration of DM. However HBA1C levels did not correlated significantly with spirometery levels. This may be most likely due to the reason that HBA1c reflects DM control over the past 3 months a period not sufficient to alter the structural effects of DM on lung architecture and microvasculature. These findings confirm that long standing diabetesmay lead to alterations in lung function necessitating regular monitoring and intervention.

Our study has certain limitations. Our cohort did not comprise of many patients with morbid obesity. The less proportion of such patients in our study population may explain the lack of correlation between BMI values and spiometery parameters. Our study population was also not segregated as per the presence or absence of confounding factors like hypertension, indoor air pollution including exposure to biomass fule smoke which is very prevalent in our settings.

Conflict of interest: None declared
Acknowledgement: None declared

REFERENCES

1. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care. 1998;21(9):1414-31.
2. Fogarty AW, Jones S, Britton JR, Lewis SA, McKeever TM. Systemic inflammation and decline in lung function in a general population: a prospective study. Thorax. 200;62(6):515-20.
3. Mittal S, Jindal M, Srivastava S, Sinha S. Evaluation of Pulmonary Functions in Patients With Type 2 Diabetes Mellitus: A Cross-Sectional Study. Cureus. 2023;15(3):e35628.
4. Walter RE, Beiser A, Givelber RJ, O'Connor GT, Gottlieb DJ. Association between glycemic state and lung function: the Framingham Heart Study. Am J Respir Crit Care Med. 2003;167(6):911-6.
5. Paek YJ, Jung KS, Hwang YI, Lee KS, Lee DR, Lee JU. Association between low pulmonary function and metabolic risk factors in Korean adults: the Korean National Health and Nutrition Survey. Metabolism. 2010 Sep;59(9):1300-6.
6. Kopf S, Groener JB, Kender Z, Fleming T, Brune M, Riedinger C, Volk N, Herpel E, Pesta D, Szendrödi J, Wielpütz MO, Kauczor HU, Katus HA, Kreuter M, Nawroth PP. Breathlessness and Restrictive Lung Disease: An Important Diabetes-Related Feature in

DOI: 10.69605/ijlbpr_13.10.2024.133

Patients with Type 2 Diabetes. Respiration. 2018;96(1):29-40.
7. Benbassat CA, Stern E, Kramer M, Lebzelter J, Blum I, Fink G. Pulmonary function in patients with diabetes mellitus. Am J Med Sci. 2001;322(3):127-32.
8. Ljubić S, Metelko Z, Car N, Roglić G, Drazić Z. Reduction of diffusion capacity for carbon monoxide in diabetic patients. Chest. 1998;114(4):1033-5.
9. Dalquen P. The lung in diabetes mellitus. Respiration. 1999;66(1):12-3.
10. Saini M, Kulandaivelan S, Bansal VK, Saini V, Sharma S, Kaur J, Sondh A. Pulmonary Pathology Among Patients with Type 2 Diabetes Mellitus: An Updated Systematic Review and Meta-analysis. Curr Diabetes Rev. 2020;16(7):759-769.
11. Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, Hallstrand TS, Kaminsky DA, McCarthy K, McCormack MC, Oropez CE, Rosenfeld M, Stanojevic S, Swanney MP, Thompson BR. Standardization of Spirometry 2019 Update. An Official American Thoracic Society and European Respiratory Society Technical Statement. Am J Respir Crit Care Med. 2019;200(8):e70-e88.
12. Sinha S, Guleria R, Misra A, Pandey RM, Yadev R, Tiwari S. Pulmonary functions in patients with type 2 diabetes mellitus and correlation with anthropometry and microvascular complications. Indian J Med Res. 2004;119:66–71.
13. He YY, Chen Z, Fang XY, Chang J, Lu Y, Wang XJ. Relationship between pulmonary function and albuminuria in type 2 diabetic patients with preserved renal function. BMC Endocr Disord. 2020;20(1):112.
14. Mori H, Okubo M, Okamura M, Yamane K, Kado S, Egusa G, Hiramoto T, Hara H, Yamakido M. Abnormalities of pulmonary function in patients with non-insulin-dependent diabetes mellitus. Intern Med. 1992;31(2):189-93.
15. Davis WA, Knuiman M, Kendall P, Grange V, Davis TM. Glycemic exposure is associated with reduced pulmonary function in type 2 diabetes, the fremantle diabetes study. Diabetes Care. 2004;27:752–7.
16. Davis TM, Knuiman M, Kendall P, Vu H, Davis WA. Reduced pulmonary function and its associations in type 2 diabetes: the Fremantle Diabetes Study. Diabetes Res Clin Pract. 2000;50(2):153-9.
17. Shah SH, Sonawane P, Nahar P, Vaidya S, Salvi S. Pulmonary function tests in type 2 diabetes mellitus and their association with glycemic control and duration of the disease. Lung India. 2013;30(2):108-12.
18. van den Borst B, Gosker HR, Zeegers MP, Schols AM. Pulmonary function in diabetes: a metaanalysis. Chest. 2010;138(2):393-406
19. Irfan M, Jabbar A, Haque AS, Awan S, Hussain SF. Pulmonary functions in patients with diabetes mellitus. Lung India. 2011;28(2):89-92.
20. Díez-Manglano J, Asìn Samper U. Pulmonary function tests in type 2 diabetes: a meta-analysis. ERJ Open Res. 2021;7(1):00371-2020.
21. Sharma A, Sharma A, Chauhan R. Spirometric lung functions in type 2 diabetes mellitus: a hospital-based study. Cureus. 2023;15(5):e38919.
22. Hayfron-Benjamin CF, Agyemang C, van den Born BH, Amoah AGB, Amissah-Arthur KN, Musah L, Abaidoo B, Awula P, Awuviri HW, Abbey JA, Fummey DA, Ackam JN, Asante GO, Hashimoto S, Maitland-van der Zee AH. Associations between spirometric impairments and microvascular complications in type 2 diabetes: a cross-sectional study. BMJ Open. 2023;13(10):e075209.
23. Lange P, Parner J, Schnohr P, Jensen G. Copenhagen City Heart Study: longitudinal analysis of ventilatory capacity in diabetic and nondiabetic adults. Eur Respir J. 2002;20(6):1406-12.
24. Uppal P, Mohammed SA, Rajashekar S, Giri Ravindran S, Kakarla M, Ausaja Gambo M, Yousri Salama M, Haidar Ismail N, Tavalla P, Hamid P. Type 2 Diabetes Mellitus and Asthma: Pathomechanisms of Their Association and Clinical Implications. Cureus. 2023 Mar 12;15(3):e36047.