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ORIGINAL RESEARCH

Pulmonary function tests in type 2 diabetes mellitus and their association with glycemic control and duration of the disease

[1]Dr. Ramesh Kumar Sharma, [2]Dr. Manoj Kumar

Associate Professor, Department of Physiology, Lt BRKM Govt Medical College, Jagdalpur, Chhattisgarh, India

[2]Assistant Professor, Department of Physiology, RSDKS, GMC, Ambikapur, Chhattisgarh, India

Correspondence:
Dr. Manoj Kumar
Assistant Professor, Department of Physiology, RSDKS, GMC, Ambikapur, Chhattisgarh, India
Email: drmanoj2k2@gmail.com

Abstract

Introduction: In the modern world, Diabetes mellitus (DM) is a well-known systemic metabolic disorder characterized by the presence of chronic hyperglycaemia which is associated with the changes in the metabolism of lipids, carbohydrates and proteins. Globally, the International Diabetes Federation (IDF) reported that prevalence of diabetes in adults aged between 20–79 years was estimated to be around 8.8% in 2017. IDF also reported that 5 million deaths and USD 727 billion health care expenditure were contributed to diabetes among people aged between 20–99 years in 2017 worldwide. The study aims to evaluate the PFTs in those affected with type 2 Diabetes and compare them with the age and gender matched healthy controls. And this study is also ought to determine the correlation of the HbA1c and duration of the disease with PFTs in type 2 DM patients.

Materials and Methodology: The study was undertaken in the Diabetes Outpatient Department. After taking the approval from the Institutional Ethics Committee, study participants of seventy male patients of type 2 DM diagnosed by the treating physician, of the age group 40-60 years who are under oral hypoglycaemic medication, were randomly selected. Patients having complaints of cough, sputum, or dyspnoea, Smokers and patients with any cardio respiratory illnesses or major diseases were excluded from the study. Sixty normal healthy males of the same age range as the study group and socioeconomic status from patient's relatives were selected as control group. The controls were also thoroughly examined clinically. Fasting and postprandial blood glucose levels were measured by glucose oxidase method to rule out type 2 DM in them. After obtaining an informed written consent from all the participants including those from controls, they were handed over 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-Spiro meters (Chandigarh, India) between 11 am and 12 pm. All the tests were conducted according to guidelines given by American Thoracic Society/European Respiratory Society (ATS/ ERS guidelines) in a quiet room in sitting posture by the trained personnel.HbA1c for all the patients were estimated by an ion exchange resin method by the diagnostic glycol-haemoglobin kits provided by Asritha Diatech as per the provided guidelines. All data were collected which were then transferred to an Excel sheet by two independent data entry operators. Discrepant values were corrected by checking the data collection form. Collected data was then analysed statistically. PFTs of diabetic patients and controls were compared by

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applying Student's unpaired't' test. Association between FVC and FEV_1 and HbA1c and duration of diabetes in patients were analysed by applying Pearson's co-efficient. Statistical analysis was done by using SPSS version 11.

Results: Table 1 tabulates the physical characteristics of the normal controls as well as the patients affected with DM. Age, height, and weight of both the groups were comparable and no statistical difference was observed between them ($P > 0.05$). This study showed that all the pulmonary parameters like FVC, FEV_1, FEF_{25}, FEF_{50}, FEF_{75}, FEF_{25-75}, $FEF_{0.2-1.2}$ and PEFR were significantly decreased except FEV_1 /FVC in patients of type 2 DM as compared with the healthy controls ($P> 0.05$) as given in Table 2. On correlating the FVC and FEV_1 with duration of illness and HbA1c, we found that there was no statistically significant correlation between them ($p>0.05$).

Conclusion: DM being a systemic disease which has the ability to affect lungs causing restrictive type of ventilatory changes probably because of glycosylation of connective tissues reduced pulmonary elastic recoil, and inflammatory changes in lungs. We found that glycaemic levels and duration of disease are probably not the major determinants of lung pathology. Further research is still being needed in this dimension.

Keywords: diabetes mellitus, type 2, pulmonary function, glycaemic control

Introduction

In the modern world, Diabetes mellitus (DM) is a well-known systemic metabolic disorder characterized by the presence of chronic hyperglycaemia which is associated with the changes in the metabolism of lipids, carbohydrates and proteins.[1] Diabetes is a global health hazard which causes multiorgan damage at ease.[2] Globally, the International Diabetes Federation (IDF) reported that prevalence of diabetes in adults aged between 20–79 years was estimated to be around 8.8% in 2017. IDF also reported that 5 million deaths and USD 727 billion healthcare expenditure were contributed to diabetes among people aged between 20–99 years in 2017 worldwide. About three quarters (79%) of those affected with diabetics were living in low and middle-income countries as surveyed in the year 2017.[3]

In the African region, IDF also reported that 321,100 deaths and USD 3.4 billion healthcare expenditure were attributed due to diabetes in 2015. The Ethiopian Diabetes Association (EDA) estimated the prevalence rate of diabetes to be 2–3% in 2013.[4]Owing to the presence of widespread lung micro vascular circulation and abundant connective tissue with a large reserve may confirms the possibility that the lung may be a target organ of the pathologic processes initiated by type 2 diabetes.[5] This depicts that extensive loss in the micro vascular bed can be tolerated without developing any significant pulmonary symptoms in type 2 diabetics. This leads to disturbed and change in pulmonary function continuing for a long time and being able to be discovered only at a later stages of diabetics.[6,7] The well-documented mechanisms for the lung dysfunction in patients with type 2 diabetes include microangiopathy of alveolar capillaries and pulmonary arterioles, glycosylation of tissue proteins, oxidative stress and autonomic neuropathy involving the respiratory muscles.[8,9]

Impaired lung functions in type 2 diabetes have not been yet received adequate attention from the healthcare community in our country. This may be due to the lack of routine screening of PFT among the diabetics, and in those where type 2 diabetics are subclinical at an early stage, lack of national spirometric guidelines and policy on spirometry, lack of previous regional or national level studies conducted on this area and inadequate trained personnel in spirometry at the diabetic clinic/hospital. As a result of which pulmonary complications among diabetics may be usually remain unnoticed clinically.[10,11] Pulmonary function tests (PFTs) are non-invasive physiologic tests that show the effectiveness of lung's performance. Pulmonary functions are generally determined by the strength of respiratory muscles, compliance of the thoracic cavity, airway resistance and elastic recoil of the lungs. Pulmonary function

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parameters are unique as there is no single "normal" value or range. These parameters vary by sociodemographic factors and change in the anthropometric characteristics.[12,13]
The study aims to evaluate the PFTs in those affected with type 2 Diabetes and compare them with the age and gender matched healthy controls. And this study is also ought to determine the co-relation of the HbA1c and duration of the disease with PFTs in type 2 DM patients.

Materials and methodology

The study was undertaken in the Diabetes Outpatient Department. After taking the approval from the Institutional Ethics Committee, study participants of seventy male patients of type 2 DM diagnosed by the treating physician, of the age group 40-60 years who are under oral hypoglycaemic medication, were randomly selected. Patients having complaints of cough, sputum, or dyspnoea, Smokers and patients with any cardio respiratory illnesses or major diseases were excluded from the study. Sixty normal healthy males of the same age range as the study group and socioeconomic status from patient's relatives were selected as control group. The controls were also thoroughly examined clinically. Fasting and postprandial blood glucose levels were measured by glucose oxidase method to rule out type 2 DM in them. After obtaining an informed written consent from all the participants including those from controls, they were handed over 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 – Spiro meter (Chandigarh, India) between 11 am and 12 pm. All the tests were conducted according to guidelines given by American Thoracic Society/European Respiratory Society (ATS/ ERS guidelines) in a quiet room in sitting posture by the trained personnel. 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 that were recorded include – forced vital capacity (FVC) in litters, 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 litres 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. Nearly 2 ml of venous blood was collected in ethylenediamine tetra acetic acid (EDTA) bulb in all the diabetic patients with aseptic precautions.
HbA1c for all the patients were estimated by an ion exchange resin method by the diagnostic glycol-haemoglobin kits provided by Asritha Diatech as per the provided guidelines. All data were collected which were then transferred to an Excel sheet by two independent data entry operators. Discrepant values were corrected by checking the data collection form. Collected data was then analysed statistically. PFTs of diabetic patients and controls were compared by applying Student's unpaired't' test. Association between FVC and FEV_1 and HbA1c and duration of diabetes in patients were analysed by applying Pearson's co-efficient. Statistical analysis was done by using SPSS version 11.

Results

Table 1 tabulates the physical characteristics of the normal controls as well as the patients affected with DM. Age, height, and weight of both the groups were comparable and no statistical difference was observed between them ($P > 0.05$). This study showed that all the pulmonary parameters like FVC, FEV_1, FEF_{25}, FEF_{50}, FEF_{75}, FEF_{25-75}, $FEF_{0.2-1.2}$and PEFR were significantly decreased except FEV_1 /FVC in patients of type 2 DM as compared with the healthy controls ($P> 0.05$) as given in Table 2. On correlating the FVC and FEV_1 with

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duration of illness and HbA1c, we found that there was no statistically significant correlation between them (p>0.05).

Table 1: Physical characteristics of subjects

Parameters	DM patients n=65 mean±SD	Controls, n=65 mean±SD	P - value
Age (years)	53.90±8.45	54.88±8.28	>0.05
Height (cms)	159.23±7.86	161.28±7.33	>0.05
Weight (kgs)	61.57±7.38	64.42±8.70	>0.05
HbA1c (%)	7.12±1.36	-	-
Duration of diabetes	6.56±5.86	-	-

Table 2: Comparison of PFTs in patients with type 2 DM and healthy controls

Parameters	Controls	DM subjects	P – value
FVC	89.36±9.71	77.97±12.99	<0.05
FEV1	88.03±6.69	78.98±14.09	<0.05
FEV1/FVC	111.36±10.62	112.83±9.35	>0.05
PEFR	77.70±12.81	59.16±99.35	<0.05
FEF_{25}	81.60±8.69	60.23±18.75	<0.05
FEF_{50}	-	61.23±17.96	<0.05
FEF_{75}	85.00±10.28	64.03±24.92	<0.05
FEF_{25-75}	73.83±10.28	67.00±15.08	<0.05
$FEF_{0.2-1.2}$	91.06±1.46	70.46±23.68	<0.05

Table 3: Correlation of HbA1c and duration of DM with PFTs

Parameters	R^2	P – value
FVC with HbA1c	0.021	0.291
FEV_1 with HbA1c	0.009	0.502
FVC with duration	8.811	0.9996
FEV_1 with duration	0.009	0.521

Discussion

All the parameters were shown in this study such as FVC, FEV_1, FEF_{25}, FEF_{50}, FEF_{75}, FEF_{25-75}, FEF0.2-1.2, and PEFR were significantly reduced except FEV1 /FVC in patients of type 2 DM as compared with those in control group. These findings were in concordance with the previous studies.[14-18] Some of the prospective and cross-sectional studies have reported that the low vital capacity or restrictive pattern associated with type 2 DM.[19,20] Meta analysis by van den Borst et al showed that DM is usually associated with impaired pulmonary function in a restrictive pattern. Moreover, these results were based irrespective of body mass index (BMI), smoking, diabetes duration, and HbA1c levels.[21] Uchida et al observed that there was reduced pulmonary diffusing capacity in patients with diabetes who were reported with having perfusion defect on ventilation perfusion scintigrams.[22] It was quite tedious to analyse the pulmonary diffusing capacity because of practical difficulties. A study was conducted by including a large number of patients affected with type – 2 diabetes by *Davis* et al in Western Australia and reported that VC, FVC,FEV_1 and PEFR decreased at an average of between 1.1% and 3.1% of predicted values/year in type 2 DM patients.[14] Ehrlich et al displayed that the patients with type 2 DM were at high risk of suffering from several pulmonary conditions such as asthma, Chronic Obstructive Pulmonary Disease (COPD), fibrosis and pneumonia.[23] Fewer studies have also mentioned that there is no significant differences among all type 2 DM patients.[24-26]

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 02, 2022

Path physiology of reduced lung function is still an interesting research issue. Normal lung mechanics and gas exchange are influenced by the pulmonary connective tissue integrity and microvasculature. Speeding of aging process in connective tissue cross links and presence of non-enzymatic glycosylation and modification of alveolar surfactant action are the documented reasons for the reduction in PFTs.[3] There have been reports of associated histopathological changes in the diabetic patients. In the study by Weynand et al[27] it was observed that alveolar epithelium, endothelium capillary and basal laminaes were thickened in lungs of type 2 DM patients when viewed under electron microscopy. Diabetic microangiopathy might be existing in the pulmonary vascular bed. Moreover, reduced pulmonary capillary blood volume was observed which favours the evidence of microangiopathy. This could lead to redistribution of the pulmonary circulation; resulting in well ventilated areas to become under-perfused.[28] the thorax and lungs are rich in collagen and elastin. Stiffening of thorax and lung parenchyma can happen because of non-enzymatic glycosylation of these structural compounds. This may lead to restrictive pattern of lungs in DM patients.[3] In our studies, since the FVC/FEV_1 ratio is not statistically significant in DM patients as compared with their normal controls, other PFT values are lower in DM patients. Studies have even shown diabetic polyneuropathy which affects respiratory neuromuscular function and thus reducing pulmonary volumes.[29] on correlating the FVC and FEV_1 with duration of illness and HbA1c, we found that there was no significant correlation between them which is tabulated in Table 3. There are certain studies showing no association between HbA1c and PFTs.[17,25] They argued that HbA1clevels are indicators of glycaemic control for a shorter period of 1-2 months, which was not adequate to conclude that the plasma glucose level was not related to decreased PFTs. While some studies have shown that the decline in PFTs was negatively correlated with HbA1c.[14,16] There are certain studies that have reported no significant correlation between PFTs and duration of diseases,[25] while some of the studies have reported a strong negative correlation of PFTs with duration.[17,18] Since DM is a disorder which involves multiple organs randomly, the study of the effect of duration of the disease on them requires further research. Several studies have also analysed the association between impaired lung function and death and found that a 10% decrease in FEV_1 was associated with a 12% increase in mortality in type 2 DM.[27]

Conclusion

DM being a systemic disease which has the ability to affect lungs causing restrictive type of ventilatory changes probably because of glycosylation of connective tissues reduced pulmonary elastic recoil, and inflammatory changes in lungs. We found that glycaemic levels and duration of disease are probably not the major determinants of lung pathology. Further research is still being needed in this dimension.

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ISSN: 0975-3583,0976-2833 VOL13, ISSUE 02, 2022

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