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Evaluation of different parameter of pulmonary function test in patients suffered from diabetes mellitus

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Abstract
Type 2 diabetes mellitus is a heterogeneous group of disorder characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production. There is an alarming increase in the incidence and prevalence of diabetes mellitus particularly in Asian Indians. The major morbidities in type 2 diabetes mellitus are due to its microangiopathic and macroangiopathic complications, which affect eyes, kidneys, nerves, heart, and major vessels. The development of these complications may be related to biochemical alterations in connective tissue constituents, particularly collagen and elastin as well as macroangiopathy due to a non-enzymatic glycosylation of proteins induced by chronic hyperglycemia. The presence of an extensive pulmonary microvascular circulation and abundant connective tissue raises the possibility that lung may also be a target organ in diabetes. The present study is undertaken to study pulmonary function tests in patients having diabetes mellitus. The present study was planned in Narayan Medical College and Hospital, Jamuhar Sasaram, Bihar. The Pulmonary function test was assessed in the diabetes cases. Total 50 cases were enrolled in the present study. The total patients were divided into the two study groups. The 25 cases were evaluated in Group A as diabetic patients and 25 cases were evaluated in the Group B as control patients. After demonstrating the technique for carrying out pulmonary function tests, subjects were made to undergo pulmonary function tests, using medspiror, for 3 times at every 15 minutes interval and best of 3 was taken into account.
The data generated from the present study concludes that diabetic patients showed impaired lung function. This reduced lung function is likely to be a chronic complication of diabetes mellitus. Lung functions need to be checked periodically to assess the severity of impairment. However, a need of larger prospective study with long observational course to confirm these observations is required. It is therefore important to increase awareness of potential damage to the lungs in our patients with diabetes and encourage ideal BMI for this group of persons. DM being a systemic disease, 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.

Keywords: pulmonary function test, PFT, diabetes, etc

1. Introduction
Pulmonary function test (PFT) is a complete evaluation of the respiratory system including patient history, physical examinations, and tests of pulmonary function. The primary purpose of pulmonary function testing is to identify the severity of pulmonary impairment [1]. Pulmonary function testing has diagnostic and therapeutic roles and helps clinicians answer some general questions about patients with lung disease. PFTs are normally performed by a respiratory therapist, physiotherapist, pulmonologist, and/or general practitioner.
Neuromuscular disorders such as Duchenne muscular dystrophy are associated with gradual loss of muscle function over time. Involvement of respiratory muscles results in poor ability to cough and decreased ability to breathe well and leads to collapse of part or all of the lung leading to impaired gas exchange and an overall insufficiency in lung strength [2]. Pulmonary function testing in patients with neuromuscular disorders helps to evaluate the respiratory status of patients at the time of diagnosis, monitor their progress and course, evaluate them for possible surgery, and gives an overall idea of the prognosis [3].
Spirometry includes tests of pulmonary mechanics – measurements of FVC, FEV1, FEF values, forced inspiratory flow rates (FIFs), and MVV. Measuring pulmonary mechanics assesses the ability of the lungs to move huge volumes of air quickly through the airways to identify airway obstruction. The measurements taken by the spirometry device are used to generate a pneumotachograph that can help to assess lung conditions such as: asthma, pulmonary fibrosis, cystic fibrosis, and chronic obstructive pulmonary disease. Physicians may also use the test results to diagnose bronchial hyperresponsiveness to exercise, cold air, or pharmaceutical agents [4].
Spirometry assesses the integrated mechanical function of the lung, chest wall, and respiratory muscles by measuring the total volume of air exhaled from a full lung (total lung capacity [TLC]) to maximal expiration (residual volume [RV]). This volume, the forced vital capacity (FVC) and the forced expiratory volume in the first second of the forceful exhalation (FEV1), should be repeatable to within 0.15 L upon repeat efforts unless the largest value for either parameter is less than 1 L. In this case, the expected repeatability is to within 0.1 L of the largest value. The patient is instructed to inhale as much as possible and then exhale rapidly and forcefully for as long as flow can be maintained. The patient should exhale for at least six seconds. At the end of the forced exhalation, the patient should again inhale fully as rapidly as possible. The FVC should then be compared with that inhaled volume to verify that the forced expiratory maneuver did indeed start from

full inflation.

Reduction in the amount of air exhaled forcefully in the first second of the forced exhalation (FEV1) may reflect reduction in the maximum inflation of the lungs (TLC); obstruction of the airways; respiratory muscle weakness; or submaximal expiratory force due to poor coaching, poor understanding, or malingering. Airway obstruction is the most common cause of reduction in FEV1. Airflow obstruction may be secondary to bronchospasm, airway inflammation, loss of lung elastic recoil, increased secretions in the airway, or any combination of these causes. Response of FEV1 to inhaled bronchodilators is used to assess the reversibility of airway obstruction, although it is now widely appreciated that a response showing a lack of a significant increase in FEV1 does not indicate the patient will not benefit clinically from bronchodilator therapy. A significant increase in the inspiratory capacity (IC) and/or vital capacity (VC) after bronchodilator therapy can occur even when the FEV1 fails to show a significant change [5].

Spirometry is used to establish baseline lung function, evaluate dyspnea, detect pulmonary disease, monitor effects of therapies used to treat respiratory disease, evaluate respiratory impairment, evaluate operative risk, and perform surveillance for occupational-related lung disease.

Relative contraindications for spirometry include hemoptysis of unknown origin, pneumothorax, unstable angina pectoris, recent myocardial infarction, thoracic aneurysms, abdominal aneurysms, cerebral aneurysms, recent eye surgery (within 2 weeks due to increased intraocular pressure during forced expiration), recent abdominal or thoracic surgical procedures, and patients with a history of syncope associated with forced exhalation. Patients with active tuberculosis should not be tested.

Two choices are available with respect to bronchodilator and medication use prior to testing. Patients may withhold oral and inhaled bronchodilators to establish baseline lung function and evaluate maximum bronchodilator response, or they may continue taking medication as prescribed. If medications are withheld, a risk of exacerbation of bronchial spasm exists. Interpretation of spirometry results should begin with an assessment of test quality. Failure to meet performance standards can result in unreliable test results (see the image below). The American Thoracic Society (ATS) defines acceptable spirometry as an expiratory effort that has the following characteristics:

Pulmonary function tests require patients to successfully perform respiratory maneuvers in a standardized manner in order to obtain clinically meaningful results. Spirometry is perhaps the most technically and physically demanding. The patient is required to inhale as fully as possible, exhale with as much force as possible, and continue their expiratory effort until they empty their lungs as completely as possible or are unable to continue. The performance standards for spirometry are summarized below. The comments of the technologist administering the test can assist the interpreting physician in determining if results of a testing session that fail to meet some of the standards can still provide clinically useful data.

Comprehensive treatment of technical acceptability of spirometry test results is beyond the scope of this review. Readers are directed to Spirometry Quality Assurance: Common Errors and Their Impact on Test Results. A booklet can also be obtained from the Department of Health and Human Services. It provides examples of common spirometry performance errors and their impact on test results.

In patients that have significant loss of lung elastic recoil (pulmonary emphysema, COPD), spirometry may show negative effort dependence of forced expiratory flow. The effort that has the highest peak expiratory effort may produce a lower FEV1 because of the dynamic compression of the airways that results from the loss of elastic recoil support of airways that is characteristic of emphysema. In this circumstance, reporting the highest FEV1 coming from an effort with submaximal expiratory effort can lead to confusing results, particularly if a setting of assessing spirometric response to bronchodilators. Although not yet a spirometry acceptability standard, it appears that when reporting the FEV1 considering only efforts that have a time to peak flow (TPEF) less than or equal to 0.12 seconds helps eliminate this effect. This parameter can be displayed on most laboratory-based spirometry testing systems. Additionally, the two largest values for FVC and the two largest values for FEV1 in the same testing session should vary by no more than 0.15 L (0.1 L if the largest value is <1 L).

Inspection of the volume-time tracing aids in identification of early termination of expiration by evaluating the presence of an expiratory plateau. In the absence of an expiratory plateau, a 12- to 15-second expiratory time ensures the quality of the FVC. Inspection of the start of the volume-time tracing can identify a hesitant start, which can result in a falsely low FEV1. Repeatability of the FVC and the FEV1 helps ensure that the results truly represent the patient's lung function. Attention should be focused on the repeatability of two key parameters: FVC and FEV1 [6].

Diabetes mellitus (DM), commonly known as diabetes, is a group of metabolic disorders characterized by a high blood sugar level over a prolonged period. Symptoms of high blood sugar include frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death. Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes. Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced. There are three main types of diabetes mellitus:

Type 1 diabetes results from the pancreas's failure to produce enough insulin due to loss of beta cells. This form was previously referred to as "insulin-dependent diabetes mellitus" (IDDM) or "juvenile diabetes". The loss of beta cells is caused by an autoimmune response. The cause of this autoimmune response is unknown.

Type 2 diabetes begins with insulin resistance, a condition in which cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". The most common cause is a combination of excessive body weight and insufficient exercise.

Gestational diabetes is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels [7].

Prevention and treatment involve maintaining a healthy diet, regular physical exercise, a normal body weight, and avoiding use of tobacco. Control of blood pressure,

maintaining proper foot care, and eye care are important for people with the disease. Type 1 diabetes must be managed with insulin injections. Type 2 diabetes may be treated with medications with or without insulin. Insulin and some oral medications can cause low blood sugar. Weight loss surgery in those with obesity is sometimes an effective measure in those with type 2 diabetes [8].

Diabetes mellitus describes a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both. It is associated with wide spread hormonal , metabolic and microvascular abnormalities as well as disturbances of the functions of many organ systems. Type 2 diabetes mellitus is a heterogeneous group of disorder characterized by variable degrees of insulin resistance, impaired insulin secretion, and increased glucose production [9]. There is an alarming increase in the incidence and prevalence of diabetes mellitus particularly in Asian Indians. The major morbidities in type 2 diabetes mellitus are due to its microangiopathic and macroangiopathic complications, which affect eyes, kidneys, nerves, heart, and major vessels [10]. The development of these complications may be related to biochemical alterations in connective tissue constituents, particularly collagen and elastin as well as macroangiopathy due to a non-enzymatic glycosylation of proteins induced by chronic hyperglycemia. The presence of an extensive pulmonary microvascular circulation and abundant connective tissue raises the possibility that lung may also be a target organ in diabetes. The present study is undertaken to study pulmonary function tests in patients having diabetes mellitus.

Methodology

The present study was planned in Narayan Medical College and Hospital, Jamuhar Sasaram, Bihar. The Pulmonary function test was assessed in the diabetes cases. Total 50 cases were enrolled in the present study. The total patients were divided into the two study groups. The 25 cases were evaluated in Group A as diabetic patients and 25 cases were evaluated in the Group B as control patients. After demonstrating the technique for carrying out pulmonary function tests, subjects were made to undergo pulmonary function tests, using medspiror, for 3 times at every 15 minutes interval and best of 3 was taken into account.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion criteria: Previously diagnosed diabetic patients of more than 1-year duration; with or without hypertension, non- smokers, body mass index (BMI) < 30 kg/m2 with no previous history of any respiratory diseases and clinically ruled out cardiovascular diseases.

Exclusion criteria: Patients with acute or chronic respiratory disease or cardiorespiratory disease, with history of smoking or tobacco chewing, underwent abdominal or chest surgery.

Results & Discussion

Major consequences of hyperglycemia are excessive non enzymatic glycosylation of various body proteins including albumin collagen and elastin. In type 2 diabetics with uncontrolled disease there is decreased pulmonary functions have been noted. There may be increased cross linkage between polypeptides of collagen which leading on to thickening leading to restriction of lung volume and alveolar gas transport, reduced membrane diffusion capacity and pulmonary capillary blood volume. The possible explanations of restrictive type of lung disease are thickening of alveolar epithelium, pulmonary microangiopathy and centrilobular emphysema. So the net effect due to collagen & elastin changes and microangiopathy. The lung complications of type 2 diabetes mellitus are mainly affects the Mechanical aspects of the organ and among that the restrictive pattern of lung disease is the commonest one, these effects are reported by using the spirometry and measuring the forced vital capacity and forced expiratory volume in first second and ratio between these two [11].

The demographic profile of the study and control groups depicted in Tables. There exists a non-significant between the anthropometric parameters, thus both the groups were comparable to one another. Although BMI was more in study group versus control group, but the difference was not significant. As expected, blood sugar levels (fasting and post parandial) were significantly higher in study group versus the control group.

Table 1: Basic Biochemical Profiles

Group	Group A	Group B
Group of	**Diabetic Cases**	**Control Cases**
No. of Cases	25	25
Sex: Males Females	 28 22	 31 19
Age in years	43 – 65	46 – 63
BMI kg/m2	23.1 – 35.2	24.5 – 33.5
Systolic BP mm of Hg	121 – 158	107 – 138
Diastolic BP mm of Hg	75 – 92	71 – 88
Fasting Blood Sugar mg/dL	121 – 223	92 – 111
Random Blood Sugar mg/dL	123 – 307	84 – 132
Low Density Lipids mg/dL	91 – 143	98 – 138
Triglycerides mg/dL	98 – 294	86 – 185
Cholesterol mg/dL	152 – 214	164 - 228

Table 2: Basic Biochemical Profiles

Group	Group A	Group B
Group of	**Diabetic Cases**	**Control Cases**
No. of Cases	25	25
FVC: Forced Vital Capacity	1.65 – 3.35	2.05 – 3.63
FEV_1: Forces Expiratory Volume in 1 second	1.29 – 2.83	1.65 – 3.03
FEV_1/FVC	74.5 – 90.3	76.3 – 88.4
SVC: Slow Vital Capacity	1.98 – 3.19	2.14 – 3.59
MMEF: Maximum mid expiratory flow	1.25 – 3.79	1.53 – 3.53

In a study by Dharwadkar AR et al done on Forty Type-2 diabetic patients, aged 30-60 years, with diabetic duration of 1-20 years showed reduction in dynamic lung functions like FEV1, FEV1% & MEP and its negative correlation to glycemic status [12].

Another study done by A.S.Agarawal et al, showed mild reduction in diffusing capacity in patients with Type 2 DM (2010) [13]

A cross sectional study by Rodolfo J Dennis suggests

inadequate glucose control may be simultaneously associated with inflammation and decreased lung function in type 2 diabetes [14].

Hsin-Chieh Yeh Et al conducted cross-sectional and prospective analyses of diabetes status and and the associated decline in lung function . Adults with diabetes had significantly lower predicted FVC and predicted FEV1 than those without diabetes. In prospective analyses, FVC declined faster in diabetic adults than in their nondiabetic counterparts [15].

In study done by Strojek K et al found that Diffusing capacity in the diabetic patients with complications was significantly lower than in both the diabetic patients without complications and the control group .Specific diffusing capacity was significantly lower in the diabetic patients than in the control subjects [16].

Maccioni FJ, studied in 22 diabetic nonsmokers, in these diabetic subjects, mean values for total lung capacity, functional residual capacity, VC, and FEV1 were similar to predicted values,so they concluded that insulin-dependent diabetes mellitus does not affect pulmonary function [17].

BMI, which is modifiable parameter, has often been neglected in various studies. The effect of BMI in reducing lung function has been well documented by Li AM. The effect of BMI in reducing lung function may be due to reduced chest wall compliance and increased airway resistance [18]. Our study revealed increase in BMI in study group versus controls but the difference was not significant.

Study by Davis TM et al., [19] showed reduction in FEV 1 , which may attribute to the thickening of the alveolar epithelium and the pulmonary capillary basal lamina and also due to the reduced recoiling of the lung caused by non-enzymatic glycosylation of the connective tissue. However, in the present study the reduction in mean FEV1 was seen to be not significant.

P.Lang et al documented the possible associations between Diabetes mellitus, plasma glucose and the spirometric values like FVC & FEV1. They did a cross sectional study covering about 11,763 subjects of Copenhagen city. It showed slight impairement in lung function which was more prominent in diabetic subjects, who were taking insulin than those taking oral hypoglycaemic agents. They finally concluded saying that both IDDM & NIDDM were having reduced lung functions since they had decreased FVC & FEV1 [20].

Davis.A.Wendy et al studied and explained about the concept of reduced pulmonary function test in Type 2 DM in association with their glycemic exposure. This study included 495 patients with Type 2 DM and were studied between 1993 to 1994 by cohort study and 125 were restudied after 7 years. They found a decrease in mean % predicted values and annual decline of FVC, FEV1, PEF and Vital capacity [21].

DM is a systemic disease, which also affects lungs causing the restrictive type of ventilatory changes, because of glycosylation of connective tissues, reduced pulmonary elastic recoil and inflammatory changes in lungs. [22] The histopathological changes in the lungs of diabetics are associated with the thickening of the alveolar epithelium and the pulmonary capillary basal lamina and also due to the reduced recoiling of the lung. This is caused by biochemical alteration of connective tissue constituents, particularly collagen and elastin. There is increased cross-linkage formation between polypeptides of collagen which leads to thickening, leading restriction of lung volume and alveolar gas transport, reduced membrane diffusion capacity and pulmonary capillary blood volume [23]. Pathophysiology for the deteriorated pulmonary capacity in diabetic patients is not fully understood. Few histopathological reports are in favor of basal lamina thickening and fibrotic changes in the lung parenchyma [24]. The pattern of abnormal pulmonary function observed in our study, low FVC and preserved FEV1/FVC ratio, is suggestive of the restrictive type of lung disease. This can be explained on basis of chronic hyperglycemia leading to nonenzymatic glycosylation of connective tissues [25]. As non-enzymatic glycosylation has been shown to occur in human lung parenchymal tissue

Conclusion

The data generated from the present study concludes that diabetic patients showed impaired lung function. This reduced lung function is likely to be a chronic complication of diabetes mellitus. Lung functions need to be checked periodically to assess the severity of impairment. However, a need of larger prospective study with long observational course to confirm these observations is required. It is therefore important to increase awareness of potential damage to the lungs in our patients with diabetes and encourage ideal BMI for this group of persons. DM being a systemic disease, 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.

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