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Original Article

Pulmonary Function Tests Among Type 2 Diabetes Mellitus Patients And Their Association With Glycemic Control At Tertiary Care Teaching Hospital.

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ABSTRACT

Introduction: Type 2 diabetes mellitus is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Type 2 DM is preceded by a period of abnormal glucose homeostasis classified as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). Respiration is the process by which oxygen and CO2 are exchanged between the atmosphere and the mixed venous blood to meet the metabolic demands of the body. Clear decrements in lung function have been reported in patients with diabetes over the past 2 decades, and many reports have suggested plausible pathophysiological mechanisms. However, at the present time, there are no reports of functional limitations of activities of daily living ascribable to pulmonary disease in patients with diabetes. ***Material and Methods:*** The study was carried out in collaboration with Diabetes Outpatient Department of Tertiary Care Teaching Hospital. One hundred and two patients of type 2 DM diagnosed by the treating physician, of the age group 40–60 years taking oral hypoglycemics, were randomly selected from the94 Diabetes Outpatient Department. One hundred and two patients' normal healthy males and females of the same age group and socioeconomic status from patient's relatives were selected as control group. The controls were also thoroughly examined clinically. Those with cardio-respiratory, musculoskeletal, or endocrine diseases were excluded from the study. Fasting and postprandial blood glucose levels were measured by glucose oxidase method to rule out type 2 DM in them. ***Results:*** The comparison of fasting blood sugar (FBS) and Glycosylated hemoglobin (HbA1c) level among cases and controls. Mean FBS level of 197.50 among cases much higher than the control group which is 86.42. HbA1c levels also show the similar trend of having a higher mean value of 7.78 comparative to 4.34 among controls. The comparison of PFT among study and control group. Blood pressure variation among cases both in males and females. In our present study we have found that female cases are mostly normotensive (81% of total female cases) comparing to only 11% in male cases. Hypertension is more prevalent in male cases constituting 67% of all male cases, whereas only 5% female cases are hypertensive. Blood pressure is found to be in pre hypertension range in 14% female cases and 22 % of male cases. The mean FVC in the control group is approximately 11.98% higher than in the study group. The mean FEV1 in the control group is approximately 12.30% higher than in the study group. The mean PEFR in the control group is approximately 6.89% higher than in the study group. The mean FEF 25%-75% in

the control group is significantly higher, approximately 27.41% higher than in the study group. The mean FEV1/FVC ratio in the control group is approximately 6.12% higher than in the study group. ***Conclusion:*** Lung function is severely affected in type 2 diabetics patients indicating that lung is a target organ of long term complication of type 2 diabetes. Long term glycaemic control i.e. HbA1c is a major determinant of this deterioration rather than the duration of disease. Females are more prone to be affected than their male counterpart.

Keywords*: Type 2 diabetes, Pulmonary function tests, Respiration.*

INTRODUCTION

DM is classified on the basis of the pathogenic process that leads to hyperglycemia. There are two broad categories of DM, designated type 1 and type 2. However, there is increasing recognition of other forms of diabetes in which the pathogenesis is better understood. Type 1 DM is the result of complete or near-total insulin deficiency. Type 2 DM is a heterogeneous group of disorders characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. Type 2 DM is preceded by a period of abnormal glucose homeostasis classified as impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). [1]

The identification of patients with diabetes or pre-diabetes by screening allows for earlier intervention, with potential reductions in future complication rates. The persons having risk factors of developing type 2 diabetes mellitus should be screened [2]. About 25% of patients with type 2 DM already have microvascular complications at the time of diagnosis suggesting that they have had the disease for more than 5 years at the time of diagnosis. [3]

Respiration is the process by which oxygen and CO2 are exchanged between the atmosphere and the mixed venous blood to meet the metabolic demands of the body. This is achieved by the integrated physiological processes of ventilation, pulmonary blood flow and gaseous diffusion. [4]

Spirometry is the most widely used noninvasive test of ventilatory function and assesses the mechanical or bellows properties of the pulmonary system by measurement of the dynamic or respired lung volumes and capacities. It is a physiological test for assessing the functional aspect of the lungs using an objective indicator by measuring the amount of air that a patient can inhale and exhale to the maximum. [5] When combined with the measurement of arterial gas tensions or pulmonary gas exchange, it provides an overall assessment of lung function suitable for the detection, differentiation and diagnosis of various respiratory diseases, and an objective method for following disease progression or improvement and therapeutic response over time. [6]

Clear decrements in lung function have been reported in patients with diabetes over the past 2 decades, and many reports have suggested plausible pathophysiological mechanisms. However, at the present time, there are no reports of functional limitations of activities of daily living ascribable to pulmonary disease in patients with diabetes. [7]

In contrast to the substantial evidence supporting the concept of the lung as a target organ for diabetic microangiopathy, reports of lung mechanical abnormalities in diabetes have been less convincing. Most reports of lung mechanical function have utilized spirometric PFTs, which are commonly interpreted as indicative of airflow obstruction. In practice, however, PFTs are influenced by a wide variety of factors: they are physically demanding, maximally forced, coordinated efforts that are subject to deterioration with any debilitating disease, aging, loss of muscle strength from any cause, and obesity.

Thus, routine clinical lung function tests may not detect the presence of modest lung function abnormalities in diabetes, either early pulmonary microangiopathy or early peripheral airway disease. While more sensitive tests reveal such abnormalities, there is no clear evidence at the present time of clinically significant lung disease in patients with diabetes who have modest lung function abnormalities. However, another more important issue has yet to be addressed, namely the increased deterioration of lung function over time in patients with diabetes, particularly with respect to the impact of inhalational delivery of pharmacological agents.

MATERIALS AND METHODS

The study was carried out in collaboration with Diabetes Outpatient Department of Tertiary Care Teaching Hospital. One hundred and two patients of type 2 DM diagnosed by the treating physician, of the age group 40–60 years taking oral hypoglycemics, were randomly selected from the Diabetes Outpatient Department.

Exclusion criteria

1. Patients having complaints of cough, sputum, or dyspnoea.
2. Smokers and patients with any cardio-respiratory illnesses or major diseases.

One hundred and two patients normal healthy males and female of the same age group and socioeconomic status from patient's relatives were selected as control group.

The controls were also thoroughly examined clinically. Those with cardio-respiratory, musculoskeletal, or endocrine diseases were excluded from the study. Fasting and postprandial blood glucose levels were measured by glucose oxidase method to rule out type 2 DM in them.

All the patients were handed a questionnaire that contained a detailed personal and medical history. PFTs of the patients as well as of the controls were performed with turbine flow sensor-based 702 Helios - Spirometer between 11 am and 12 pm. All the tests were conducted according to American Thoracic Society/European Respiratory Society (ATS/ERS guidelines) in a quiet room in sitting position by the trained personnel. [8,9] The controls and patients performed spirometry three times at the interval of 15 minutes and the best of the three was taken into account.

Parameters recorded were - forced vital capacity (FVC) in liters, forced expiratory volume in 1 second (FEV1), FEV1/FVC in percentage (%), forced expiratory flow during 25% of FVC (FEF25), forced expiratory flow during 50% of FVC (FEF50), forced expiratory flow during 75% of FVC (FEF75), forced expiratory flow during 25–75% of FVC (FEF25–75), forced expiratory flow during 0.2–1.2 liters of FVC (FEF0.2–1.2), 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.

Nearly 2 ml of venous blood was collected in ethylenediamine tetra acetic acid (EDTA) bulb in all the diabetic patients with aseptic precautions. HbA1c of all the patients was estimated by ion exchange resin method by the diagnostic glycohaemoglobin kits of Asritha Diatech as per the guidelines provided. [10]

All data were collected in a data collection form and then transferred to an Excel sheet by two independent data entry operators. Discrepant values were corrected by checking the data collection form. Clean data was then analyzed statistically.

Statistical Analysis

PFTs of diabetic patients and controls were compared by applying Student′s unpaired ′t′ test. Correlations between FVC and FEV1 and HbA1c and duration of illness in diabetic patients were analyzed by applying Pearson′s coefficient. Statistical analysis was done by using SSPS version 11 and Graphic Prism Pad version 5.

RESULTS AND OBSERVATIONS

Table 1: Comparison of Age, Height, Weight and BMI among study group and control group.

	Study group (n=102) (Mean ± SD)	Control (n=102) (Mean ± SD)
Age (Years)	51.94 ± 7.060	52.58 ± 6.990
Height (cm)	160.30 ± 5.791	162.18 ± 5.359
Weight (Kgs)	61.47 ± 8.201	60.66 ± 7.122
BMI	23.85 ± 2.307	23.09 ± 2.862

Table 1 shows the comparison of age, height, weight and BMI among cases and controls. Statistical analysis shows that both of these groups are comparable as no significant difference exists between the study group and the control.

Table 2: Comparison of fasting blood sugar and HbA1c among cases and controls

	Study group (n=102) (Mean ± SD)	Control group (n=102) (Mean ± SD)
FBS (gm/dl)	197.50 ± .548	86.42 ± 7.052
HbA1c	7.78 ± 1.784	4.34 ± .358

Table 2 shows the comparison of fasting blood sugar (FBS) and Glycosylated hemoglobin (HbA1c) level among cases and controls. Mean FBS level of 197.50 among cases much higher than the control group which is 86.42. HbA1c levels also show the similar trend of having a higher mean value of 7.78 comparative to 4.34 among controls.

Table 3: Comparison of PFT values among study group and controls

Percentage of predicted value	Study group (n=102) (mean ± SD)	Control (n=102) (mean ± SD)	P Value
FVC	77.63 ± 8.719	88.19 ± 9.718	.000*
FEV1	77.21 ± 10.305	88.05 ± 7.389	.000*
PEFR	70.25 ± 10.853	75.45 ± 12.506	.002*
FEF 25%-75%	56.36 ± 8.573	90.80 ± 4.367	.000*
FEV1/FVC	100.16 ± 9.640	106.69 ± 17.723	.002*

Table 3 shows the comparison of PFT among study and control group. In present study, 5 pulmonary function parameters have been taken into consideration namely Forced vital capacity (FVC), Forced vital capacity in 1st minute (FEV1), Peak expiratory flow rate (PEFR), Forced expiratory flow in between 25% and 75% (FEF 25%-75%) and FEV1, FVC ratio (FEV1/FVC). It shows that the values of all the 5 parameters are significantly reduced in study population (p value <0.05) than the control.

Table 4: Correlation between PFT data and duration of disease

Duration of Disease	P Value	Pearson Correlation (r)
FVC	.164	.139
FEV1	.144	.146
PEFR	.834	.021
FEF 25%-75%	.759	.031
FEV1/FVC	.638	.047

Table 4 shows the correlation between PFT data and duration of disease. In this study it was found that none of these variable have any statistically significant relationship (p value >0.05). There is weak positive correlation exists between FVC vs duration of disease and FEV1 vs duration of disease as the magnitude of association is $.1 < | r | < .3$.

Table 5: Blood pressure variation among study group

BP	Male	Female	Total
Normotensive	9 (11%)	17 (81%)	26
Pre-hypertensive	18 (22%)	3 (14%)	21
Hypertensive	54 (67%)	1 (5%)	55
Total	81 (100%)	21(100%)	101

Table 5 shows blood pressure variation among cases both in males and females. In our present study we have found that female cases are mostly normotensive (81% of total female cases) comparing to only 11% in male cases. Hypertension is more prevalent in male cases constituting 67% of all male cases, whereas only 5% female cases are hypertensive. Blood pressure is found to be in pre hypertension range in 14% female cases and 22 % of male cases.

DISCUSSION

In this study attempts have been taken to justify any relation between pulmonary function and type 2 diabetes mellitus and its correlation with duration of disease and long term glycaemic control.

It was observed that in most of the type 2 diabetes patients fasting blood glucose level and HbA1c was significantly high pointing towards the fact that there was poor glycaemic control.

This may be because of irregular drug intake, inappropriate drugs, sub-dosing, overeating, lack of diabetic life style discipline, etc practiced by the patients [11].

The above results are in agreement with the famous Fremantle diabetes study. This was a community based study done at western Australia, Davis WA et. al.[12] found that FVC, FEV1, VC, and PEF decreased significantly in type 2 diabetes mellitus patients when followed up after 7 years. Declining lung function measures were consistently predicted by poor glycaemic control in the form of a higher mean HbA1c.

Asanuma Y et. al. [13] found that forced vital capacity and timed vital capacity were lower in diabetics. Diffusing capacity was also decreased in male diabetics. Diabetic patients showed abnormal lung function which increased with age and gas transfer was also affected by diabetic microangiopathy as well as the duration of diabetes.

Meo SA et. al. [14] reported decrease in lung function in type 2 diabetic patients reflected as decrease in FVC, FEV1 and PEF, as compared to their matched controls. Stratification of results by years of disease showed a dose-response effect on lung function.

In Indian scenario Swati S. et. al. [15] conducted a study on pulmonary function of 60 type 2 diabetes mellitus patients in western India and found that all the pulmonary function parameters (FVC, FEV1, PEFR, FEF 25%-75%) were decreased in diabetes patients except FEV1/FVC ration. Though they found no correlation between FVC, FEV1 with glycaemic control (HbA1c level) and duration of disease.

In a similar study in our neighbouring country Pakistan, Muhammad Irfan et al. [16] found among 64 diabetic

subjects significant reduction in the forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and slow vital capacity (SVC, relative to nondiabetic controls. There was no significant difference noted in the forced expiratory ratio and maximum mid-expiratory flow between the groups.

A study conducted at Nellore, Andhra Pradesh [17] among 50 type 2 diabetes patients shows the mean FVC, FEV1, FEV1/FVC%, PEFR, FEF25-75%, MVV values are low in diabetics (p value <0.001) compared to non-diabetics. Also, female diabetics show greater decrease in PFT values than male diabetics and suggested that the female diabetics are more prone to have pulmonary dysfunction than their male counterpart.

In a recent study, Kanya Kumari et al. [18] found that among 90 type 2 diabetes mellitus patients 70 had restrictive, 12 had obstructive and remaining 8 had normal spirometric pattern. Even though Type2 diabetic patients did not have any respiratory symptoms they did have underlying sub clinical restrictive patterns of lung functions. They also concluded that the duration of diabetes increases the restrictive profile become more prominent.

In this study there was significant reduction in mean FVC and the mean FEV1 values in all diabetic patients irrespective of blood sugar level, however there was more significant decrease in subjects who had poor controlled blood sugar level. Though there were significant decrease in the FVC and FEV1, FEV1/FVC ratio was within the normal range indicating a restrictive pattern of lung involvement.

These findings were consistent with findings of Davis et al., [19]. The FEV1/FVC ratio was within normal range in all diabetics. The decrease in FVC, FEV1 and normal value of (FEV1/FVC) shows restrictive pattern of lung disease in the diabetics. Similar findings were observed by Kanyakumari DH et al. [20].

Sandler M [21] also concluded that 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. This may lead to restrictive pattern.

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 the presence of nonenzymatic glycosylation and modification of alveolar surfactant action cause reduction in PFTs [22].

Pulmonary function abnormalities, in particular a reduction in diffusion capacity, were commonly found in patients with NIDDM by Marvisi M et al. [23]. Microangiopathy in cases of NIDDM is related to an impaired pulmonary microvasculature and thickened alveolar epithelial basal lamina.

CONCLUSION

Lung function is severely affected in type 2 diabetics patients indicating that lung is a target organ of long term complication of type 2 diabetes. Long term glycaemic control i.e. HbA1c is a major determinant of this deterioration rather than the duration of disease. Females are more prone to be affected than their male counterpart.

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