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Effect of duration of Type 2 Diabetes Mellitus on Lung Function Tests --- Original research article

Dr. Garima Charak[*1], Dr.Anupama Kaur[2], Dr.Surinder Kaur[3], Dr.Sonia Kocchar[4]

[1]*Senior Resident, Department Of Physiology Ascoms & Hospitals, Sibhra, Jammu*
[2]*Associate Professor, Department Of Physiology Mmimsr, Mullana*
[3]*Professor, Department Of Physiology Mmimsr, Mullana*
[4]*Professor, Department Of Physiology Mmimsr, Mullana*

Abstract: *India is called Diabetic capital of the world as there are going to be 80% of all diabetes from the entire world population, concentrated here. The complications which are caused by diabetes mellitus have become a challenging health problem. Like other target organs lung is also affected in diabetes.the present study was conducted to see the effect of duration of Type 2 Diabetes Mellitus on Lung function tests***.**
Method*: Study Group consisted of 50 subjects with type 2 Diabetes mellitus and is further divided into 2 subgroups:Sub-Group A:-Patients with duration of diabetes for 5 to 10 years. Sub-Group B:-Patients with duration of diabetes for more than 10 years. Pulmonary function tests were performed using computerized spirometer, Spiro – Excel.*
Summary And Conclusion *Observations of various parameters are that Diabetics for more than10 years had statistically significant reduction in FVC with p value (0.046) when compared with those Diabetic for 5-10 years. However, in Diabetics for more than10 years there was no significant difference for FEV1/FVC% relative to the other group with p value (0.490), no significant difference in PEFR relative to Group with Diabetics less than 5 years with p value (0.087) and no significant difference in FEV1 relative to Diabetics with duration of Diabetes less than 5 years with p value (0.053). Hence, as duration of Diabetes increases there is decline in Pulmonary function tests.Spirometry remains a simple and cost effective tool and its judicious use can warn patients to take early preventive measures.*

I. Introduction

The prevalence of Type 2 Diabetes in Asian Indians is the highest prevalence in the world.[1,2] India is called Diabetic Capital of World as there are going to be 80% of all diabetes from the entire world population, concentrated here. Type 2 Diabetes comprises 90% of people with diabetes all around the world, and is largely the result of excess body weight and physical inactivity. Diabetes mellitus is associated with long term damage, dysfunction and failure of various organs and its complications are mostly due to macro vascular and micro vascular damage; include cardiovascular disease, nephropathy, diabetic retinopathy, neuropathy and lung damage.[3,4] As we know Diabetes Mellitus is a multisystem disorders that affects many organs of the body. These complications are mainly a consequence of macrovascular and microvascular damages of the target organs. The microvascular complications appear early within 5 to 10 years and macro vascular complications appear within 15 to 20years from the onset of diabetes.

Like other target organs lung is also affected in diabetes. The presence of an extensive micro vascular circulation and abundant connective tissue in the lungs, raises the possibility that lung tissue may be affected by micro angiopathy process and non-enzymatic glycosylation of tissue proteins,included by chronic hyperglycemia, there by rendering the lung a "target organ" in diabetic patients. Hyperglycemia causes thickening of basal lamina in pulmonary capillaries leading to decreased diffusion capacity. The alteration in scleroproteins in turn affects mechanical properties of lungs. In this chronic disease susceptibility and severity of systemic inflammation increases which may cause peripheral airway obstruction .[5,6]

II. Review of literature

Diabetes mellitus is one of the world's oldest known disease. A remedy for diabetes was discovered in the 20th century though diabetes mellitus was first described 3500 years ago. The discovery of insulin for the tr atment of diabetes represents one of the major humanitarian and scientific milestones of the 20th century.[7] Schuyler M R et al observed that decreased elastic recoil at low lung volumes in juvenile diabetes mellitus was similar to that found in aging and was consistent in functional integrity of elastin. The authors further reported that in diabetes, total lung capacity (TLC) was significantly smaller than that of normal control subjects which could be due to alteration of collagen matrix which renders it less distensible at high lung volumes, limits the expansion of lungs or causes difference in lung maturation.

The changes observed in pressure volume curve could be due to alteration of collagen and elastin. It was postulated that these changes were related to subtle abnormalities in lung scleroproteins. The authors also observed similar changes in other organs.[8] Kida et al reported that an ultrastructural study of lungs from patients with both juvenile and adult onset diabetes mellitus showed that the alveolar basal laminae were slightly thicker than those of age matched control subjects. Biochemical data indicated that Lysyl oxidase activity, an enzyme related to cross linking of elastin and collagen was elevated in experimental diabetes. Administration of β aminopropionitrile, which inhibits Lysyl oxidase activity in rats in early postnatal life produced lungs that had too few but enlarged alveoli therefore it was possible that Lysyl oxidase might induce structural alterations of the elastic-collagen network with consequent changes in lung structure and lung function.[9]Sandler reported that major long-term complications of diabetes mellitus is currently thought to involve both microangiopathic process and non-enzymatic glycosylation (NEG) of tissue proteins. The most consistent abnormalities were reduced lung volumes in young (aged < 25 years) insulin dependent diabetic subjects, reduced pulmonary elastic recoil in both young and adult (aged > 25 years) diabetic subjects and impaired diffusion due to reduced pulmonary capillary blood volume in the adult age group. Non-enzymatic glycosylation induced alteration of lung connective tissue was the most likely pathogenic mechanism underlying mechanical pulmonary dysfunction in diabetic subjects while most tenable explanation for impaired diffusion in these patients was the presence of underlying pulmonary microangiopathy. [10] Lange et al reported from the subjects enrolled in the Copehhagen city heart study that there was slight reduction in FEV1 and FVC in all age groups among subjects with both IDDM and NIDDM. In addition authors reported that subjects with more prounced hyperglycemia had the most pronounced reduction of ventilator function.

The study showed that the subjects with newly developed Diabetes mellitus have almost twice as high a decline of ventilator functions as the non diabetic subjects. Subjects who have had Diabetes mellitus for some year experience a decline of ventilatory function which is not significantly greater than decline observed among non-diabetic subjects. So authors suggested that the excessive decline of ventilator function in subjects with newly developed Diabetes mellitus might be due to cross linking of pulmonary collagen.[11]Meo S A et al conducted the study in the Department of Physiology, College of Medicine, King Khalid University Hospital and Diabetic Centre, King Abdul-Aziz University Hospital, Riyadh, Saudi Arabia and randomly selected a group of 32 apparently healthy volunteer male type 2 diabetic patients with an age range from 24-73 years. They matched the diabetic patients with another group of 40 control healthy male subjects in terms of age, height, weight, and socioeconomic status. Spirometry was performed using Electronic Spirometer (Schiller AT-2 Plus, Switzerland) and results were compared using the 2-tailed student t-test. It was found that Diabetic patients showed a significant reduction in the forced vital capacity (FVC), forced expiratory volume in one second (FEV1) and peak expiratory flow (PEF) relative to their matched controls. However, there were no significant difference in the forced expiratory ratio (FEV1/FVC%) and middle half of the FVC (FEF 25-75%) between the groups. So it was concluded that lung function in type 2 diabetic patients is impaired by a decrease in FVC, FEV1 and PEF, as compared to their matched controls.[12]Swaty H Shah et al conducted a study to analyze the pulmonary function parameters in diabetic patients and compare them with age and gender matched healthy subjects.

Pulmonary function tests (PFTs) were recorded in 60 type 2 diabetic male patients and 60 normal healthy male controls aged 40-60 years by using Helios 702 spirometer. The PFTs recorded were - FVC, FEV1, FEV1/FVC, FEF25, FEF50, FEF75, FEF25–75, FEF0.2–1.2, and peak expiratory flow rate (PEFR). HbA1c of all the patients was estimated by ion exchange resin method, which is a very standard method of estimation. PFTs of diabetic patients and controls were compared by applying Student′s unpaired t test. Associations between FVC and FEV1 and HbA1c and duration of illness in diabetic patients were analyzed by applying Pearson′s coefficient. In the study it was seen that the PFTs were significantly decreased in diabetic patients compared with the healthy controls except FEV1/FVC. There was no correlation found between FVC and FEV1 and duration of illness as well as HbA1c and thus concluded that DM being a systemic disease, which also affects lungs causing restrictive type of ventilatory changes probably because of glycosylation of connective tissues, reduced pulmonary elastic recoil and inflammatory changes in lungs.[13]

Aims And Objectives

- To study the pulmonary function of individuals with Type 2 Diabetes mellitus.
- To assess the extent of impairement in lung functions and its relation to the duration of Diabetes Mellitus.

The anthroprometric data i.e height, weight, Body Mass Index (BMI) were recorded and pulmonary function tests performed.

Technique

The equipment used was computerized spirometer, Spiro-Excel (Medicaid systems Chandigarh). It had a turbine flow meter and the range for flow measurement is 0.03

L/sec. Range for volume measurement is 0-10 L. The subject was made to sit comfortably. The subject was asked to breathe in and out to familiarize himself with of disease.

III. Material And Methods

This study was conducted in the Department of Physiology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana (Ambala) in collaboration with Department of Medicine. Subjects were selected from patients visiting O.P.D or admitted in the hospital of M.M.I.M.S.R during January 2014 to January 2015

Study Group consisted of 50 subjects with type 2 Diabetes mellitus and is further divided into 2 subgroups:
Sub-Group A:-Patients with duration of diabetes for 5 to 10 years.
Sub-Group B:-Patients with duration of diabetes for more than 10 years.

Inclusive Criteria:-

- Age 45 years and above.
- Patients suffering from Type 2 Diabetes mellitus and attending O.P.D or admitted in hospital of M.M.I.M.S.R.

Exclusive Criteria:-

- Subjects with gross abnormalities of the vertebral column or thoracic cage. The subject was then asked to inhale to his maximum capacity and forcefully blow out into the sensor (nose clipped) as hard as possible for as long as possible. This procedure was repeated and the best of three readings was considered for analysis. Data was tabulated and statistically analysed.

The parameters recorded were:-

A) Physical Parameters
Height:-A vertical measuring rod was fixed to the wall and the subjects were asked to remove the shoes and stand on flat floor in front of measuring rod with feet parallel and heels, buttocks, shoulders and back of head touching upright side. The head was held comfortably erect with lower border of the orbit in the same horizontal plane as the external auditory meatus. The arms were kept hanging by the sides in natural manner. The horizontal bar of the measuring rod was lowered to touch the head. The height was recorded to the nearest centimetre (cm). WEIGHT:-The platform beam balance was used to record the weight. The subjects were asked to remove the shoes and wear minimum clothing"s and stand on the center of the platform. The reading was recorded to the nearest kilogram (kg).

Body Mass Index:- **Body mass index was calculated by:-**
Quetelet's Index i.e $\frac{\text{Weight(kg)}}{\text{Height(m2)}}$

B) Pulmonary Function Parameters:-
Medspiror was used to calculate the following parameters:-

1. Forced Vital Capacity (FVC):- It is maximum volume of gas that can be expired when the patient exhales as forcefully and rapidly as possible after a maximal inspiration. FVC will be smaller in both obstructive and restrictive disorders and is not of a concern unless it is 75-85% of predicted volumes. FVC alone cannot give the diagnosis of obstructive or restrictive. FVC is measure in litres.

2. Forced Expiratory Volume in 1 second (FEV1):- FEV1 measures the volume of air expired forcefully over the first second of an FVC maneuver. FEV1 reported as a volume, although it measures flow over specific intervals. Healthy individuals are able to expel 75-80% of their vital capacity in 1 second of FVC test. Low FEV1 is highly suggestive of obstructive diseases.

3. FEV1/FVC ratio: - The most standardized index of airway obstructive disease, related to ability to work and function in life. FEV1/FVC ratio expressed as % is used to determine of the pattern is obstructive, restrictive or normal. A low FEV1/FVC ratio indicates an obstructive pattern where as if ratio is normal and FVC value is low, it indicates restrictive pattern and a normal FVC value indicate normal pattern.

4. Peak Expiratory Flow Rate:- It is the maximum rate of airflow observed during a sudden forced expiration, from the position of full inspiration. It is measured in litres per second .

Table 1: Table showing overall comparison of physical parameters of the subjects belonging to different groups i.e. Group B (Diabetic above 10 yrs) and Group A (Diabetic for 5-10 yrs).

	Group	N	Mean	SD	T-Test	P value
Age (Years)	B	25	51.92	4.82	0.077	0.939
	A	25	51.80	6.10		
Height (cms)	B	25	163.28	8.44	0.329	0.744
	A	25	162.56	6.99		
Weight (Kg)	B	25	68.88	9.77	0.612	0.543
	A	25	66.96	12.27		
BMI (Kg/m2)	B	25	26.16	3.77	0.413	0.682
	A	25	25.60	5.71		

Table shows mean age of Group A as (51.80± 6.10) and mean age of Group B as (51.92 ± 4.82) which is found to be statistically insignificant (p = 0.939).It also shows mean height of Group A as (162.56±6.99) and mean height of Group B as (163.28± 8.44) which is also found to be statistically insignificant (p=0.744).Also depicting mean weight of Group A as (66.96± 12.27) and mean weight of Group B as (68.88±9.77) which was also statistically insignificant (p = 0.543).Mean B.M.I of Group A was found to be (25.60±5.71) and mean B.M.I of Group B was (26.16±3.77)
which was statistically insignificant (p=0.682).

B) Pulmonary Function Parameters

Table 2:- Table showing overall comparison of Lung Volumes among Group B (Diabetic > 10 years) and Group A (Diabetic for 5-10 years).

	Group	N	Mean	SD	T-Test	P value
FVC (L)	B	25	2.18	0.40	2.051	0.046
	A	25	2.41	0.37		
FEV1 (L)	B	25	1.83	0.56	1.980	0.053
	A	25	2.11	0.43		
PEFR (L/Sec)	B	25	5.06	1.38	1.748	0.087
	A	25	5.79	1.57		
FEV1/FVC%	B	25	84.84	10.75	0.696	0.490
	A	25	86.90	10.22		

Table shows mean FVC of Group A as (2.41± 0.37) and mean FVC of Group B as (2.18 ± 0.40) which is found to be statistically significant (p = 0.046).It also shows mean FEV1 of Group A as (2.11±0.43) and mean FEV1 of Group B as (1.83± 0.56) which is also found to be statistically insignificant (p=0.053).Also depicting mean PEFR of Group A as (5.79± 1.57) and mean PEFR of Group B as (5.06±1.38) which was also statistically not significant (p = 0.087). Mean FEV1/FVC of Group A was found to be (86.90±10.22) and mean FEV1/FVC of Group B was (84.84±10.75) which was also statistically insignificant (p=0.490)

B) Biochemical Parameters

Table 3:- Table showing overall comparison of mean BGF among Group B (Diabetic > 10 years) and Group A (Diabetic for 5-10 years).

	Group	N	Mean	SD	T -Test	P value
BGF(mg%)	B	25	146.76	38.26	1.785	0.081
	A	25	130.92	22.48		

The overall mean BGF ± S.D in Group B was 146.76 ± 38.26 mg% and in Group A was 130 ± 22.48 mg%. There was no statistical significant difference seen in the mean BGF of the subjects on intergroup comparison.

IV. Discussion

The present study was conducted in the Department of physiology, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana (Ambala) in collaboration with Department of Medicine to observe the alterations in lung functions in patients with Diabetes Mellitus. Various observations depending on duration of disease and pulmonary function impairment were analysed.

The aim of present study was to assess the extent of impairement in lung functions and its relation to the duration of disease. Pulmonary functions i.e PEFR, FEV1, FVC, FEV1/FVC% were determined using computerized spirometer (spiro-excel) .

Total 50 subjects were taken. All subjects were males. Study group was further divided into 2 groups according to the duration of diabetes mellitus.

GROUP A - Duration of Diabetes 5-10 years – 25 Subjects.

GROUP B - Duration of Diabetes more than 10 years – 25 Subjects.

Physical Parameters:-

The mean age is comparable in Group A & Group B. There is no significant difference in the age between the two groups.($p = 0.939$).

There is no statistically significant difference in weight of Group A & B. ($p = 0.345$).

The mean height of Group A vs Group B is also not significant ($p = 0.744$).

The mean BMI in the two groups is compared.The mean B.M.I of Group A vs Group B is also not significant ($p = 0.682$).

The observations of present study are in agreement with observations made by Shravya Keerthi G et al[15] who reported that there is no significant difference in the anthropometric data such as age, height, weight and body mass index between the two groups.

Pulmonary Function Parameters

Forced Vital Capacity:-

The forced vital capacity represents the largest amount of air that can be expired after a maximal inspiratory effort, is frequently measured as an index of pulmonary function. It gives useful information about the strength of the respiratory muscles and other aspects of pulmonary function.[14] In the present study, the mean value of FVC were 2.41 litres, 2.18 litres in males of Group A, Group B respectively.

On Comparison Of Duration Of Disease Between (5-10 Years) & (>10 years)

Type 2 Diabetic Patients with disease for > 10 years (Group B) showed a significant reduction in FVC 2.18 ± 0.40 litres relative to their matched Type 2 Diabetic Patients with disease for 5-10 years (GroupA) with FVC 2.41 ± 0.37 litres. Type 2 diabetic patients > 10 years also had a statistically significant reduction in FVC ($p = 0.046$).

Our observations are in agreement with Meo S A et al who in their studies on Saudi diabetic patients showed significant reduction in FVC as compared to their matched control. They also showed a strong association with a dose-effect response of duration of disease and decreased pulmonary function impairment in diabetic patient.[16] Shravya Keerthi G et al demonstrated that there was significant reduction in mean FVC in all diabetic patients and the reduction was more pronounced with increased duration of diabetes.[17] Amal Abd El-Azeem et al reported that impairement of lung functions was obvious with a longer duration of diabetes and thus concluded that Diabetes is associated with a significant impaired pulmonary function in a restrictive pattern as compared to nondiabetics. The pulmonary function impairement was found to be more marked with diabetic duration especially after 10 years.[18]

Forced Expiratory Volume In One Second (Fev1):-

The fraction of the vital capacity expired during the first second of a forced expiration is referred to as FEV1.

In the present study, the mean value of FEV1 were 2.11 litres, 1.83 litres in males of Group A, Group B respectively On Comparison Of Duration Of Disease Between (5-10 Years) & (>10 Years)

Type 2 Diabetic Patients with disease for > 10 years (Group B) showed a reduction in FEV1 1.83 ± 0.56 litres relative to their matched Type 2 Diabetic Patients with disease for 5-10 years (Group A) with FEV1 2.11 ± 0.43 litres. Type 2 diabetic patients > 10 years had no statistically significant reduction in FEV1 with ($p = 0.046$).

Our observations are quite in agreement with Davis et al who demonstrated that FEV1 were decreased in type 2 Diabetic patients and also suggested that the reduced lung volumes and airflow limitations are likely to be chronic complication of type 2 diabetes.[19]Shravya Keerthi G et al demonstrated that there was significant reduction in mean FVC in all diabetic patients and the reduction was more pronounced with increased duration of diabetes.[20]

Peak Expiratory Flow Rate (Pefr):-

In the present study, the mean value of PEFR were 5.79 litres/sec, 5.06 litres/sec in males of Group A, Group B respectively.

On Comparison Of Duration Of Disease Between (5-10 Years) & (>10 YEARS) Type 2 Diabetic Patients with disease for > 10 years (Group B) showed a reduction in PEFR 5.06 ± 1.38 litres/sec relative to their matched Type 2 Diabetic Patients with disease for 5-10 years (Group A) with PEFR 5.79 ± 1.57 litres/sec. Type 2 diabetic patients > 10 years had no statisticaly significant reduction in PEFR with ($p = 0.087$).Studies done by Timothy M E Davis and Sreeja et al also showed a decrease in PEFR.[21,22]FEV1/FVC **Ratio:-** FEV1/FVC% is the volume of air expired in the first second, expressed as percentage of FVC. It is more

sensitive indicator of airway obstruction than FVC or FEV1. The alteration in collagen and elastic ratio is the main factor in the diabetic patient. The decrease in FEV1/FVC% in diabetic subjects may be related with the poor mechanical properties of the lung, like lung compliance and elastic recoil of lung. Loss of elastic recoil leads to dynamic collapse of small airways during expiration. In addition, myopathic or neuropathic changes affecting the respiratory muscles further impairs the endurance, efficiency of ventilator pump.[17] In the present study, the mean value of FVC/FEV1% were 86.90%, 84.84% in males of Group A, Group B respectively.

On Comparison Of Duration Of Disease Between (5-10 Years) & (>10 Years)

Type 2 Diabetic Patients with disease for > 10 years (Group B) showed a reduction in FEV1/FVC% i.e 84.84% relative to their matched Type 2 Diabetic Patients with disease for 5-10 years (Group A) with FEV1/FVC i.e 86.90%. Type 2 diabetic patients > 10 years had reduction in FEV1/FVC% but it was not statistically significant with ($p = 0.490$).

Similar observations were reported by Meo et al who reported that there was no significant difference for FEV1/FVC% relative to control.[16]

V. Summary And Conclusion

Observations of various parameters i.e FVC, FEV1,PEFR and FEV1/FVC% in all subjects were as follows:-

Group B (Diabetic for more than10 years) had statistically significant reduction in FVC with p value (0.046) when compared with Group A (Diabetic for 5-10 years).

However in Group B (Diabetic for more than10 years) there was no significant difference for FEV1/FVC% relative to Group A with p value (0.490), no significant difference in PEFR relative to relative to Group A with p value (0.087) and no significant difference in FEV1 relative to Group A with p value (0.053).

BGF on intergroup comparison of GroupB (Diabetic for more than 10 years) and Group A (Diabetic for 5-10 years) revealed that no statistical significant difference existed between the groups with p value (0.081). The values were much less in the subjects with diabetes for more than 10 years of disease (Group B) when compared with that of subjects having diabetes for 5-10 years (Group A). The differences were not statistically significant except for FVC. It is also observed that as the duration of diabetes increases, the values of pulmonary function tests are significantly reduced and the lowest values are seen in Group B who had been suffering from diabetes for more than 10 years. Hence, as duration of Diabetes increases there is decline in Pulmonary function tests.Spirometry remains a simple and cost effective tool and its judicious use can warn patients to take early preventive measures.

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DR.ANUPAMA KAUR is no longer affiliated with M.M.I.M.S.R. However this work was done during her stay in the organization.