Section: General Medicine

Original Research Article

EVALUATION OF PULMONARY FUNCTION TEST AND CRP IN TYPE 2 DIABETES MELLITUS – A CROSS-SECTIONAL STUDY

M.Dhanasekar[1], A.Shivaprakasam[2], P.Anandeswari[2], A. Chitrakumar[3]

[1]Consultant, Department of General Medicine, Shri Mani Hospital, Erode, Tamilnadu, India
[2]Assistant Professor, Department of Thoracic Medicine, Government Mohan Kumaramangalam Medical College, Salem, Tamilnadu, India
[3]Professor, Department of Respiratory Medicine, Karpaga Vinayaga Institute of Medical Sciences & Research Centre, Chengalpet, Tamilnadu, India

Received : 15/10/2024
Received in revised form : 04/12/2024
Accepted : 19/12/2024

Keywords:
Type 2 Diabetes Mellitus, Pulmonary function test, CRP, HbA1c and Cross-Sectional Study.

Corresponding Author:
Dr. P.Anandeswari,
Email: anandhipalanivelu1@gmail.com

DOI: 10.47009/jamp.2024.6.6.115

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2024; 6 (6); 607-611

Abstract

Background: Diabetes is a chronic metabolic disease that is characterised by elevated blood glucose levels. This study aimed to determine the association between type 2 Diabetes Mellitus and pulmonary function tests, and to explore the association between pulmonary function and blood glucose, insulin resistance, and C-reactive protein (CRP) levels. **Materials and Methods:** This cross-sectional study included 126 patients and was conducted for 7 months from November 2022 to May 2023 on physically active newly diagnosed T2DM patients in a rural population who attended Shri Mani Hospital, Bhavani, Tamil Nadu. The vital signs of all patients were recorded. Spirometry was performed, and forced vital capacity (FVC) and forced expiratory volume in 1s (FEV1) were measured. The FEV1/FVC ratio was then calculated. Patient's history included gender, in-depth clinical history, physical examination and laboratory investigations were assessed. **Result:** Of 126 newly diagnosed type 2 diabetic patients there was no statistically significant difference in the proportion of HbA1c according to the pulmonary dysfunction pattern (p = 0.111). There was a significantly negative and moderate correlation of HbA1c with FEV1 and FVC, while the correlation with the FEV1/FVC ratio was not statistically significant. FBS and CRP levels also showed a positive and strong correlation (p <0.001). **Conclusion:** There is a possibility of increased restrictive impairment of pulmonary function in the presence of T2DM. It can also be concluded that lung function in T2DM patients is reduced, while there is an increase in CRP values as fasting blood glucose and HBA1c increases.

INTRODUCTION

Diabetes is a chronic metabolic disorder characterised by chronic hyperglycaemia resulting from elevated blood glucose levels. It is characterised by disturbances in the metabolism of carbohydrates, fats, and proteins due to inadequate insulin production. Different and distinct types of diabetes mellitus exist.[1] Diabetes mellitus (DM) is linked to several well-documented comorbidities and chronic complications, such as hypertension, dyslipidaemia, microangiopathy, macroangiopathy, neuropathy, and subclinical pulmonary function impairment.[2]

The understanding of type 2 Diabetes Mellitus (T2DM) has transformed from being considered primarily a metabolic disorder to an inflammatory condition, influenced by the effects of pro-inflammatory and anti-inflammatory cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin-6 (IL-6), and C-reactive protein (CRP).[3] Numerous studies have reported elevated levels of CRP in T2DM, identifying it as an independent biomarker for the disease. While the pathogenesis of type I diabetes has long been recognized for the significant roles played by inflammation and immune mechanisms, recent epidemiologic studies have also highlighted that higher levels of systemic inflammatory markers are linked to type II diabetes.[4]

The decrease in lung volume, impaired pulmonary function, and particularly reduced alveolar gas exchange along with airflow limitations are chronic complications associated with T2DM. Specifically, diabetes-related respiratory complications may lead to alterations in the diffusion capacity and elastic properties of the lungs, as well as the performance of respiratory muscles. Glycemic control plays a significant role in determining the severity of lung dysfunction.[5]

The association between diabetes and abnormal lung function was investigated using spirometry, along with patient history, physical examination, and chest radiography.Spirometry is crucial in detecting the presence and severity of pulmonary impairment and would assist in managing lung diseases.[6] Pulmonary function parameters, including forced expiratory volume in the first second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio, peak expiratory flow rate (PEFR), and FEF25–75%, exhibit significant changes in diabetic patients compared to healthy individuals. The outcomes of pulmonary function tests (PFTs) in patients with Type 2 DM can assist clinicians in enhancing their intervention and management strategies.[7]

Exercise serves as a crucial therapeutic approach and positively influences the prevention of cardiovascular disease in individuals with DM. Individuals with diabetes mellitus (DM) exhibit a reduced capacity for submaximal exercise, as evidenced by lower peak oxygen uptake (VO2peak), a slower rate of increase in oxygen uptake (VO2), and increased ventilatory demand during incremental exercise. Furthermore, a decrease in lung volume has been observed in DM, and reduced exercise capacity is associated with DM and cardiovascular events. Regular respiratory exercises can help strengthen the respiratory muscles, and tight glycaemic control can enhance pulmonary function in type 2 diabetic patients.[8]

Aim

The primary aim of this study was to determine the association between Type2 Diabetes mellitus and pulmonary function test and to explore the association between pulmonary function and blood glucose and C- reactive protein (CRP).

MATERIALS AND METHODS

This cross-sectional study was conducted on 126 newly diagnosed T2DM patients for seven months, from November 2022 to May 2023, attending the Shri Mani Hospital, Bhavani, Tamil Nadu. This population was purposively selected to determine the effect of pulmonary function in a rural population with diabetes who were mostly physically active.

Inclusion Criteria

Patients aged 18–65 years diagnosed with diabetes based on fasting plasma glucose (>125 mg/dl), post-prandial (>199 mg/dl), and HbA1c (>6.4%) levels were included in the study.

Exclusion Criteria

Patients showing chest X-ray (CXR) changes, changes on electrocardiogram (ECG), chronic obstructive pulmonary disorder (COPD), bronchial asthma, gestational diabetes mellitus, or known diabetic were excluded from the study.

All included patients were informed about the study, and written informed consent was obtained from them before the commencement of the study. The informed consent form was administered in English as well as in the local language, and confidentiality was maintained.

An in-depth clinical history, physical examination, and laboratory investigations of all included patients were performed. Data for each patient were collected in a specifically prepared proforma which contained sociodemographic details of the patients, date of diagnosis of T2DM, present and past medical history including peripheral vascular diseases and stroke, and history of habits such as smoking, alcoholism, and diet history. The vital signs of all patients were recorded, including the blood pressure, heart rate, respiratory rate, and SPO2 values. Physical examination was performed to calculate height, weight, and body mass index (BMI). Laboratory investigations included complete blood count (CBC), fasting plasma glucose, post-prandial plasma glucose by GOD PAP method, HBA1c values by capillary tube method, C reactive protein values (CRP) by Latex Enhanced Immunoturbimetry (LEIT) assay, electrocardiography (ECG) and Chest X-ray (CXR).

Spirometry was performed using an NDD Easy One Air portable device and a PC spirometer. The following parameters were measured: forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV1). The FEV1/FVC ratio was then calculated. These tests were conducted using the standard operating protocol at Shri Mani Hospital. The results of all investigations were recorded in the proforma.

Statistical Analysis

Descriptive analysis was performed using frequencies and proportions for categorical variables. Continuous variables were presented as mean ± SD. Pearson’s Correlation coefficient was used to determine the relationship between the two continuous variables. One-way ANOVA with Dunnett’s T3 post-hoc test was used to compare the mean ± SD of continuous variables between more than two groups. Statistical significance was set at $p < 0.05$. Machines IB. IBM SPSS Statistics for Windows, IBM Corp Armonk, NY; Version 22.0 (2013) was used for statistical analysis.

RESULTS

Of 126 patients, 66 (52.4%) were male, and 60 (47.6%) were female. Based on occupation/activities, 97 (77%) patients had moderate activity, 27 (21.4%) engaged in sedentary activities, and 2 (1.6%) involved in heavy activities. Based on the pattern of pulmonary dysfunction, 81 (64.3%) patients had airway restriction, 22 (17.5%) had normal airways, 13 (10.3%) had small airway disease, and 10 (7.9%) had airway obstruction. Based on the HbA1c categories, 53 (42.1%) patients had 6.5 to 8.5, 39 (31%) patients had 8.6 to 10.5, and 34 (27%) had > 10.5. Based on laboratory parameters, the mean ± SD of TC (/µL) was 7400.88 ± 1779.89, PPBS (mg/dL) was 317.72 ± 85.38, FBS (mg/dL) was 199.11 ± 59.12, HB (g/dl) was 11.90 ± 1.93, HbA1c (%) was 9.39 ± 1.74 and CRP (mg/dL) was 9.23 ± 5.14 (Table 1).

Based on the inter-relation patterns of HbA1c and pulmonary dysfunction, out of 15 normal patients, 15 (68.2%) had an HbA1c level of 6.5 to 8.5, 5 (22.7%)

ISSN (O): 2687-5365; ISSN (P): 2753-6556

of patients had 8.6 to 10.5, and 2 (9.1%) of patients had >10.5. Of the 10 patients with airway obstruction, 4 (40%) had an HbA1c level of 6.5 to 8.5, 3 (30%) of patients had 8.6 to 10.5, and the remaining 3 (30%) had >10.5. Out of 81 patients with airway restriction 29 (35.8%) of patients had an HbA1c of 6.5 to 8.5, 27 (33.3%) of patients had >10.5, and 25 (30.9%) of patients had 8.6 to 10.5. Of the 13 patients with small airway disease, six (46.2%) had 8.6 to 10.5, five (38.5%) had 6.5 to 8.5, and the remaining two (15.4%) had HbA1c values of >10.5. There was no statistically significant difference in the proportion of HbA1c according to the pulmonary dysfunction pattern (p = 0.111) (Table 2).

HbA1c and Pulmonary function test

Table 3 depicts a variation in the mean values of pulmonary function parameters in the group of HbA1c and a lack of variation in the mean values of FEV1/FVC in the group of HbA1c. A statistically significant and high correlation was found with HbA1c and CRP (r = 0.889, p<0.001). There was a significantly negative and moderate correlation of HbA1c with FEV1 (r = -0.361, p<0.001), similarly negative and moderate correlation of HbA1c with FVC (r = -0.337, p<0.001) while correlation with FEV1/FVC (r = -0.05, p = 0.580) was statistically not significant.

CRP Vs HBA1c and FBS

A positive and very high correlation between HbA1c and CRP (p<0.001) (Table 4). Similarly, FBS and CRP had a positive and high correlation (p<0.001).

Table 1: Demographic details of the patients

Variable		**Frequency**
Sex	Male	66 (52.4%)
	Female	60 (47.6%)
Occupation/Activities	Moderate	97 (77%)
	Sedentary	27 (21.4%)
	Heavy	2 (1.6%)
Pattern of pulmonary dysfunction	Normal	22 (17.5%)
	Obstruction	10 (7.9%)
	Restriction	81 (64.3%)
	Small Airway Disease	13 (10.3%)
HbA1c Categories	6.5 to 8.5	53 (42.1%)
	8.6 to 10.5	39 (31%)
	>10.5	34 (27%)
Laboratory parameters		Mean ± SD
	HB (g/dl)	11.90 ± 1.93
	TC (/µL)	7400.88 ± 1779.89
	FBS (mg/dL)	199.11 ± 59.12
	PPBS (mg/dL)	317.72 ± 85.38
	HbA1c (%)	9.39 ± 1.74
	CRP (mg/dL)	9.23 ± 5.14

Table 2: Crosstabs between Hba1c and pulmonary dysfunction pattern

Pulmonary dysfunction pattern	**HbA1c**			**P-value**
	6.5 to 8.5	**8.6 to 10.5**	**>10.5**	
Normal (n=22)	15 (68.2%)	5 (22.7%)	2 (9.1%)	0.111
Obstruction (n=10)	4 (40%)	3 (30%)	3 (30%)	
Restriction (n=81)	29 (35.8%)	25 (30.9%)	27 (33.3%)	
Small Airway (n=13)	5 (38.5%)	6 (46.2%)	2 (15.4%)	

Table 3: CRP, FEV1, FVC and FEV1/FVC according to HbA1c

Variable	**HbA1c**			**P-value (One-way ANOVA)**
	6.5 to 8.5 (n=53)	8.6 to 10.5 (n=39)	>10.5 (n=34)	
CRP (Mean ± SD)	5.10 ± 1.51	9.54 ± 2.29	15.31 ± 5.01	<0.001
FEV1 (Mean ± SD)	72.55±16.24	66.15 ± 16.37	57.41 ± 15.90	<0.001
FVC (Mean ± SD)	74.32 ± 14.81	68.82 ± 17.11	60.82 ± 14.90	<0.001
FEV1/FVC (Mean ± SD)	101.23 ± 16.97	99.54 ± 14.16	96.15 ± 16.23	0.351

Table 4: Correlation between CRP Vs HBA1c and FBS

Correlation between:	**Correlation coefficient (95% CI)**	**P-value**
CRP and HbA1c	0.889 (0.831 - 0.939)	**<0.001**
CRP and FBS	0.746 (0.640 - 0.824)	**<0.001**

DISCUSSION

The relationship between diabetes mellitus and lung function remains unclear, and studies on diabetes and lung impairment have shown variable results. Few studies have reported minimal changes in pulmonary function, whereas others have shown major abnormalities.[9,10] The link between T2DM and

ISSN (O): 2687-5365; ISSN (P): 2753-6556

pulmonary function has not been adequately proven. The main findings of this study were negative and moderate correlations between HbA1c values and FVC, FEV1, and FEV1/FVC. This correlation between HbA1C values and FVC and FEV1 was statistically significant, whereas that with the FEV1/FVC ratio was statistically insignificant. The study also showed a statistically insignificant difference in the proportion of HbA1c according to pulmonary dysfunction pattern. A statistically significant and strong correlation was found between CRP and HbA1c, as well as FBS.

Van den Borst et al. reported their study findings which showed that diabetes was associated with a significantly decreased forced expiratory volume in 1 second (FEV1%) and forced vital capacity (FVC%) predicted value with a preserved FEV1/FVC ratio. Similar findings were reported in our study with a significantly negative and moderate correlation of HbA1c with FEV1, and FVC values.[11] The insignificant negative correlation with FEV1/FVC ratio was however opposite to the study conducted by Walter et al. which revealed that the ratio of FEV1/FVC increased by 1.5% in diabetic individuals, and was statistically significant. The difference could be attributed to the fact that they have included COPD patients also in their study.[12]

A previous study conducted by Davis et al. found that there was an average decrease of 9.5% in mean FVC values in diabetic individuals.[13] On similar lines a study by Agarwal and Kaur conducted on 50 diabetics and 50 matched healthy volunteers found that there was a significant reduction in all the PFT parameters (FVC%, FEV1% and FEV1/FVC) in diabetics as compared to controls.[14]

In a study conducted by Kumari et al., 45 patients diagnosed with DM for more than five years and 45 controls were selected. Spirometry was performed for all cases and controls. Patients had lower FVC, FEV1, FEV1/FVC, and PEF than controls, and the difference was statistically significant. A negative weak and insignificant correlation was found between spirometry and Hba1c level and disease duration.[15] Our study findings were consistent with these previous studies, and a negative and moderate correlation of HbA1c with FVC, FEV1, and FEV1/FVC was observed.

In our study, a positive and very high correlation was observed between HbA1c and CRP levels. This coincides with the findings of a study by Kanmani et al. which also showed that there was an association between CRP levels and the incidence of T2DM. It was more prominent among the older group (≥ 50 years) in the latter study.[16] Age correlation was not conducted in our study. Karintholil et al. performed a study that included 80 patients with type 2 diabetes, who were tested using spirometry. The mean predicted values of FEV1/FVC and FVC% showed a restrictive pattern. Thus, the results are consistent with those of the present study. HbA1c was negatively correlated with FEV1/FVC which is consistent with our study findings. BMI had a negative correlation with FVC% predicted.[17]

CONCLUSION

This study indicates that in T2DM patients, lung function is reduced, while CRP values increase as fasting blood glucose and HBA1c increase. There is also a possibility of increased restrictive impairment of pulmonary function in the presence of T2DM. Detecting reduced pulmonary function at early stages can help improve the quality of life of T2DM patients and reduce the burden on healthcare providers. Longitudinal studies with a larger number of participants are required to better understand the link between the duration of diabetes, plasma glucose concentration, and body habits with pulmonary function tests.

REFERENCES

1. Mukhtar Y, Galalain A, Yunusa U. A modern overview on diabetes mellitus: A chronic endocrine disorder. European Journal of Biology 2020;5:1–14. https://doi.org/10.47672/ejb.409.
2. Francisco CO, Catai AM, Moura-Tonello SCG, Lopes SLB, Benze BG, Del Vale AM, et al. Cardiorespiratory fitness, pulmonary function and C-reactive protein levels in nonsmoking individuals with diabetes. Braz J Med Biol Res 2014;47:426–31. https://doi.org/10.1590/1414-431x20143370.
3. Bashir H, Ahmad Bhat S, Majid S, Hamid R, Koul RK, Rehman MU, et al. Role of inflammatory mediators (TNF-α, IL-6, CRP), biochemical and hematological parameters in type 2 diabetes mellitus patients of Kashmir, India. Med J Islam Repub Iran 2020;34:5. https://doi.org/10.34171/mjiri.34.5.
4. Silva LT, Figueiredo MP. Inflammatory markers in chronic diabetic complications: a literature review. Health and Society 2023;3:294–314. https://doi.org/10.51249/hs.v3i03.1415
5. Ali E, Priel E, Brister D, Diab N, Freitag A, Byrne O, et al. The effects of diabetes on gas transfer capacity, lung volumes, muscle strength and cardio-pulmonary responses during exercise. n.d. https://doi.org/10.21203/rs.3.rs-4487541/v1.
6. Al-Khlaiwi T, Alsabih AO, Khan A, Habib SH, Sultan M, Habib SS. Reduced pulmonary functions and respiratory muscle strength in Type 2 diabetes mellitus and its association with glycemic control. Eur Rev Med Pharmacol Sci 2021;25:7363–8. https://doi.org/10.26355/eurrev_202112_27430.
7. Díez-Manglano J, Asìn Samper U. Pulmonary function tests in type 2 diabetes: a meta-analysis. ERJ Open Res 2021;7:00371–2020. https://doi.org/10.1183/23120541.00371-2020.
8. Syeda USA, Battillo D, Visaria A, Malin SK. The importance of exercise for glycemic control in type 2 diabetes. Am J Med Open 2023;9:100031. https://doi.org/10.1016/j.ajmo.2023.100031.
9. Pal YS, Tiwari D, Malik AK, Tiwari DP, Singh M. Pulmonary function tests in diabetes mellitus type 2: a case-control study in a tertiary care centre of Uttar Pradesh. Int J Med Public Health 2024;14:94–8. https://doi.org/10.5530/ijmedph.2024.2.19.
10. Mathur T, Kumar B, Dubey M, Annepu K, Annepu YR, C SG. Evaluating the role of glycemic control in modulating pulmonary function among smokers with diabetes mellitus: A systematic review. Cureus 2024;16:e56895. https://doi.org/10.7759/cureus.56895.

11. Van den Borst B, Gosker HR, Zeegers MP, Schols AMWJ. Pulmonary function in diabetes: a meta-analysis. Chest 2010;138:393–406. https://doi.org/10.1378/chest.09-2622.
12. Walter RE, Beiser A, Givelber RJ, O'Connor GT, Gottlieb DJ. Association between glycemic state and lung function: the Framingham Heart Study: The Framingham heart study. Am J Respir Crit Care Med 2003;167:911–6. https://doi.org/10.1164/rccm.2203022.
13. 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;50:153–9. https://doi.org/10.1016/s0168-8227(00)00166-2.
14. Agarwal N, Kaur S. Pulmonary function tests in type 2 diabetes mellitus. Arch Med Health Sci 2016;4:35. https://doi.org/10.4103/2321-4848.183350.
15. Kumari R, Goswami P, Bhattacharyya DK, Kakati S. Pulmonary function test by spirometry in patients with diabetes mellitus and correlation with disease duration and Hba1c level: a case-control study. Int J Contem Med Res 2021;8:1-5. https://doi.org/10.21276/ijcmr.2021.8.4.4.
16. Kanmani S, Kwon M, Shin M-K, Kim MK. Association of C-reactive protein with risk of developing type 2 diabetes mellitus, and role of obesity and hypertension: A large population-based Korean cohort study. Sci Rep 2019;9:4573. https://doi.org/10.1038/s41598-019-40987-8.
17. Karintholil AR, Aroor AR, Sabu J, Chacko J. Correlation of pulmonary function tests with anthropometry and glycaemic control in type 2 diabetes mellitus-A cross-sectional study. J Clin Diagn Res 2021. https://doi.org/10.7860/jcdr/2021/47275.14778.