**Original Research**

# Spirometric evaluation of Diabetic patients and its correlation with elevated Glycated Haemoglobin levels.

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**ABSTRACT**
**AIM** – To show association between elevated Glycated Haemoglobin levels and its effect on pulmonary function test.
**INTRODUCTION** Diabetes mellitus is a syndrome of hyperglycemia leading to micro as well as macrovascular complications. Diabetes is not directly interlinked with any specific pulmonary symptoms and hence periodic screening for lung disease is not done in diabetic patients. However an extensive micro-vascular circulation and an abundant connective tissue in the lung raise the possibility that the lung may also be a "target organ" in diabetic patients.
**MATERIALS AND METHOD-**. 50 patients of both Type 1 and type 2 DM of the age group 20–70 years taking anti diabetic medications were randomly selected. Controls includes 50 non-diabetic apparently healthy individuals.
**RESULTS-**The mean age for all cases was 45.84 ± 15.40 years. The percentage of the male and female in both the groups were 60% (30) and 40% (20) respectively. Out of 50 diabetes patients, 34 were diagnosed for 5 -10 years and 16 were diagnosed for >10 year. 2 were Type 1 DM and 48 were Type 2 DM. 3 cases were with well controlled diabetes (HbA1c ≤ 7) whereas 47 cases were having uncontrolled diabetes (HbA1c >7). The mean HbA1c was 9.75 ± 2.62.
**CONCLUSION-** DM being a systemic disease, also affects lungs causing both restrictive and obstructive type of ventilatory changes probably because of glycosylation of connective tissues, reduced pulmonary elastic recoil, and inflammatory changes . So, we may conclude that patients with diabetes mellitus have underlying pulmonary dysfunction
**Keywords-** Spirometry, HbA1c,Diabetes mellitus



## INTRODUCTION

Diabetes mellitus is a syndrome of hyperglycemia leading to micro as well as macrovascular complications. It may be either due to impaired insulin secretion or resistance to peripheral actions of insulin, or both[1]. Chronic hyperglycemia along with other metabolic aberrations can cause various complications like retinopathy, nephropathy and neuropathy. T2DM is most commonly seen in elderly population however it is increasingly seen in children, adolescents and younger adults due to rising levels of obesity, physical inactivity and dietary food habits[2]. Investigations for diagnosis of diabetes mellitus include Glycated Hemoglobin (HbA1c), fasting blood sugar (FBS) and post-prandial blood sugar (PPBS). Glycated Hemoglobin (HbA1c) is the most accurate test that reflects average plasma glucose over the previous 3 months. It can be performed at any time of the day and does not require any special preparation such as fasting[3]. HbA1c has now been recommended by an International Committee and by the American Diabetes Association (ADA) as a means to diagnose diabetes. According to American Diabetes Association (ADA), diabetes is diagnosed at an HbA1c of greater than or equal to 6.5 Diabetes is not directly interlinked with any specific pulmonary symptoms and hence periodic screening for lung disease is not done in diabetic patients. However an extensive micro-vascular circulation and an abundant connective tissue in the lung raise the possibility that

the lung may also be a "target organ" in diabetic patients[4]. There are many histopathological changes seen in lungs of diabetics such as thickened alveolar epithelium and pulmonary capillary basal lamina ultimately resulting into reduced pulmonary elastic recoil and lung volumes[5]. Also there is impaired diffusion due to reduced pulmonary capillary blood volume and thickening of the basement membrane. Non–enzymatic glycosylation induced alteration of lung connective tissue is the most likely mechanism underlying the mechanical pulmonary dysfunction in diabetic subjects. The chronic hyperglycaemia damages the connective tissue elements like collagen and elastin associated with pulmonary damage eventually resulting in dysfunction[6]. The patients with diabetes mellitus have impaired immune system which might be the major cause for pulmonary insufficiency.

Clinically diabetic patients present with dyspnoea, wheezing and easy fatigability directing medical professionalstowards coronary artery disease (CAD) than respiratory illness[7]. The respiratory system is also targeted in diabetics and such clinical features might be due to pulmonary complications rather than CAD alone, so prompt evaluation of cardio-respiratory system is must in diabetic patients[8].

The most widely used investigation for determining the pulmonary function is spirometry.

Spirometry is a method of assessing lung function by measuring the volume of air that the patient can expel from the lungs after a maximal inspiration[9]. Pulmonary Function Test (PFT) can assessthe lung volumes and flows, helps in detecting obstructive and restrictive impairment oflung function.

Spirometry findings include -

- FVC – Forced Vital Capacity – the total volume of air that the patient can forcibly exhale in one breath.
- FEV1 – Forced Expiratory Volume in One Second – the volume of air that the patient is able to exhale in the first second of forced expiration.
- FEV1 /FVC – the ratio of FEV1 to FVC expressed as a fraction (previously this was expressed as a percentage).

There are 3 basic patterns to recognize -

NORMAL: FEV1 and FVC above 80% predicted with FEV1/FVC ratio above
0.7

OBSTRUCTIVE: FEV1 below 80% predicted FVC can be normal or reduced – usually to a lesser degree than FEV1 with FEV1/FVC ratio below 0.7

RESTRICTIVE: FEV1 normal or mildly reduced FVC below 80% predicted with FEV1/FVC ratio normal - above 0.7.

Spirometry is now regarded as an important component of any respiratory medical surveillance programme.

## MATERIALS AND METHOD

The study was carried out atNoida International Institute of Medical Sciences , Greater Noida.,–50 patients of both Type 1 and type 2 DM diagnosed by the treating physician, of the age group 20–70 years taking anti diabetic medications were randomly selected from various departments presenting to OPD. Controls includes 50 non-diabetic apparently healthy individuals with similar characters as cases, regarding age group, sex and with similar exclusion criteria as the study group

Inclusion Criteria:

1. Both male and female subjects with type 1 and type 2 diabetes mellitus, 2. Age 20-70 years
3. HbA1c> 6.5%.

Exclusion Criteria:

1. History of smoking,
2. Acute or chronic respiratory disease,
3. History of occupational exposure affecting lung function,
4. Neuromuscular, cardiovascular or end stage kidney disease
5. Physical disability that may affect lung function as kyphoscoliosis, pectus excavatum and pectus carinatum

Detailed personal and medical history of all 50 cases and controls were recorded. PFTs of the patients are measured in a quiet room in sitting position by the trained personnel. Parameters recorded were - forced vital capacity (FVC) in liters, forced expiratory volume in 1 second ($FEV_1$), $FEV_1$/FVC in percentage (%), forced expiratory flow during 25% of FVC ($FEF_{25}$), forced expiratory flow during 50% of FVC ($FEF_{50}$), forced expiratory flow during 75% of FVC ($FEF_{75}$), forced expiratory flow during 25–75% of FVC ($FEF_{25–75}$), forced expiratory flow during 0.2–1.2 liters of FVC ($FEF_{0.2–1.2}$), and peak expiratory flow rate (PEFR). For all these parameters, percentage of predicted values for the respective age, height, and weight were taken into consideration.

HbA1c of all the patients was estimated by ion exchange resin method by the diagnostic glycohemoglobin kits.

PFTs of diabetic patients with increased HbA1c measured and data collected.

## RESULT

The mean age for all cases was 45.84 ± 15.40 years. The maximum age and the minimum was 70 years and 21 years for cases and 70years and 21years for control. The percentage of the male and female in both the groups were 60% (30) and 40% (20) respectively. Out of 50 diabetes patients, 34 were diagnosed for 5 -10 years and 16 were diagnosed for >10 year. 2 were Type 1 DM and 48 were Type 2 DM. 3 cases were with well controlled diabetes (HbA1c ≤ 7) whereas 47 cases were having uncontrolled diabetes (HbA1c >7). The mean HbA1c was 9.75 ± 2.62.

The spirometry parameters were significantly reduced in diabetic subjects compared with controls. 38% of patients have deranged PFT. 24 % of cases had restrictive type of spirometry and 14% had obstructive or mixed pattern of spirometry and the rest had normal pulmonary function.

| Result | A1C |
|---|---|
| **Normal** | less than 5.7% |
| **Prediabetes** | 5.7% to 6.4% |
| **Diabetes** | 6.5% or higher |

**Table 2: Characteristics of selected population**

| | | Case | Control |
|---|---|---|---|
| Age | | 21-70 | 21-70 |
| Gender | Male<br>Female | 30<br>20 | 30<br>20 |
| HbA1c | | >6.5 | |
| Duration ofdiabetes | | >5 YEARS | |
| | TYPE 1<br>TYPE 2 | 2<br>48 | |

**Table 3: Spirometric Findings Of Cases and Controls**

| | CASES | CONTROL |
|---|---|---|
| TOTAL | 50 | 50 |
| OBSTRUCTIVE | 7(14%) | 00 |
| RESTRICTIVE | 12 (24%) | 00 |
| NORMAL | 31 (62%) | 50 |

**DISCUSSION**

Diabetes mellitus being an important risk factor for precipitating micro and macrovascular complications[11]. Various studies on diabetes and pulmonary function test shows variable results, with a few showing minimal changes and others showing significant lung abnormalities. This study aimed to assess the extent of impairment in lung function based on glycaemic control i.e HbA1c values.

The study spirometry, showed that out of 44 subjects 12 were presented with restrictive pattern and 7 presented as obstructive cases of respiratory system. Spirometry findings revealed 27.2% of restrictive cases. Study shows that diabetes mellitus was more common in old age group (< 50 years of age) especially in males[11]. Majority of the patients had abnormal HbA1c values along with deranged FEV1 and FVC values that shows significant association of T2DM and pulmonary fuction. The obstructive cases were 15.9% of the subjects studied. Majority of the diabetics exhibited impaired pulmonary function with reduced FVC and FEV1 and preserved FEV1/FVC indicating a restrictive pattern. The incidence of restrictive pattern was more in patients with HbA1c greater than 9% which may probably be due to the poor control of diabetes associated with impairment in lung function[12]. Amal Abd El-Azeem et al. in 2013,reported predominant reduction in all the spirometry parameters in diabetic patients toward the restrictive pattern as well as there was significant deterioration in DLCO in comparison with healthy controls. Impairment of lung functions was more with a longer duration of diabetes[15].

In a study by Swati H. Shah et al. in 2013, pulmonary function tests (PFTs) of 60 type 2 diabetic male patients and 60 normal healthy male controls aged 40-60 years were compared and associationsbetween FVC and FEV1 and HbA1c and duration of illness in diabetic patients were analysed[16]. It was found that the PFTs were significantly decreased in diabetic patients compared with the healthy controls. Dhiraj Kapoor et al in 2015 studied 90 cases and 90 matched controls. Patients with type 2 DM patients as compare to its controls were observed to have restrictive pattern of lung dysfunction[17]. In addition, it was found that long duration of DM was significantly correlated with lung dysfunction. Simran Kaur et al in 2016 studied 50 diabetics and 50 matched apparently healthy volunteers. It was seen that there was significant change in all the PFT parameters in diabetics as compared to controls. The major potential mechanisms underlying the association between glycaemic exposure and abnormal lung function are microangiopathy of the pulmonary vascular network and chronic low-grade tissue inflammation[18]. Normal lung mechanics and gas exchange are influenced by the integrity of the pulmonary connective tissue and microvasculature. Acceleration of aging process in connective tissue cross links and presence of nonenzymatic glycosylation and modification of alveolar surfactant action causes reduction in PFTs. There have been reports of histopathological changes in the diabetic patients.

In the study by Weynand *et al*., it was found that alveolar epithelium, endothelium capillary, and basal laminas were thickened in lungs on electron

microscopy, when compared with the controls. In addition, the thickening of basal lamina was of the same magnitude in lung and kidney. Diabetic microangiopathy might be existing in the pulmonary vascular bed[19]. Moreover, reduced pulmonary capillary blood volume was found, favouring the evidence of microangiopathy. This could lead to redistribution of the pulmonary circulation, resulting in well-ventilated areas to become hypoperfused. The thorax and lungs are rich in collagen and elastin. Stiffening of thorax and lung parenchyma can occur because of nonenzymatic glycosylation of these structural compounds ultimately leading to restrictive physiology. Our data also provide insight into the relationship between HbA1c level and impaired lung function that reveals a non-linear association between deranged PFTs and elevated Hb1Ac values indicating the long-term effects of T2DM on the lungs. This is supported by the Sweet Breath Study, in which 60 subjects received a 3-month intensified treatment for diabetes and this short-term benefit of glycaemic control on pulmonary function was profound for good responders (defined as an HbA1c decrease > 0.5% after treatment), who exhibited a significant improvement in spirometry values between baseline at the end of the study[20]. This clearly depicts that poor glycaemic control is associated with decline in pulmonary function.

## SUMMARY AND CONCLUSION

DM being a systemic disease, also affects lungs causing both restrictive and obstructive type of ventilatory changes probably because of glycosylation of connective tissues, reduced pulmonary elastic recoil, and inflammatory changes in lungs. So, we may conclude that patients with diabetes mellitus have underlying pulmonary dysfunction and the assessment of pulmonary function is an important investigation. Early detection of functional impairment and its appropriate treatment will probably help to reduce morbidity and mortality especially in situation of acute on chronic lung diseases. We found that impaired glycemic control can be one of the determinants of lung pathology, which requires further research.

## REFERENCES

1. Kumari, et al. Pulmonary Function Test by Spirometry in Patients with Diabetes Mellitus International Journal of Contemporary Medical Research Section: Medicine ISSN (Online): 2393-915X; (Print): 2454-7379 | Volume 8
2. World Health Organization. Fact sheet: Diabetes No 312, November 2008. [Last accessed on 2009 Apr 14]
3. King H, Aubert RE, Herman WH. Global burden of diabetes 1995 to 2025.
4. Prevalence, numerical estimates and projections. Diabetes Care. 1998;21:1414–31.
5. Sandler M. Is the lung is target organ in diabetes mellitus? Arch Intern Med. 1990;150:1385–8.
6. Klein OL, Krishnan JA, Jlick S, Smith LJ. Systematic review of association between lung function and type 2 diabetes mellitus. Diabet Med. 2010;27:977–87.
7. Hamlin CR, Kohn RR, Luschin JH. Apparent accelerated aging of human collagen in diabetes mellitus. Diabetes. 1975;24:902–4
8. Alfino Validita Sidiq//Yetti Hernaningsih//Puspa Wardhani//Soebagijo Adi Soelistijo, Differences in AGEs and hs-CRP between Type 2 Diabetes Mellitus with and without Complications.
9. The Journal of Bucharest College of Physicians and the Romanian Academy of Medical Sciences, June 26, 2023
10. Larsen, Kronenberg, Melmed P. Williams's textbook endocrinology. 10th ed. Elsevier India Publisher.
11. Marvisi M1, Bartolini L, del Borrello P, Brianti M, Marani G, Guariglia A CA. Pulmonary function in non-insulin-dependent diabetes mellitus. Respiration. 2001;68:268–72.
12. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. 2005;26:319–38.
13. Kaparianos A. AE and SF. Pulmonary complications in diabetes mellitus. Chron Respir Dis. 2008;5:101–8.
14. Michael. DG. Lung dysfunction in diabetes. Diabetes Care. 2003;26:1915
15. Leahy T.L., Clark N.G., Cefalu WT, editor. Medical management of diabetes mellitus. CRC Press; 2000 Feb 17.
16. Diabetes Control and Complications Trial Research Group, Nathan DM, Genuth S, Lachin J, Cleary P, Crofford O, Davis M, Rand L SC. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus,. N Eng J Med,. 1993;329:977–86.
17. Sreeja C.K, Elizabeth Samuel, C.Kesava Chandra SS. Pulmonary function in patients with diabetes mellitus. IJPP. 2003;47:87–93.
18. Irfan M, Jabbar A, Haque AS, Awan S, Hussain SF. Pulmonary functions in patients with diabetes mellitus. 2011;28:89–92.
19. Kumar M AS. Diabetes in Elderly: Pulmonary Complication in Elderly Diabetics. Bangalore Micro Labs Ltd; 2005;119–25.
20. Borst BB, Gosker HR, Zeegers MP SA. Pulmonary function in Diabetes: A Metaanalysis. Chest. 2010;138:393–406.
21. Shravya Keerthi G, Sharan B Singh M, Hari Krishna Bandi, Suresh M, Preetham J K MRN. Deterioration of Pulmonary Functions in Type 2 Diabetes Mellitus. OSR J Pharm Biol Sci. 2012;1:39–43.
22. Kaur S, Agarwal N. Pulmonary function tests in type 2 diabetes mellitus.2016;4:35–9