A STUDY OF PULMONARY FUNCTION TEST IN TYPE II DIABETES MELLITUS – SPIROMETRY BASED

Dissertation submitted to

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CERTIFICATE

This is to certify that this Dissertation entitled **"A STUDY OF PULMONARY FUNCTION TEST IN TYPE II DIABETES MELLITUS – SPIROMETRY BASED"** is submitted to the **Tamilnadu Dr. M.G.R Medical University, Chennai** which was done under the guidance of our Professor Dr.R.Vinodha M.D., Professor and HOD, Department of Physiology, Thanjavur Medical College, Thanjavur.

This dissertation is a record of fresh work done by the candidate Dr.S.Suguna during the course of the study (2010-2013). This work was carried out by the candidate herself under my supervision.

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DECLARATION

I hereby declare that this dissertation entitled **"A study of pulmonary function test in type II diabetes mellitus – Spirometry based"** is a bonafide and genuine research work done by me under the guidance of our Professor Dr.R.Vinodha M.D., Professor and Head of Department, Department of Physiology, Thanjavur Medical College, Thanjavur.

This dissertation is submitted to the Tamilnadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the university requirements for the award of degree M.D in physiology.

Place:

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INTRODUCTION

INTRODUCTION

Diabetes mellitus is one of the most common chronic diseases in nearly all countries, and continues to increase in numbers and significance, as changing lifestyles lead to reduced physical activity, and increased obesity [(1)].

According to WHO survey, India will be the world diabetic capital in 2025. As the prevalence of diabetes is increasing, with type II diabetes accounting for 90 – 95% of all cases [(2)]. It is often asymptomatic in its early stages and can remain undiagnosed for many years.

The etiogenesis of type II diabetes reflects the heterogeneous genetic, pathologic, environmental and metabolic abnormalities that can exist in different patients and all lead to a final common pathway of hyperglycemia [(3)]. Chronic hyperglycemia is associated with continuing damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart, lungs and blood vessels [(4)].

The pathogenesis is thought to involve both a microangiopathic process and non enzymatic glycosylation of tissue proteins. This process results in impaired collagen and elastin cross-linkage with a reduction in strength and elasticity of connective tissue. Due to the presence of an abundant connective tissue and an extensive microvascular circulation raises the possibility that lung may be a target organ in diabetic patients [(5)].

It has been demonstrated that pulmonary complications in diabetes are due to thickening of walls of alveoli, alveolar capillaries and pulmonary arterioles and these changes cause pulmonary dysfunction [4].

These microvascular complications appear early within 5 to 10 yrs and macrovascular complications appear within 15 to 20 yrs from the onset of diabetes [6].

In type I diabetes lung function has been investigated in several clinical studies and evidenced reduced lung volume, reduced elastic recoil, diminished respiratory muscle performance, decrease in pulmonary diffusion capacity for carbon monoxide [7] .

As the prevalence of type II DM is increasing, particularly in developing countries like India, and since these changes can potentially incapacitate the patients, it is of utmost importance to define these changes. It is also important to find ways of retarding the progression of disease so that they do not become irreversible thus allowing millions of patients to be economically productive [2].

It has been suggested that pulmonary dysfunction may be one of the earliest measurable non metabolic alteration in diabetes. So it is important to determine whether these lung function changes also occur in type II diabetes.

Thus, this study was under taken to correlate the lung function in type II diabetes with duration of diabetes and to find out whether it is obstructive or restrictive pattern.

AIMS

&

OBJECTIVES

AIMS & OBJECTIVES

- To study lung function in type II diabetic patients.
- To correlate pulmonary function test with duration of diabetes mellitus.
- To find out whether it is obstructive or restrictive.

REVIEW

OF

LITERATURE

REVIEW OF LITERATURE

DIABETES MELLITUS

The term diabetes is derived from the greek word meaning ‘siphon’ was named by Aretaeus of cappadoica. Cullen added the word ‘mellitus’ meaning honey, to the name diabetes [8].

Diabetes mellitus is a syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiencies in insulin secretion or insulin action.

The characteristic symptoms of diabetes mellitus are polyphagia, polydipsia, polyuria and weight loss [6].

HISTORY:

Diabetes was described more than 2000 years ago. Polyuric states, clinically resembling diabetes mellitus were described as early as 1550 B.C, by Georg Ebers [6].

The sugar in diabetic urine was identified as glucose by Chevreul in 1815. In the 1840’s , Bernard showed that glucose was normally present in blood and showed that it was stored in the liver as glycogen for secretion into the blood stream during fasting.

In 1889, Minkowski and von Mering reported that pancreatectomy causes severe diabetes in the dog. In 1893, Laguesse suggested that the

pancreatic ‘islets’ described by Langerhans in 1869 produced as internal secretion that regulated glucose metabolism.

Insulin was discovered in 1921 by Banting, Best, Macleod and Collip in acid – ethanol extracts of pancreas. For this, Banting and Macleod were awarded the noble prize in 1923 and they shared it with Best and Collip. Insulin was first used for treatment in January 1922 [9].

INSULIN:

Insulin is a polypeptide containing 2 chains of amino acids linked by disulfide bridges, secreted by beta cells of pancreas.

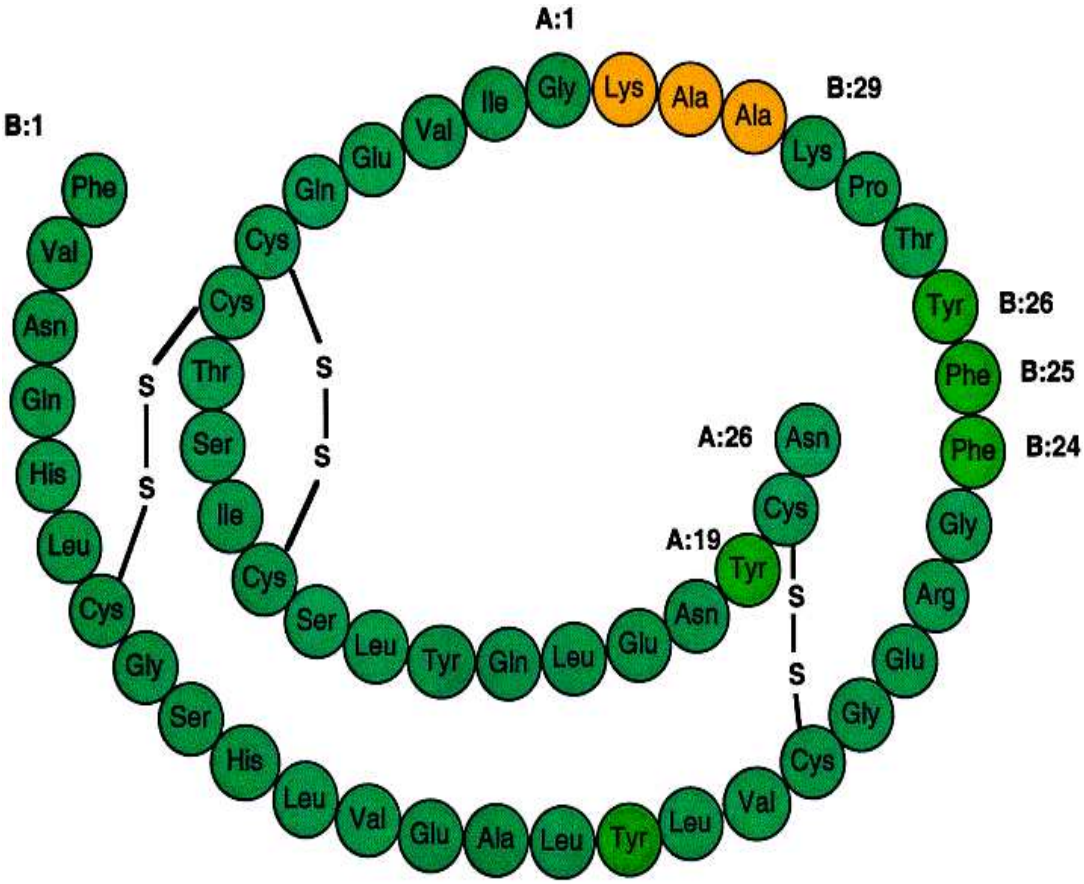


Figure 1: Structure of Human Insulin.

In humans, the gene encoding preproinsulin, the precursor of insulin, is located on the short arm of chromosome 11. It is 1355 base pairs in length and its coding region consists of three exons. The first encodes the signal peptide at the N – terminus of preproinsulin, the second the B chain and part of C peptide and the third the rest of the C peptide and the A chain.

Preproinsulin, an 11.5 KDa polypeptide is rapidly discharged into the rough endoplasmic reticulum where proteolytic enzymes immediately cleave the signal peptide, generating proinsulin.

Proinsulin is a 9-KDa peptide, containing the A and B chains of insulin joined by the C peptide. It is transported in micro vesicles to the golgi apparatus where it is packaged into membrane – bound vesicles known as secretory granules. It is converted into insulin by two endopeptidases.

Insulin and C peptide are stored together in the secretary granules and are ultimately released in equimolar amounts by a process of regulated exocytosis [(9)].

Mechanism of action of insulin:

Insulin exerts a broad spectrum of anabolic effects on multiple tissues. The regulation of whole body fuel homeostasis primarily involves insulin action in skeletal muscle, adipose tissue and liver. In these organs, insulin promotes uptake and storage of carbohydrates, fat and amino acids. It also antagonizes the catabolism of these fuel reserves. Therefore, it is appropriately called the “Hormone of abundance”.

Insulin receptor is a tetramer made up of two α and two β glycogen subunits. All these are synthesized on a single mRNA and then proteolytically separated and bound to each other by disulfide bonds. The subunits bind insulin and are extracellular, whereas the β subunit span the membrane and the intracellular portion have tyrosine kinase activity.

Binding of insulin with α subunit of insulin receptor triggers the tyrosine kinase activity of the β subunits, producing autophosphorylation of the β subunits on tyrosine residues. This autophosphorylation of insulin receptor is essential for insulin to exert its metabolic effects. In the tissue insulin increases the number of glucose transporters in the cell membrane (GLUT) [(10)].

The primary function of insulin is to lower the plasma glucose concentration by increasing glucose entry into the cell and stimulates its oxidation and also promotes its storage. At the same time insulin inhibits glucose production.

In skeletal muscle, insulin stimulates glucose transport and glucose storage as glycogen, as well as glycolysis and tricarboxylic acid cycle activity. Insulin also lowers hepatic glucose output by inhibiting glycogenolysis, gluconeogenesis and augments glycogen formation.

Insulin is the only anti-ketogenic hormone. Insulin increases storage of fat and decreases the level of free fatty acids and ketoacids in the plasma. Insulin is an anabolic hormone, promotes protein synthesis and inhibits proteolysis [(10)].

Insulin also enhances cell growth, differentiation and survival as a consequence of mitogenic and anti-apoptotic process. Thus oxidative stress, endoplasmic reticulum stress and inflammation are associated with insulin resistance, obesity and metabolic syndrome [9].

DIABETES MELLITUS

The constellation of abnormalities caused by insulin deficiency is called diabetes mellitus. It is characterized by polyuria, polydipsia, polyphagia, hyperglycemia, glycosuria, ketosis, acidosis, and coma.

The fundamental changes are

- Decrease in the entry of glucose into peripheral tissues.
- Increased synthesis of glucose by the liver.

Therefore there is an excess extracellular glucose and in many cells an intracellular glucose deficiency-a situation called “starvation in the midst of plenty” [10].

Based on the pathogenesis responsible for hyperglycemia, diabetes mellitus is classified as

1. Type I Diabetes Mellitus.
2. Type II Diabetes Mellitus.
3. Other specific types [Maturity-Onset Diabetes of the Young (MODY), due to endocrine disorder, infection]
4. Gestational diabetes.

TYPE I DIABETES MELLITUS:

It is characterized by the development of a state of complete insulin deficiency, as a result of cellular mediated autoimmune destructive process which ultimately destroys the β cells.

TYPE II DIABETES MELLITUS:

It represents a heterogeneous constellation of disease syndromes, all leading to a final common pathway of hyperglycemia. It is due to impaired insulin secretion, insulin resistance and increased hepatic glucose production.

OTHER SPECIFIC TYPE:

1. Defects in insulin secretion are the Maturity-Onset Diabetes of the Young (MODY) family, which are a group of autoimmune – dominant inherited disorder where there is hyperglycemia at an early age, generally of a mild nature.

2. Diseases of the exocrine pancreas often cause diabetes through destruction of islets – eg: Pancreatitis, Hemochromatosis, Cystic fibrosis.

3. Several endocrinopathies are associated with diabetes – cushing syndrome, acromegaly, pheochromocytoma, hyperthyroidism and glucagonoma.

4. Infections are also associated with the development of diabetes – mumps, congenital rubella, coxsackie B virus and cytomegalovirus.

GESTATIONAL DIABETES:

Gestational diabetes is hyperglycemia first detected during pregnancy. Screening for GDM is generally undertaken at around 28 wks [3].

Of these, type II DM is a predominant form of diabetes worldwide. The complications of type II DM are due to microangiopathy and macroangiopathy, which affect the eyes, kidneys, nerves, heart and major blood vessels [11].

WHO – recommended criteria for the diagnosis of diabetes and intermediate hyperglycemia

TEST	NORMOGLYCEMIA	IFG (mg/dl)	IGT (mg/dl)	DIABETES
Fasting plasma glucose	< 100	100-125		≥126mg / dl
2 hr plasma glucose	< 140		149 -199	≥200mg / dl
Causal plasma glucose				≥200mg/ dl & symptoms of diabetes

TYPE II DIABETES MELLITUS

Diabetes is renowned as a “silent epidemic” due to the slow progression and lack of symptoms in the early stages of disease preclude seeking medical attention and preventive care. [9]

An epidemic of type II diabetes is underway in both developed and developing countries like India due to change in life style, junk foods, sedentary life, environmental factors and stressful life .

MAJOR RISK FACTORS FOR TYPE II DIABETES MELLITUS:

- Over weight (Body Mass Index $\geq$ 25 kg / m^2).
- Physical inactivity.
- Race / ethnicity.
- Previously identified Impaired Fasting Glucose or Impaired Glucose Tolerance.
- Hypertension (Blood pressure $\geq$ 140 /90 mm Hg).
- Triglyceride $\geq$ 250 mg / dl or HDL cholesterol $\leq$ 35 mg / dl.
- History of Gestational Diabetes Mellitus or delivery of a baby weighing > 4.1 kg.
- Poly cystic ovarian disease [11].

The three major metabolic abnormalities that coexist in type II diabetes are

1. Increased hepatic glucose production.
2. Target tissues are insulin resistant (skeletal muscle)
3. Abnormal islet cell function.

These metabolic abnormalities depend on the genetic, pathologic and environmental factors.

Genetic factors:

Type II diabetes is not simply the result of a single gene defect. The disease appears to be a polygenic disorder, meaning that different combinations of gene polymorphisms may exist among patients. Individuals may be predisposed to develop type II diabetes through their inheritance of particular combination of genes, but acquired environmental factors are necessary to bring out the phenotypic manifestation of hyperglycemia.

Acquired factors:

1. Westernized life style is associated with change to a diet that has a higher content of total calories, fats, and refined carbohydrates.
2. The reduced level of physical activity and obesity leads to develop diabetes.
3. Low birth weight is one of the risk factor for the development of insulin resistance.
4. Decline in insulin secretion and insulin sensitivity, results in decreased glucose tolerance in aged individuals.

Pathophysiology of type II diabetes mellitus:

1. **Abnormal beta cell function:**

The beta cell mass is decreased, due to accelerated β cell apoptosis and failure of islet neogenesis and β cell replication to compensate for this loss. Glucotoxicity and Lipotoxicity play a major role in impaired β cell function.

Glucose stimulated insulin secretion involves transport of glucose into cells by a specific glucose transporter termed GLUT2. Genetic deletion of GLUT2 leads to loss of glucose stimulated insulin secretion.

2. **Peripheral insulin resistance:**

Insulin resistance is a metabolic state where there is normal insulin production but less biological response.

One of the most important effects of insulin was stimulation of glucose uptake into skeletal muscle, adipocytes and heart muscle. Tissue glucose uptake is mediated by a family of at least five facilitative glucose transporters. Out of them, GLUT4 was uniquely expressed in skeletal muscle, adipocytes and heart muscle. Upon insulin stimulation, GLUT4 are translocated from the intracellular vesicular pool to the plasma membrane, where they begin to transport glucose into cell.

The major manifestation of insulin resistance is decreased glucose disposal. The cause for this may be due to

- Decrease in cellular insulin receptors.
- Abnormal coupling between the glucose transporters and insulin receptors.
- Decrease in the activity of the glucose transporters.
- Intracellular defects in various pathways of glucose metabolism [(9)].

Mechanism of hyperglycemia induced damage:

Due to generalized hyperglycemia, certain types of cells are potentially damaged. Because these cells fails to down regulate the glucose uptake, even when the extracellular glucose concentrations are elevated.

The major target for hyperglycemic damage are vascular endothelial cells, which shows no significant change in glucose transport even when the glucose concentration is elevated, resulting in intracellular hyperglycemia.

1. Hyperglycemia increases glucose metabolism by sorbital pathway. This leads to cellular dysfunction, as a result of increase in cellular osmolarity, altered redox potential, generation of reactive oxygen species.

2. Increased intracellular advanced glycation end products, formed by reaction of glucose and other glycating compounds with proteins and to some extent, nucleic acids.

3. Increase in the expression of Advanced Glycated End products receptor and its activating ligand.

4. Increase in the formation of diacylglycerol, which activates protein kinase C and alters the transcription of genes for type IV collagen, fibronectin, contractile proteins and extracellular matrix proteins in endothelial cells and neurons.

5. Increased hexosamine pathway flux which generates fructose -6-phosphate, a substrate for O – linked glycosylation and proteoglycan production.

Finally a single process due to increased mitochondrial production of oxygen free radicals activates each of this mechanism.

The consequence of persistent hyperglycemia is increased superoxide production which explains the continuing progression of tissue damage even after the improvement of glycemic levels (glycemic memory). So early glycemic control appears to be important in order to reduce vascular complications in subsequent decades [9].

Biochemical test to be done to diagnose and monitor the efficacy of treatment to DM:

Glycated hemoglobin and blood glucose are the two most frequently used measure of glycemia in current practice.

1. **Fasting blood glucose** should be obtained after an approximately 10 hr fast. Urine glucose measurement is not used in diabetic diagnosis; however some patients use this measurement for monitoring purposes.

In an asymptomatic patient, if fasting blood glucose is 126 mg/dl or above on more than one occasion, the diagnosis of DM is confirmed.

2. **Oral glucose tolerance test:**

Patient should be on a normal to high carbohydrate intake for 3 days before the test. The patient should be fasting for at least 10 hrs and not more than 16 hrs. The test should be performed in the morning because of the hormonal diurnal effect on glucose.

Fasting blood sample is collected. A solution containing 75gm of glucose is given orally and blood for plasma glucose measurement is drawn 2hrs later. If the two hr glucose is 149 -199 mg/dl is called **impaired glucose tolerance** and > 200 mg/dl is called **diabetes**.

3. **Glycosylated hemoglobin** is the most reliable method to monitor long term diabetes control rather than random blood glucose. HbA1c is the most commonly detected hemoglobin, is a glucose molecule attached to one or both N- terminal valine of the β- polypeptide chain of normal adult hemoglobin[(9)] .

HbA1c levels serve as a retrospective indicator of the average glucose concentration over the previous 6-8 wks, as the average life span of red blood cell is about 120 days. The rate of formation is directly proportional to the plasma glucose concentration. The levels of HbA1c are directly related to the risk of developing diabetic complications [(9)].

HbA1c	Mean plasma glucose	
	mmol/L	mg/dl
6	7.0	126
7	8.6	154
8	10.2	183
9	11.8	212
10	13.4	240
11	14.9	269
12	16.5	298

Complications of diabetes mellitus:

1. Acute complications:
    - Metabolic – diabetic ketoacidosis.

      Hyperglycemic hyperosmolar syndrome.

      Hypoglycemia.
    - Others – acute infections.

      Acute coronary syndromes.

      Cerebrovascular accidents.
2. Chronic complications:
    - Microvascular – Neuropathy and Retinopathy.
    - Macrovascular – Hypertension, Coronary arterial disease.

- Others – Diabetic foot, Gastro intestinal and genitourinary dysfunction.
- Dermatological disorders.
- Infections.

Management of Type II Diabetes:

The management of type II diabetes mellitus was very important to achieve good glycemic control, in order to prevent or reduce the severity of chronic complications.

1. **Lifestyle intervention.**

Diet –the caloric content of the diet is based on the patient's current weight. 150 kJ / kg for men and 140 kJ/kg for women are reasonable initial values in most patients.

The protein requirement for good nutrition is about 1.0 to 1.5 g/kg of body weight/ day. The average fat intake should be 30 % of total calories and the remaining calories are assigned to carbohydrate. Increasing the fiber content of the diet is helpful.

Not only the amount of carbohydrate, but also the quality of carbohydrate is important for individuals with diabetes. The amount of carbohydrate is an essential factor for post-prandial glucose results in people with type I DM and type II DM. In the process of achieving desirable glycemic control, many individuals use either carbohydrate counting, carbohydrate

exchanges or experience – based estimation of consumption of carbohydrate at meals or snacks.

The **glycemic index (GI)** of a carbohydrate – containing food describes its post prandial glucose response over 2hrs in the area under the good glucose curve compared with a reference food with the same amount of carbohydrate, usually 50 g glucose. Foods can be differentiated into high (GI: 70-100) average (GI: 55-70) or low (GI: 55) glycemic index food.

High GI foods (e.g.: mashed potatoes, sugary drinks, cookies) should be substituted with low GI foods (e.g. oats, whole grain breads, certain raw fruits) as they lower post-prandial hyperglycemia [(9)].

Exercise: One of the important lifestyle modifications in diabetes is exercise. It is associated with improved glycemic control, insulin sensitivity, and cardiovascular fitness and remodeling.

Self-monitoring of blood glucose is an integral part of the process, allows the patients to assess the effect of their lifestyle and pharmacologic efforts in controlling post prandial glucose levels [(3)].

2. **Pharmacotherapy.**

   The available oral hypoglycemic agents are

- Bigunaide Metformin which counters insulin resistance and decreases blood glucose by reducing hepatic glucose production and also increases the glucose uptake by the liver.

- Sulfonylureas (eg: gliclazide, glimepride) act on the pancreas β cells to stimulate insulin secretion.
- Meglitinides, also known as prandial insulin releasers, taken before meals to boost insulin levels during digestion, thereby reducing prandial hyperglycemia.
- Thiazolidinediones alter the expansion of certain insulin sensitive genes by stimulating the peroxisome-proliferator-activated receptor γ and produce a slow –onset-glucose lowering effect, attributed mainly to increased insulin sensitivity.
- α – glucosidase inhibitor (eg: acarbose) show the digestion of carbohydrates by competitive inhibition of intestinal α – glucosidase enzymes.

The advanced stages of type II diabetes insulin therapy should be initiated, along with oral hypoglycemic agents [9].

RESPIRATORY SYSTEM

The organ that supports gas exchange comprises the respiratory system. They are the upper airways, lower airways, lung parenchyma, chest wall, respiratory muscle, pulmonary blood vessels, support nerves and lymphatics. Lung is a sophisticated conglomerate of alveolar air sacs, whose primary function is continuous absorption of O_2 and excretion of CO_2 [12].

Lungs are multilobed, cone shaped, sponge like organs that lie within the pleural cavities bounded by chest wall & diaphragm. The average adult

lungs are low – density organs that occupy a volume of approximately 3.5 liters and weight approx 900gm.

The chest wall and the lungs are elastic structures that can expand and recoil when inflated with air. This elasticity results from surface tension forces in the alveoli & from the elastic properties of the tissues & various connective tissue fibers. The presence of elastin fibers in the alveolar walls, the small airways and pulmonary capillaries produces elastic recoil.

Collagen and reticulin fibers located in the visceral pleurae and airway walls combine to create a basket like helical network of connective tissue fibers around the alveoli and airway walls that extends to the lumen.

Tendency of the lung to collapse is counteracted by the thoracic walls tendency to spring outward and to hold the lung inflated. The tension developed by these two opposing tendencies result in the development of subatmospheric intrapleural pressure [13].

INSPIRATION AND EXPIRATION:

Inspiration is an active process. The muscles of inspiration are diaphragm, external intercostals, sternocleidomastoid muscle, serratus anterior and scalene muscle. Their contraction increases the lung volume.

During inspiration the intrapleural pressure becomes more negative i.e. from -2.5 mm Hg to -6 mm Hg due to expansion of the chest wall. This pulls

the surface of lungs with greater force creating negative intrapulmonary pressure.

At the end of inspiration, the inspiratory muscles relax and the recoiling force of the lungs begins to pull the chest wall back to expiratory position. The pressure in the airway becomes slightly positive, and the air flows out of the lungs.

Expiration during quiet breathing is passive. At the end-expiratory position where the recoil force of the lungs and recoil force of thoracic cage balance, the pleural pressure returns back to -2.5 mm Hg [10].

RESPIRATORY UNIT:

It is composed of a respiratory bronchiole, alveolar ducts and alveoli. There are about 300 million alveoli in the lungs; each alveolus is about 0.2 mm in diameter. The alveolar walls are thin and has solid network of interconnecting capillaries. Gas exchange occurs between the alveoli and pulmonary capillary blood.

RESPIRATORY MEMBRANE:

The layers of the respiratory membrane are

1. A fluid layer containing surfactant.
2. A layer of alveolar epithelium.
3. The epithelial basement membrane layer.

4. A thin interstitial space between the alveolar epithelium & the capillary membrane.
5. A capillary basement membrane.
6. The capillary endothelial cell layer.

Despite the large number of layers, the thickness of the respiratory membrane is 0.2 µm and the total surface area is about 70 square meters [14].

PULMONARY FUNCTION TEST

The pulmonary function tests are very important age old test to assess the respiratory function of a person. They are important for clinical, diagnostic and prognostic values [7].

The factors that determine the lung functions at a particular point in adult life are

1. The maximally attained level of lung function.
2. The onset of decline of lung function.
3. The rate of decline of lung function.

Normally the maximum lung function is around the ages of 20 and 25 years. After the age of 30-35 years there is decline in lung function [15].

It has been observed that the lung function have been mild to moderately reduced before they are appreciated by the patient or clinical signs are observed.

Therefore, the subjective assessment of the severity of the disease is sometimes difficult. It may lead to inadequate treatment interventions and control of the disease.

Measurements of the lung function tests are important in diagnosis and monitoring of treatment of lung disorders [16].

The ability of the lungs to perform gas exchange depends upon

1. The diaphragm and thoracic muscles which are capable of expanding the thorax and lungs to produce a subatmospheric pressure.
2. The airways must be unobstructed so that it allows gas flow into the lungs and reach the alveoli.
3. The cardiovascular system must circulate blood through the lungs and ventilated alveoli.
4. O_2 and CO_2 must be able to diffuse through the alveolar – capillary membrane.

Pulmonary function tests can provide valuable information about these important individual processes that support gas exchange i.e. ventilation, diffusion & perfusion [13].

Pulmonary function tests can be divided into categories based on the aspect of lung function they measure

1) Airway function
2) Lung volume and ventilation

3) Diffusion capacity tests.
4) Blood gases and gas exchange tests.
5) Cardiopulmonary exercise tests.
6) Metabolic measurements.

Airway function and lung volumes are almost always measured with spirometry.

SPIROMETRY

Spirometry is a powerful tool that can be used to detect, differentiate, follow and also to manage patients with pulmonary disorders. It typically assesses the lung volumes and flows. It is also useful to determine the patterns of lung dysfunction [(4)].

In the middle of 18th century, Hutchinson developed a simple water sealed spirometer that allowed measurement of vital capacity. He also observed that VC was related to the standing height of the patient [(17)].

In 1679, Borelli first measured the volume of air inhaled by single deep breath. The need for temperature correlation was pointed out by Goodwyn (1788). In 1831, Thackrah showed the volume of air to be less in women than in men.

Davy (1800) measured the residual volume by gas dilution method. DuBois and colleagues (1956) developed a method called whole body plethysmography [(17)].

Forced vital capacity is a refinement of the simple VC test. During the 1930s, Barach observed that patients with asthma exhaled more slowly than healthy patients. He noted that airflow out of the lungs was important in detecting obstruction of the airways. He also used kymograph to display VC changes as a spirogram.

In 1950, Gaensler began using a microswitch in conjuction with water – sealed spirometer to time FVC. He observed that healthy patients consistently exhaled approximately 80% of their FVC in 1 second and almost all of the FVC in 3 seconds. He used the FEV1 to assess airway obstruction.

In 1955, Leuallen and Fowler demonstrated a graphic method to assess airflow. They measured airflow between the 25% and 75% points on a forced expiratory spirogram. This was described as maximal mid expiratory flow rate [MMFR] and now referred to as Forced Expiratory Flow 25% - 75%.

In the late 1950s, Hyatt and others began using the flow – volume display to assess airway function. The tracing was termed the Maximal Expiratory Flow Volume (MEFV) curve. By combining it with an inspiratory maneuver, a closed loop was displayed called the flow – volume loop.

In the 1960s, Wright used the peak flow to monitor asthmatic patients. Peak Expiratory Flow (PEF) is measured using either a flow – sensing spirometer or a peak flow meter.

Maximal Voluntary Ventilation (MVV) was described as early as 1941. Cournand and Richards originally called it the maximal breathing

capacity. The MVV gives an estimate of the peak ventilation available to meet physiologic demands [17].

Nowadays, modern computerized pulmonary function systems allow very sophisticated data handling and storage, graphic display of maneuvers, accurate calculations and enhanced reporting capabilities. They combine physical transducers, analog to digital converters, and computer software to process and record physiologic data. Microprocessor-based spirometers are now small enough to be handheld and portable [17].

TYPES OF SPIROMETERS:

Broadly there are two types of spirometers:

I.VOLUME DISPLACEMENT SPIROMETERS:

These records the amount of air exhaled or inhaled within a certain time.

These widely used types of volume spirometer are

1) Water seal spirometer.
2) Dry rolling seal spirometer.
3) Bellows spirometer.

II. FLOW SENSING SPIROMETER OR PNEUMOTACHOMETER:

These measures how fast the air flows in or out as the volume of air inhaled or exhaled increases.

The most common types of flow spirometers are

1) Rotating vanes (Turbines)
2) Pressure differential flow sensing spirometers.
3) Hot wire anemometers.
4) Pitot tube flow sensing spirometers [16].

Spirometry can be performed in either the sitting or standing position for adults and children. The use of nose clips is recommended for spirometric measurements that require rebreathing, even if just for a few breaths.

American Thoracic Society Standards for Spirometry are

The spirometer should be able to measure up to 30 seconds, while measuring the slow vital capacity and for FVC, the time capacity should be at least 15 seconds.

It should have a capacity of at least 8 Liters and should measure volumes with less than 3% error or within 50ml of a reference value, whichever greater.

A diagnostic spirometer should measure flow of about 95% accurate over the entire 0 to 14 L/sec range of gas flow.

The values produced by spirometer is corrected for body temperature, ambient pressure, and saturated with water vapour (BTPS).

The standards include verifying volume accuracy with a 3 liter calibration syringe at least daily [13].

INDICATIONS OF SPIROMETRY:

1. To detect the presence or absence of lung disease.
2. To monitor the progress of the disease.
3. To monitor the efficiency of treatment.
4. To evaluate the respiratory fitness prior to surgery.
5. To measure effects of occupational or environmental exposure
6. To evaluate disability or impairment [17].

CONTRAINDICATIONS OF SPIROMETRY:

1. Hemoptysis of unknown origin.
2. Respiratory infections.
3. Pneumothorax.
4. Recent myocardial infarction or pulmonary embolus.
5. Recent eye surgery or surgery of thorax or abdomen.
6. Thoracic, abdominal or cerebral aneurysms [4].

LUNG VOLUMES AND CAPACITIES

Lung volume determination usually includes the VC and its subdivisions, along with functional residual capacity. From these two basic measurements, the remaining lung volumes and capacities can be calculated. The most common reason for measuring lung volumes is to identify restrictive lung

disease. Lung volumes are almost airways measured in conjunction with spirometry.

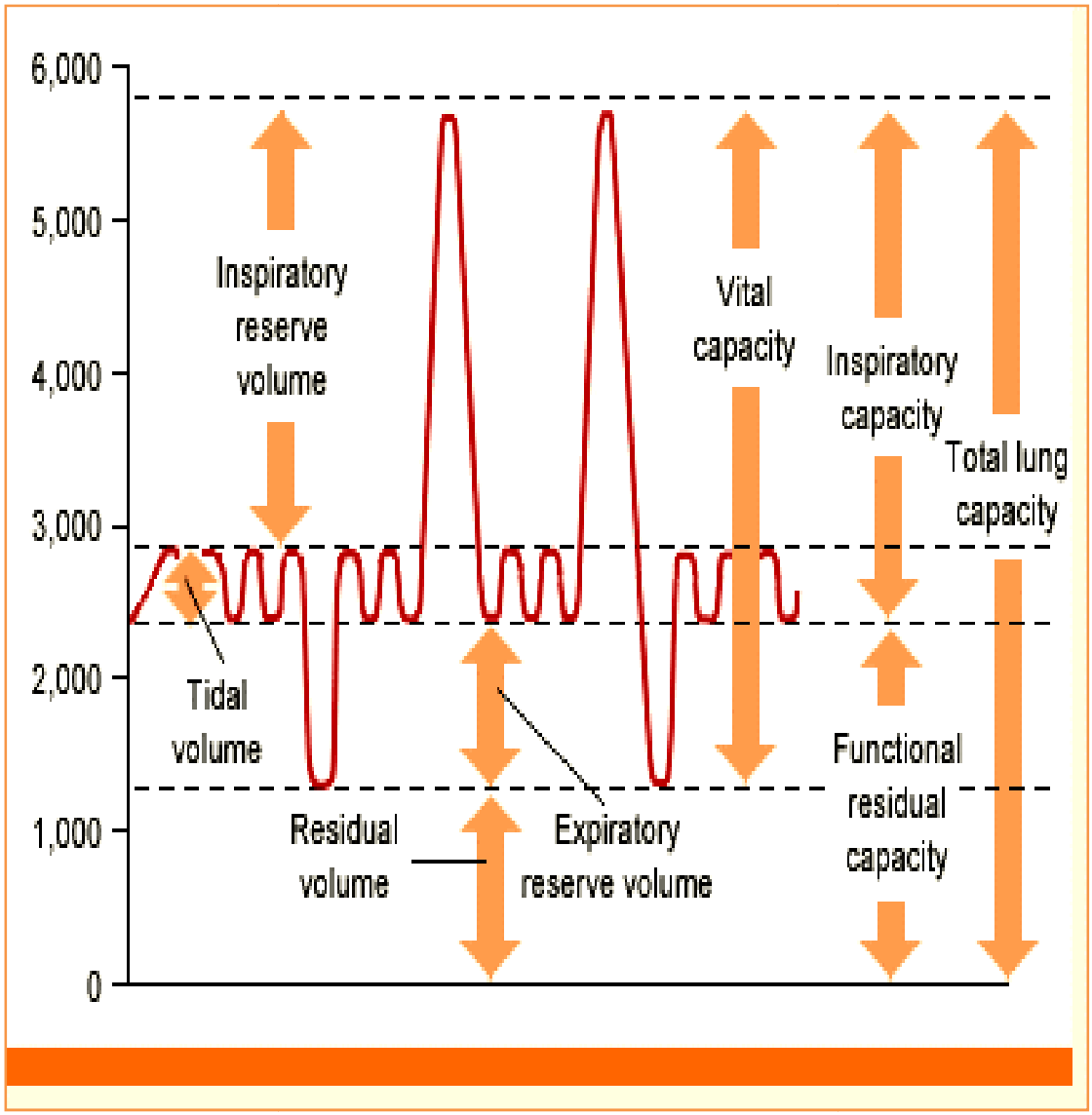


Figure 2: Diagrammatic representation of lung volumes and capacities based on a simple spirogram.

The four lung volumes are

1. **Tidal volume** is the volume of air inspired or expired during quiet breathing and is about 500ml.
2. The amount of air inspired with maximum inspiratory effort above the normal tidal volume is called **inspiratory reserve volume**: it is about 3000ml.
3. The **expiratory reserve volume** is the volume of air expired with maximum expiratory effort after the normal tidal expiration: this normally amounts to about 1100ml.
4. The volume of air remaining in the lungs after the forceful expiration is known as **residual volume**: it is normally about 1200ml.

The pulmonary capacities are

1. The maximum amount of air inspired after completing the tidal expiration is defined as **inspiratory capacity** and is about 3500ml.
2. The **functional residual capacity** is the amount of air remaining in the lung at the end of normal expiration and is about 2300ml.
3. The **vital capacity** is the maximum amount of air expired forcefully after a maximum inspiratory effort and is about 4600ml.
4. The **total lung capacity** is the volume of air present in the lung after a maximum inspiration and is about 6 liters [(14)].

Indices based on volume:

The volume of gas measured from a slow, complete expiration after a maximal inspiration, without forced or rapid effort is known as vital capacity. It is also referred to as the **slow vital capacity**, distinguishing it from forced vital capacity.

Forced vital capacity is defined as the maximum volume of expired forcefully and rapidly after a maximal inspiration.

In healthy individuals FVC equals VC or FVC & VC should be within 200ml of each other. Reduced FVC is a non specific finding. Values lower than 80% of predicted or less than the 95% confidence limit are considered abnormal. Low FVC may be caused either by obstruction or restriction.

FEV_1 is the volume of air expired in the first second of an FVC maneuver. It is reported as a volume, although it measure flow over a specific interval. The index was pioneered by Tiffeneau and Pinelli and by Gaensler. FEV_1, like FVC may be reduced in either obstructive or restrictive patterns.

FVC is measured concurrent with FEV_1 and its main application is to standardize FEV_1 for lung size using the relationship:

$$FEV_1\% = (FEV_1/FVC) \times 100$$

The relationship is a component of most lung function reports [12].

$FEF_{25-75\%}$ is the indicative of the status of the medium to small airways. It is measured from a segment of the FVC. Typical values for healthy young

adults average 4 to 5 L / sec. It is useful in to detect air flow limitation in the early stage itself.

PEF primarily measures large airway function. Effort dependence of PEF makes it a good indicator of patient effort during spirometry. It is particularly useful for monitoring asthma patients at home.

Maximal voluntary ventilation (MVV) is the maximum volume of air expired in a specific period of time (12 sec for normal subjects). It tests the overall function of the respiratory system. It is influenced by airway resistance, respiratory muscle, compliance of the lung/ chest wall and ventilatory control mechanisms. Values in healthy young men average between 150 – 200 L/min.

MVV is decreased in patients with moderate or severe obstructive disease. MVV may be normal in patients who have restrictive pulmonary disease. They can compensate by performing the MVV maneuver with V_T and breathing rates [17].

Indices based on time:

The time taken to expire a specified portion of the forced vital capacity is known as **forced expiratory time (FET)**. A time in excess of 4s is evidence for some degree of airflow limitation. Spirogram or volume-time curve, the volume of air exhaled is plotted against time. It reports four major test results. They are FVC, FEV_1, FEV_1/FVC % and $FEF_{25-75\%}$ [18].

Indices from the relationship of flow to volume:

The flow – volume curve reflects the relationship between the respiratory flows and lung volume. The curve can be for expiration alone or for expiration and inspiration (flow – volume loop). The shape of the flow- volume curve has proved to be a value for diagnosis.

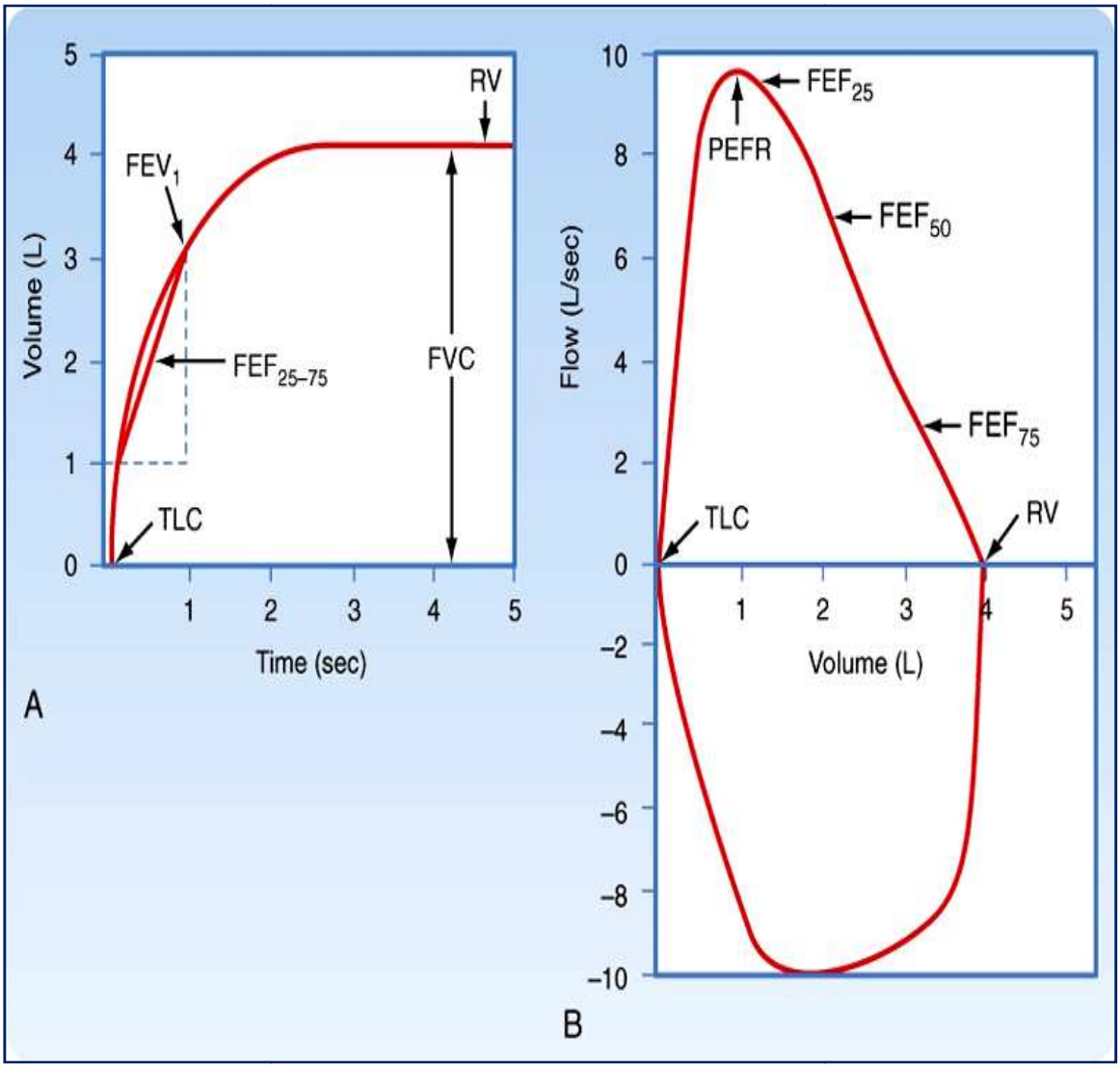


Figure 3: A – shows volume – time graph. B – Shows flow-volume loop.

Flow is plotted on the vertical axis and volume is plotted on the horizontal axis. Expiratory flow is plotted upward and inspiratory flow is

plotted downward. Peak flows for expiration and inspiration (PEF and PIF) can be read directly and the instantaneous flow (FEF) at any point in the FVC also can be measured directly [17].

The procedure to record the flow-volume loop is to ask the patient to perform FVC maneuver, inspiring fully and then exhaling as rapidly as possible. To complete the loop, the patient inspires as rapidly as possible from the maximal expiratory level back to maximal inspiration.

The flow-volume loop gives data for FVC, PEFR and Expiratory flow rates. When the expiratory flow-volume curve is divided into quarters, the instantaneous flow rate which 50% of the VC remains to be exhaled is called the $FEF_{50\%,}$ the instantaneous flow rate which 75% of the VC remains has been exhaled is called the $FEF_{75\%}$ and the instantaneous flow rate which 25% of the VC has been exhaled is called the $FEF_{25\%}$ [18].

PATTERNS OF ABNORMALITIES IN PFT RESULTS

The three main types of ventilatory dysfunctions observed in spirometry are

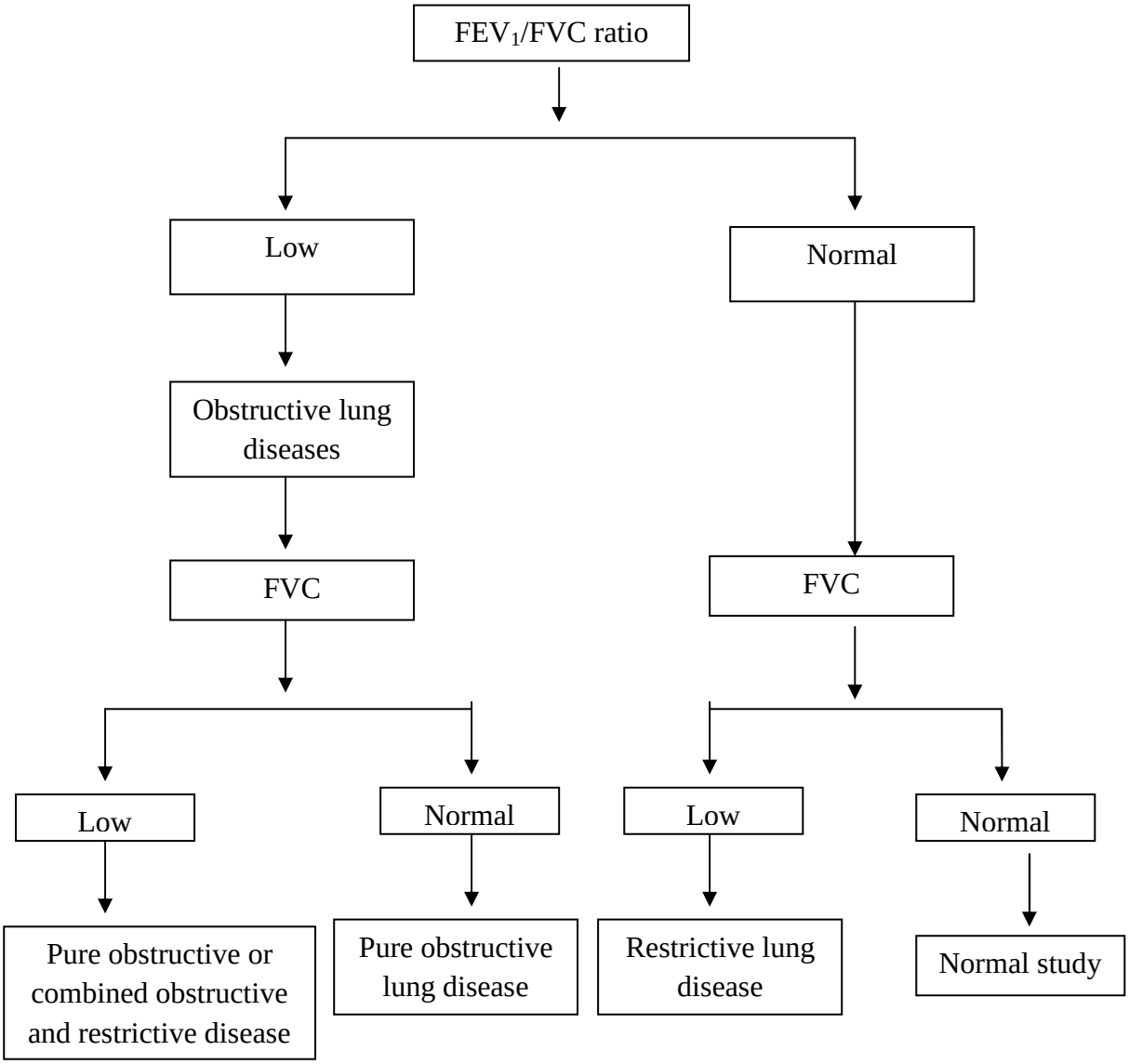
1. **Obstructive lung disorders** in which the FEV_1 is decreased, the FVC is usually normal and the FEV_1/ FVC ratio is decreased. Obstructive lung disease can be caused by conditions such as asthma, bronchitis, COPD, etc.

2. **Restrictive lung disorders -** the FEV_1 and FVC are both decreased, leaving a normal FEV1/ FVC. Restrictive lung disease can be caused by conditions

such as fibrosis, interstitial lung disease, pneumoconiosis, sarcoidosis, obesity, pregnancy and loss of lung tissue due to surgery etc.

3. **Mixed function disorders** - all the three parameters FVC, FEV_1 and FEV_1/ FVC are reduced. Mixed pattern may be seen in conditions such as bronchiectasis, cystic fibrosis, post-tubercular fibrosis, allergic bronchopulmonary Aspergillosis etc [13].

INTERPRETATION OF SPIROMETRY RESULTS [16]



Pulmonary Function Parameter	Obstructive Type	Restrictive Type
FVC (L)	↓	↓
FEV_1	↓	↓
FEV_1/ FVC%	↓	Normal
$FEF_{25-75\%}$ (L/SEC)	↓	Normal to ↑
PEFR	↓	Normal

Severity of pulmonary impairments based on a percentage (%) of the predicted values

Degree of impairment	Obstruction based on FEV_1	Restriction or Obstruction based on TLC,FRC,RV
Normal	80%-120%	80%-120%
Mild	70%-79%	70%-79% or 121%-130%
Moderate	60%-69%	60%-69% or 131%-140%
Moderately Severe	50%-59%	50%-59% or 141%-150%
Severe	35%-49%	35%-49% or 151%-165%
Very Severe	□35%	□35% or >165%

LUNG FUNCTION IN DIABETES

Spirometry is the non-invasive test that quantifies the physiological reserves that are not clinically affected by diabetes.

The pathogenesis of diabetic complications is due to involvement of both microangiopathy and non-enzymatic glycosylation of tissue proteins. This results in impaired collagen and elastin cross-linkage, reduction of strength and elasticity of connective tissue [(5)].

Since the lung has an abundant connective tissue, it may be a 'target organ' in diabetic patients [(5)]. Lung function also provides useful measures of the progression of systemic microangiopathy in diabetic patients [(4)].

The another important issue is that the lungs have a large surface area which has the ability to transfer large amounts of oxygen from the air to blood, favours a convenient portal of entry of therapeutic agents [(55)].

It was formerly thought that diabetes did not affect the lungs. However in the mid 1980s, the FVC, FEV_1, TLC, FRC & RV were observed to be reduced in diabetes. There was no evidence of airflow limitation. The finding was attributed to a reduction in lung compliance [(12)].

The decreased lung function is due to

1. Glycosylation of proteins such as collagen in the lungs and chest wall.
2. Decrease in muscle strength [(15)].

The pulmonary pathologic changes such as thickened alveolar epithelial and pulmonary capillary basal laminae are secondary to pulmonary microangiopathy [20].

Long term diabetes mellitus is characterized by widespread alterations of basal lamina. The classic morphologic findings in diabetic microangiopathy are the thickening of basement membranes in capillaries. This is a generalized phenomenon which affects both vascular and nonvascular tissues. Weynand et al demonstrated the thickenings of basal lamina of pulmonary capillaries are homogenous throughout the whole lung parenchyma [21].

All pulmonary function parameters were lower in diabetics of both sexes than non diabetic controls with greater reduction in males than in females and were due to diminished elastic recoil of lungs [22].

The reasons are some genetic factor involved for abnormal collagen structure linked to genetic predisposition of diabetes mellitus or age related changes in lung functions which might appear early in diabetic males than females [22].

The effects of diabetes on the respiratory system are numerous. They are

- Decreased lung volumes.
- Reduced vital capacity.
- Reduced TLC.
- Reduced pulmonary elastic recoil.
- Impaired pulmonary diffusion.

- Decreased inspiratory muscle strength.
- Increased bronchial responsiveness with increased threshold for cough response.
- More prone to develop respiratory tract infections.
- Sleep apnea is common in those having autonomic neuropathy [19].

Diabetes mellitus and lung function have a two way relationship. It is important to assess respiratory dysfunction caused by diabetes mellitus. It is even more pertinent, in non- diabetic subjects, to assess the risk of diabetes mellitus.

The impaired lung function may be the forecast quite reliably many years before the actual diagnosis of diabetes mellitus [23].

Augusto A. Litonjua et al observed that the diabetics had reduced lung function (especially FEV_1 and FVC but not FEV_1 / FVC ratio) than non – diabetic subjects. This decreased lung function is found to be present many years before the subjects are diagnosed as having diabetes mellitus [15].

In a retrospective analysis diabetics were found to have significantly lower mean FEV_1 and FVC values than for the control group. Diabetes also had an effect on the age related changes in lung function [24].

Dharwadkar et al observed that all the values of FVC, FEV_1, FEV_1 / FVC % and PEFR are reduced significantly in diabetics when compared with healthy controls. They also reported a negative correlation between the

respiratory parameters and glycemic status of diabetic patients. The reason for this reduced lung function is respiratory muscle weakness [7].

Muhammad Irfan et al observed that the diabetic patients had impaired lung function independent of smoking. There was a decrease in FVC, $FEV_{1,}$ and SVC as compared to their controls. They also reported that respiratory muscle endurance was impaired which was determined by MVV test [25].

Davis et al conducted a large community-based study in Western Australia in type II diabetic patients. They demonstrated that VC, FVC, FEV_1 and PEF were decreased in type II diabetic patients. An increase of 1% in mean HbA_{1C} was associated with a decrease of 4% in predicted FVC. They also suggested that the chronic complications of type II diabetes are reduced lung volumes and air flow limitation [26].

Sreeja et al reported that there was a significant decrease in FEV_1 / FVC% and $FEF_{25-75\%}$ in diabetic subjects as compared to controls [27].

Yel and associates observed in their cross- sectional study that middle – aged type II diabetics had significantly lower FEV_1, FVC, FEV_1 % predicted and FVC% predicted compared with non diabetics [28].

Diabetics with inadequate glucose control had reduced lung function than those with adequate control and the impairment is more consistent with a restrictive lung disorder [29].

McKeever et al demonstrated that in adults without diabetes, but impaired glucose regulation as indicated by glucose tolerance testing, higher levels of glycosylated hemoglobin, plasma insulin and C peptide are associated with impaired lung function in a dose – response manner [30].

O.L.Klein et al conducted a retrospective study and observed that FEV_1 and FVC were significantly reduced in patients with diabetes than those without diabetes [31].

Banu S et al, found that Mean Expiratory Pressure (MEP) was significantly reduced which was due to respiratory muscle weakness [32].

P.Lange et al in their longitudinal study in diabetic and non diabetic adult's participants of the Copenhagen City Heart study found that FEV1 and FVC were significantly lower in diabetic subjects when compared with healthy individuals with an average reduction of nearly 8% of the predicted value [33].

LUNG FUNCTION AND DURATION OF DIABETES

There is a definite correlation between the duration of diabetes mellitus and the tissue abnormalities. As the duration of diabetes increases, there is an increase in thickening of capillary basement membrane, capillary permeability, blood flow and viscosity and decrease in platelet function. These changes were observed in diabetics, particularly in the ones who are genetically susceptible.

As a result of these alterations, there are chances for the formation of microthrombi and ischemic tissue damage [34].

The duration of diabetes was a significant determinant of FEV_1 and a trend was seen for the FVC. The underlying mechanism of reduced pulmonary function in diabetes was due to inflammation which leads to progressive decrease in lung function and the severity of which would increase with duration of diabetes [35].

Mori showed that $DL_{CO\%}$ decreased significantly as the duration of DM increased and the reduction was greater in patients with diabetic microangiopathy and in type I diabetes mellitus [36].

In a cross sectional study the diabetic population were found to have abnormal pulmonary function, viz, mild reduction of lung elastic recoil and a reduction in pulmonary diffusing capacity because of a reduced pulmonary capillary blood volume which was correlated with duration of diabetes mellitus[37].

Timothy et al observed that duration of diabetes was an independent predictive of reduced lung function whereas HbA_{1C} was not [38]. Kanya kumara DH et al found that as the duration of diabetes increases, the restrictive profile becomes more prominent [39].

PATTERN OF LUNG DISEASE IN DIABETES

The most abundant protein in the human lung is collagen, which is important in defining lung structure and function. This collagen network confers strength to the structure and is dependent on cross-linkage between collagen and elastin. This is most important in conferring elasticity to the lung. However, increased collagen cross – link may increase lung stiffness.

The plausible mechanisms for restrictive respiratory defect are increased elastic recoil, decreased chest wall compliance and muscular weakness [(40)].

The markers of inflammation are Interlukein-1, Interlukein-6, and tumor necrosis factor. These are associated with insulin resistance and this has been demonstrated in recent epidemiologic studies.

In another study by Arnalich et al, found that the inflammatory markers are reduced with the treatment of diabetes, suggesting that diabetes may be a cause of systemic inflammation. This is due to the proinflammatory effects of advanced glycation end-products.

Walter, Beiser, Givelber, et al demonstrated relationship between glycemic state and reduced lung function. They also observed a slightly increased FEV_1 / FVC ratio suggesting a restrictive pattern of respiratory impairment [(10)].

Nakajima et al observed a restrictive pattern of pulmonary function but not obstructive pattern due to decrease in FVC and normal FEV1/FVC ratio.

This was due to metabolic disorders and metabolic syndrome in a severity dependant manner [41].

Sanjeev Verma et al reported a significant reduction in mean FVC and mean FEV_1 but no significant change was observed in FEV_1 / FVC ratio, PEFR, $FEF_{25 - 75\%.}$ They concluded that there was a restrictive type of respiratory function in diabetic patients [2].

Meo et al observed that there was a drop of FVC, FEV1, $FEF_{25 - 75\%}$ and PEF parameters suggests that type II diabetes adversely affect the lung function. This impairment shows a restrictive pattern of airways disease and is associated with dose-effect response of period of exposure to disease [23].

Nandhini et al also reported that there was a predominant restrictive pattern of the disease in type II diabetes mellitus, with a significant reduction of FVC and normal FEV_1 / FVC % [42].

The pattern of abnormal pulmonary function observed in Boulbou et al study, low TLC, DL_{co} and preserved FEV1 / FVC % was suggestive of a restrictive type of lung disease. The possibility exists that the reduced TLC was due to the result of increased chest wall stiffness, but it seems that the alteration of lung connective tissue at a biochemical level was responsible for the development of abnormal lung mechanics [43].

In a morbid obese woman, Diabetes is a risk factor for respiratory function impairment. In Lecube et al study, detected that inadequate control of diabetes was associated with an obstructive pattern of pulmonary

abnormalities. It is possible that type II diabetic patient's exhale less air from the lungs at a slower rate than non-diabetic individuals, so there was an increase in residual volume [44].

In a prospective study of middle-aged men and women without known lung disease, lower vital capacity predicted and the subsequent development of type II diabetes. The possible explanation are hypoxia induced insulin resistance, adverse fetal or early- life conditions through long-standing altered gene expression, inflammatory precursors and decreased muscle strength [45].

Chance and associates observed in their study that alveolar microvascular reserves were reduced in type II diabetes, reflecting restriction of lung volume, alveolar perfusion and capillary recruitment. This reduction correlates with glycemic control and is aggravated by obesity [46].

Wannamethee and Associates in a large prospective study observed that restrictive lung function is associated with the development of type II diabetes. This association was due to inflammatory pathways [47].

Role of breathing exercise:

Regular breathing exercises are important to improve the lung function in diabetics. The exercises to improve the respiratory muscle strength are

1) Walking or bicycling that improves overall conditioning.

2) Breathing control techniques such as pursed lip breathing, diaphragmatic breathing improves ventilation, decreases air trapping, decreases work of breathing and improves breathing patterns.
3) Respiratory muscle training using resistive respiratory loading may strengthen both the inspiratory and expiratory muscles [13].

MATERIALS

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METHODS

MATERIALS AND METHODS

40 healthy volunteers were randomly recruited from the general population residing around Thanjavur Medical College. 40 type II diabetic patients were selected from the diabetic outpatient department of age group 35 – 55yrs with duration of diabetes more than 2 yrs. This was a case-control type of study done in the period may 2011-2012.

The study group was divided into two groups based on the duration of diabetes as 2-5yrs and 6-10yrs.

Group I - 40 healthy controls.

Group II - type II diabetic patients having diabetes for 2-5 years.

Group III - type II diabetic patients having diabetes for 6-10 years.

An informed written consent was obtained from all the participants prior to their participation in the study. The study protocol was approved by the Institutional ethical committee of Thanjavur Medical College.

Anthropometric measurements like height, weight were measured and BMI was calculated. Glycemic status for the participants was measured by doing fasting & post prandial blood sugar. HbA1c was determined by turbidimetric immunoassay and its value less than 7 % was taken for study. Detailed history and thorough clinical examination was carried out.

Inclusion criteria:

Apparently healthy individuals with type II diabetic patients on oral hypoglycemic drugs and having diabetes for more than 2 years duration of age group 35 – 55years. Thorough clinical examination and history was obtained from the subjects in order to determine the health status of the individual.

Exclusion criteria:

- Smokers.
- Patients with history of cardiac/respiratory disease (hypertension, myocardial infarction, bronchial asthma, bronchitis, tuberculosis).
- History of recent surgery.
- History of recent respiratory tract infection.
- History of occupational exposure.

Pulmonary function tests were done using computerized spirometer which was standardized according to American Thoracic Society performance criteria [Spiro Excel – Digital Spirometer – Medicaid systems].

The pulmonary function parameters like forced vital capacity [FVC], FEV_1, FVC/FEV_1%, PEFR, slow vital capacity [SVC] and maximum voluntary ventilation [MVV] are recorded. The Pulmonary function test was performed 3 times on the same day in sitting posture with two minutes interval and the best of the three was taken.

Blood samples were drawn for estimation of fasting blood sugar and glycated hemoglobin after 6 hours of fasting. The subject was asked to take breakfast and post-prandial blood sugar was also checked after 2 hours.

The pulmonary function data are represented in three columns. These columns show the predicted values, measured values obtained during testing and the percent of predicted values for each test. A common method of comparison is to compute a percentage of the predicted value.

PRECAUTIONS:

i. The subject must be comfortable and relaxed.
ii. The apparatus should be sterilized and cleaned properly.
iii. The subject should sit with his spine erect and nostril closed.
iv. The mouth piece is placed in the subject's mouth in such a way that the mouth piece remains fitted between the teeth and the lips.
v. The subject should be demonstrated and trained about the different maneuver.
vi. Minimum three recordings should be taken for each maneuver at a gap of two minutes each and the best of the three should be taken.

PROCEDURE:

Forced vital capacity:

The subject is asked to breathe out forcefully with a maximum effort possible after taking a deep inspiration and this is followed by a forced

inspiration to produce a complete image of forced breathing called a flow – volume loop.

Criteria for acceptability:

1. Maximal effort; No cough or glottis closure during the first second; no leaks or obstruction of mouth piece.
2. Good start- of- test ; extrapolated volume < 5% of FVC or 150ml
3. Duration-6 seconds of exhalation.
4. Three acceptable spirograms are obtained; two largest FVC values within 200ml and two largest FEV_1 values within 200ml are taken.

Slow vital capacity:

The subject is instructed to inhale and exhale normally to record the tidal volume. Then the subject is asked to breathe in as much as possible after the normal expiration and exhale maximally to record inspiratory and expiratory volume.

Criteria for acceptability:

1. Two acceptable VC maneuvers should be obtained and volumes within 200ml
2. VC should be within 200ml of FVC value.

Maximum voluntary ventilation:

The subject is asked to breathe as deeply and as rapidly as he can for 15 seconds.

Criteria for acceptability:

1. Volume – time tracing shows continuous, rhythmic effort for at least 12 seconds.
2. End – expiratory lung volume is relatively constant.
3. Two acceptable maneuvers are obtained; MVV values are within 10%.
4. MVV is approximately equal to $35 \times FEV_1$ [17].

Statistical analysis:

Pulmonary function parameters were analyzed by using statistical software Microsoft excel and SPSS 18.0 for windows. The statistical analysis was done by the Student's t test, which was used to find the significant difference of pulmonary function parameters between the healthy non- diabetic controls and type II diabetic cases.

FIGURE 4: Computerized Digital Spirometer-Spiro Excel

RESULTS

RESULTS

Totally 80 subjects were participated in the study. Out of 80 participants, 40 were type II diabetes forming the study group and the remaining 40 were normal subjects forming the control group. The study group was divided into 2 subgroups based on the duration of diabetes as 2-5 years and 6-10 years.

The anthropometric, biochemical and the lung function parameters were analyzed by arithmetic mean and standard deviation. The mean values of pulmonary function parameters of the diabetics were compared with healthy controls using Independent Student's t test. The pulmonary function parameters were correlated with duration of diabetes by using Pearson's correlation coefficient test.

TABLE I

DESCRIPTIVE STATISTICS

	Control & Study (n=80)			
	Min	**Max**	**Mean**	**S.D**
Age	35	55	43.99	6.657
Height	152	169	162.56	3.464
Weight	41	91	60.85	10.713
BMI	16.41	32.63	22.9709	3.65167
HbA1c	2.34	6.80	4.2711	1.42972
FEV_1	44	115	86.28	14.956
FVC	39	100	77.80	12.423
FEV_1/FVC%	91	128	116.81	7.119
PEFR	38	168	92.40	23.799
$FEF_{25-75\%}$	44	213	131.18	34.592
MVV	28	98	62.00	16.015

The baseline characteristics of the control and study group are shown in the table.

TABLE II

Anthropometric parameters of subjects of Control and Diabetic groups

	Control (n=40)				Study (n=40)			
	Min	**Max**	**Mean**	**S.D**	**Min**	**Max**	**Mean**	**S.D**
Age(years)	35	54	40.47	5.630	35	55	47.50	5.724
Height (cms)	152	169	162.38	3.814	157	169	162.75	3.111
Weight (kg)	41	91	61.68	11.796	42	81	60.03	9.588
BMI (kg/m^2)	16.41	32.63	23.34	4.087	16.61	30.49	22.60	3.167
HbA1c%	2.34	4.32	3.1607	0.483	2.40	6.80	5.38	1.174

The Mean (±SD) of HbA1c of controls is 3.16 ± 0.482 and for the study group is 5.38 ± 1.174, shows that the controls and study group with good glycemic control are selected for the study.

TABLE III

Pulmonary function parameters of subjects of control and diabetic groups

	Control (n=40)				Study (n=40)			
	Min	**Max**	**Mean**	**S.D**	**Min**	**Max**	**Mean**	**S.D**
FEV_1	64	115	91.40	11.236	44	115	81.15	16.523
FVC	59	100	81.85	9.211	39	100	73.75	13.933
FEV_1/FVC %	91	126	117.05	7.250	94	128	116.58	7.071
PEFR	59	168	98.85	21.996	38	153	85.95	24.045
$FEF_{25-75\%}$	85	212	136.73	26.056	44	213	125.63	41.009
MVV	42	98	65.20	15.010	28	96	58.80	16.530

The mean (±SD) of the pulmonary function parameters of both study group and control group are shown in the table.

TABLE IV

Comparison of pulmonary function tests parameters between the controls and type II diabetes

PARAMETER	Control group (n =40)	Diabetic group (n = 40)	P value
FEV_1	91.40±11.236	81.15±16.523	0.002*
FVC	81.85±9.211	73.75±13.933	0.003*
FEV_1/FVC%	117.05±7.250	116.58±7.071	0.768
PEFR	98.85±21.996	85.95±24.045	0.014*
$FEF_{25-75\%}$	136.73±26.056	125.63±41.009	0.152
MVV	65.20±15.010	58.80±16.530	0.074

(* P value less than 0.05 was considered to be statistically significant)

The mean (±SD) of FEV_1 for the control group are 91.40±11.236 and for diabetic group are 81.15±16.523. It was found to be significantly reduced (P = 0.002).

The mean (±SD) of FVC for the control group is 81.85±9.211and for diabetic group is 73.75±13.933. The mean (±SD) of PEFR for the control group is 98.85±21.996 and for diabetic group is 85.95±24.045. The mean values of FVC and PEFR are found to be reduced in diabetic group when compared to controls and are statistically significant.

The mean (±SD) of FEV_1/FVC% for the control group is 117.05±7.250 and for diabetic group is 116.58±7.071. The mean (±SD) of $FEF_{25-75\%}$ for the control group is 136.73±26.056 and for diabetic group is 125.63±41.009. The mean (±SD) of MVV for the control group is 65.20±15.010 and for diabetic group is 58.80±16.530.

The mean values of FEV_1/FVC%, $FEF_{25-75\%}$ and MVV are reduced in diabetic group when compared with control group but not statistically significant.

FIGURE 5: Comparison between the controls and type II diabetes – with parameters of pulmonary function tests

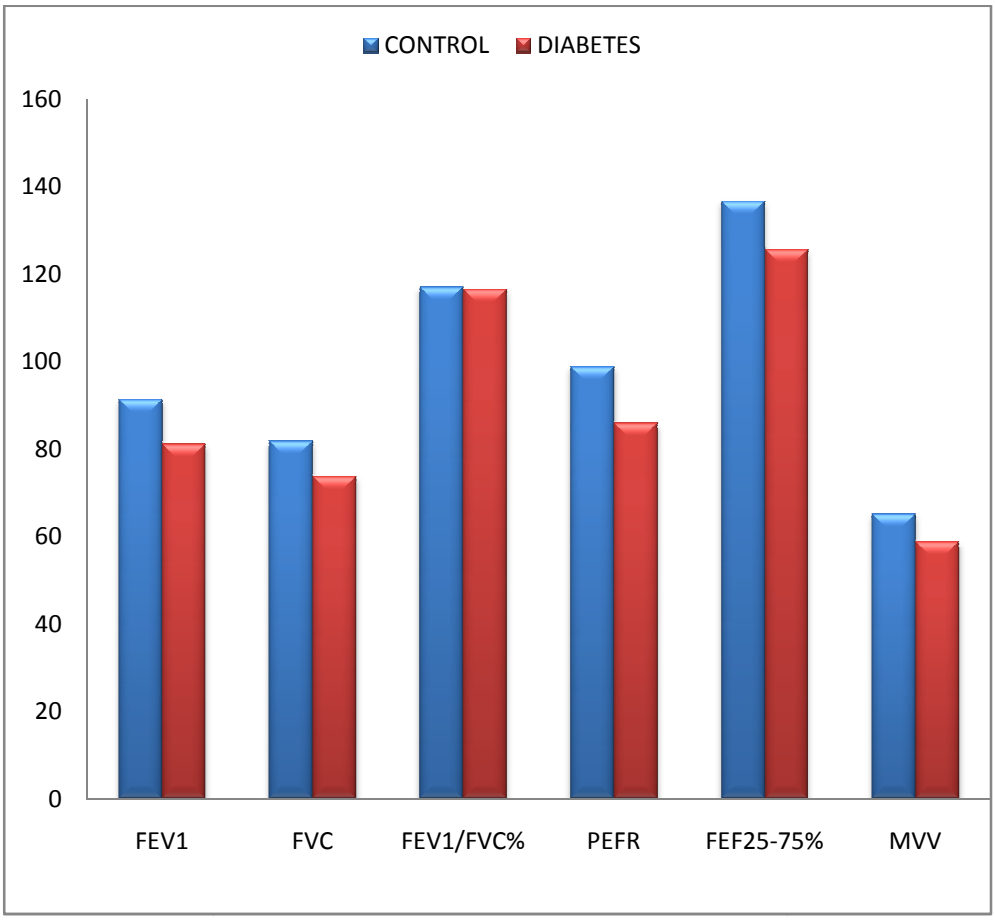


TABLE V

Comparison of pulmonary function parameter based on duration of diabetes mellitus between 2-5 years.

Parameters	Group I (n=40) Mean ± SD	Group II (n=26) Mean ± SD	P value
FEV_1	91.40±11.236	86.46±15.73	0.18
FVC	81.85±9.211	78.23±12.99	0.19
FEV_1/FVC%	117.05±7.250	117.62±6.25	0.75
PEFR	98.85±21.996	91.65±18.36	0.17
$FEF_{25-75\%}$	136.73±26.056	135.08±39.84	0.84
MVV	65.20±15.010	63.88±15.35	0.73

The mean ± SD of FEV_1 of diabetics with duration of 2-5yrs was 86.46±15.73 and found to be reduced when compared with the controls, but not statistically significant (P = 0.18) .

The mean ± SD of FVC of diabetics in group II was 78.23±12.99. When compared with the control group, it was not significantly reduced.

The mean ± SD of FEV_1/FVC % of diabetics in group II was 117.62±6.25 and for the control group was 117.05±7.250. The P = 0.75, which was not statistically significant.

Similarly the mean values of PEFR (91.65±18.36), FEF $_{25-\ 75\%}$ (135.08±39.84) and MVV (63.88±15.35) of group were found to be reduced when compared with control group but not statistically significant.

FIGURE 6: Comparison of pulmonary function parameter based on duration of diabetes mellitus between 2-5 years.

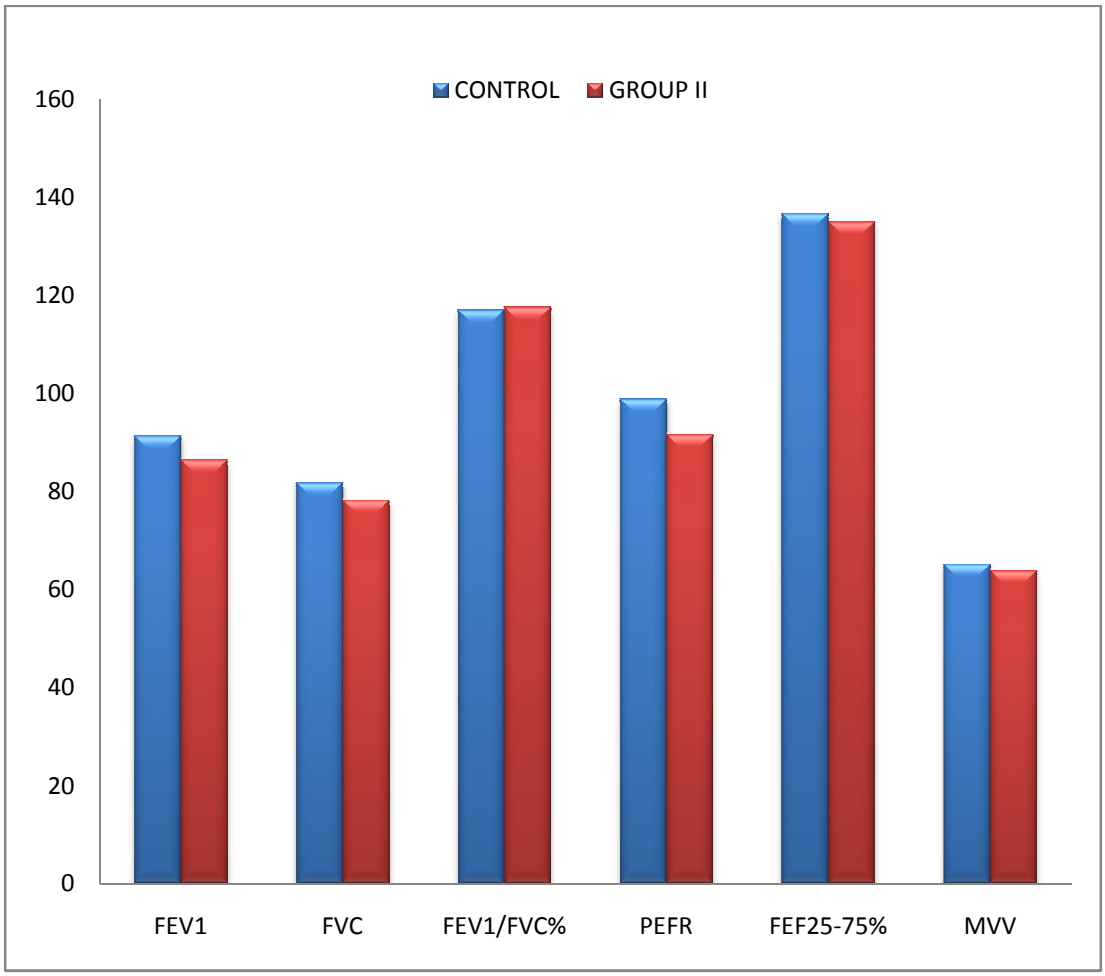


TABLE VI

Comparison of pulmonary function parameter based on duration of diabetes mellitus between 6-10 years.

Parameters	Group I (n=40) Mean ± SD	Group III (n=14) Mean ± SD	P value
FEV_1	91.40±11.236	71.28±12.29	< 0.001*
FVC	81.85±9.211	65.428±10.97	< 0.001*
FEV_1/FVC %	117.05±7.250	114.64±7.80	0.30
PEFR	98.85±21.996	75.35±28.49	0.003*
$FEF_{25-75\%}$	136.73±26.056	108.07±35.54	0.003*
MVV	65.20±15.010	49.36±13.66	0.001*

The mean (±SD) duration of disease for diabetic patients was 8.64 ± 1.23 years.

The mean (±SD) of FEV_1, FVC and MVV of study group having diabetes for 6-10years showed a highly significant reduction (P = 0.001) when compared with the control group.

The mean (±SD) of FEV_1/FVC % of group III having diabetes for 6-10 years was 114.64±7.80 and it was found to be statistically insignificant (P = 0.30).

FIGURE 7: Comparison of pulmonary function parameter based on duration of diabetes mellitus between 6-10 years.

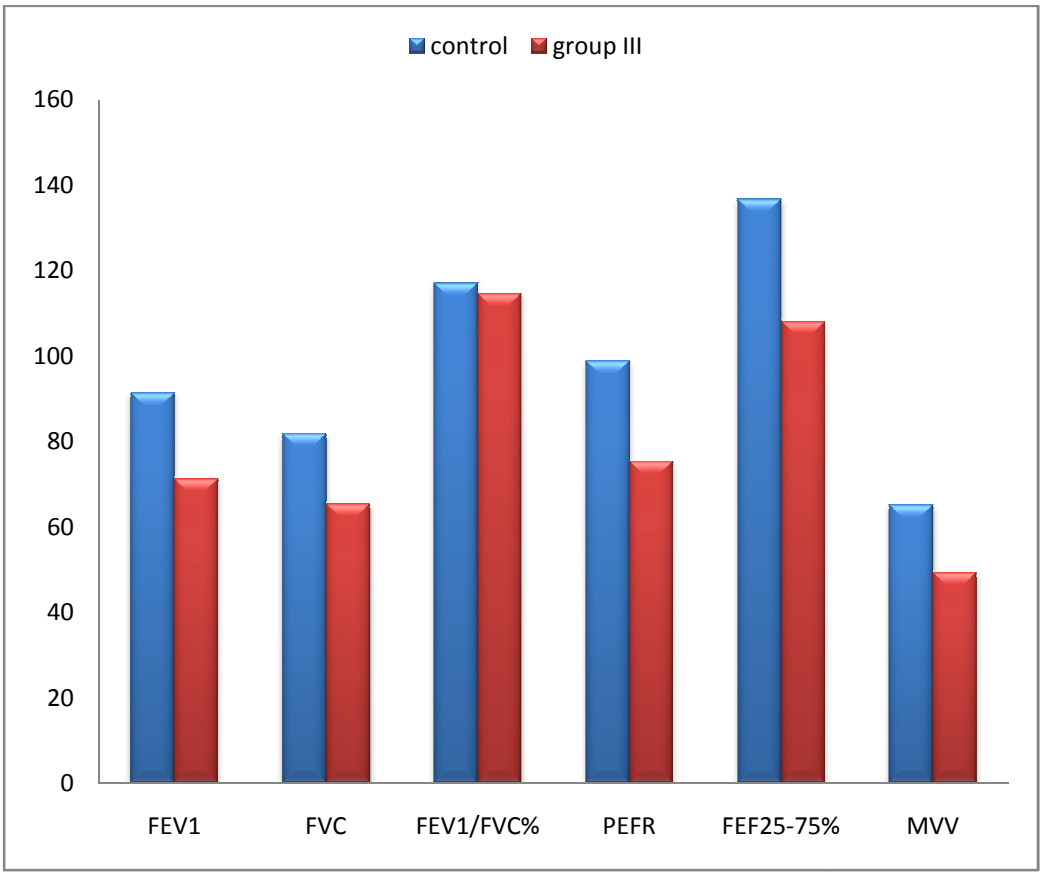


TABLE VII

Comparison of pulmonary function parameter based on duration of diabetes mellitus between 2-5years and 6-10 years.

Parameters	Group II (n=16) Mean ± SD	Group III (n=14) Mean ± SD	P value
FEV_1	86.46±15.73	71.28±12.29	0.004*
FVC	78.23±12.99	65.428±10.97	0.004*
FEV_1/FVC %	117.62±6.25	114.64±7.80	0.21
PEFR	91.65±18.36	75.35±28.49	0.04*
$FEF_{25-75\%}$	135.08±39.84	108.07±35.54	0.045*
MVV	63.88±15.35	49.36±13.66	0.006*

The mean values of pulmonary function parameters of the diabetic group II and III are compared based on the duration. The mean (±SD) values of FEV_1, FVC, PEFR, $FEF_{25-75\%}$ and MVV of type II diabetics with duration 6-10 years was found to be reduced when compared with diabetics of 2-5 years duration and it was found to be statistically significant.

The mean (±SD) values of FEV1/FVC % of group III was 114.64±7.80 and of group II was117.62±6.25. It was found to be reduced but not statistically significant.

FIGURE 8: Comparison of pulmonary function parameters based on duration of diabetes mellitus.

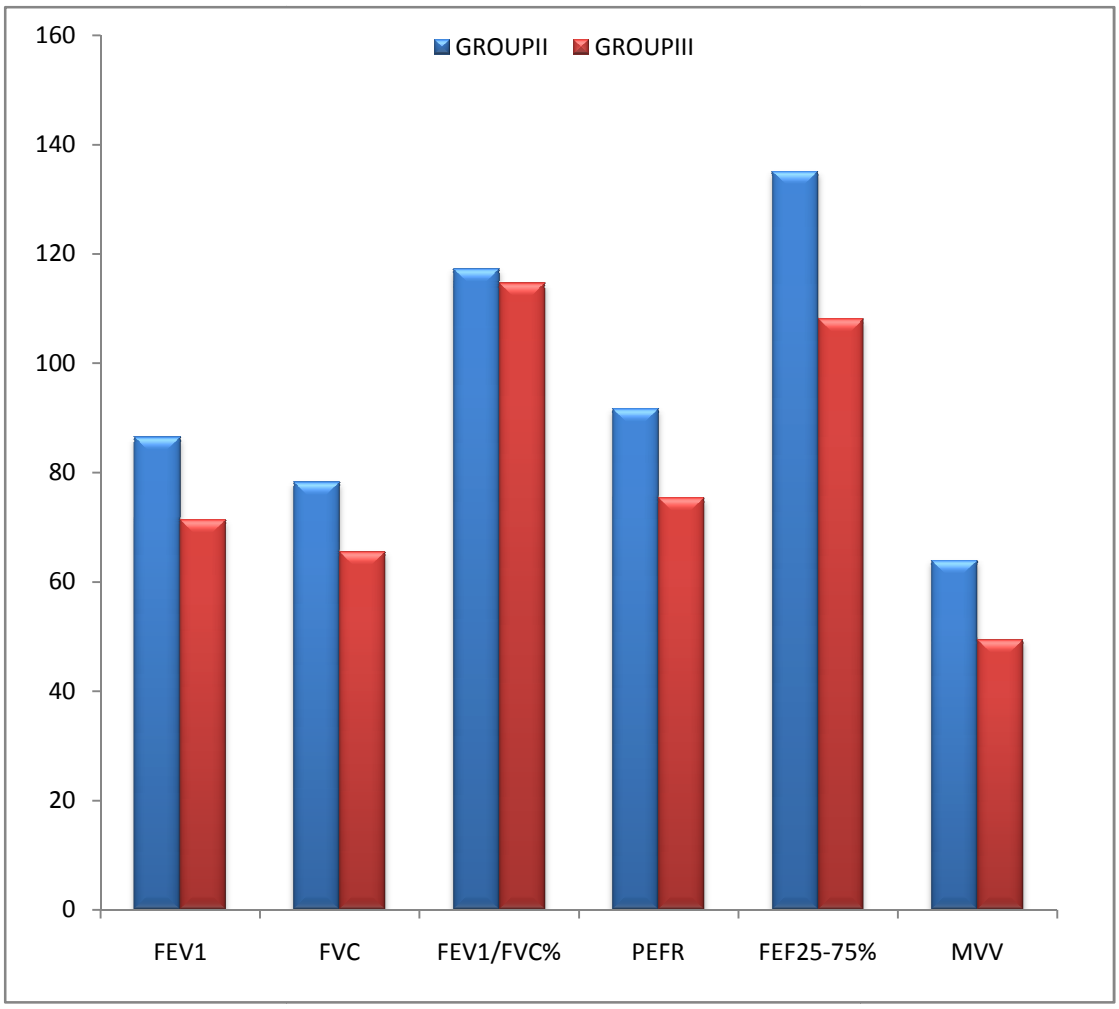


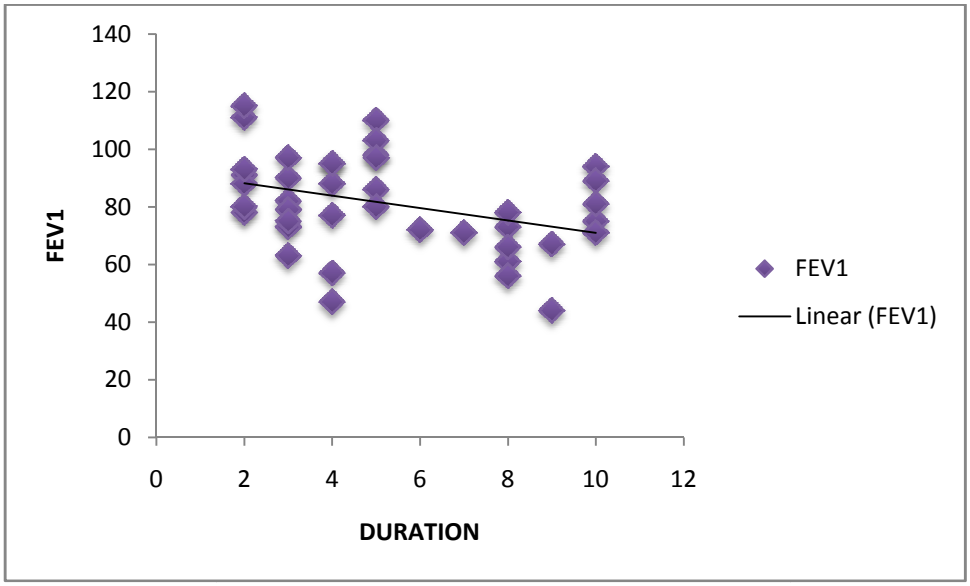
TABLE VIII

Correlation between duration of diabetes and the parameters of lung function

Parameter	Pearson correlation	P value - sig (2 tailed)	
FEV_1	-0.0368	0.022	S
FVC	-0.3478	0.028	S
FEV_1/FVC	-0.1301	0.423	NS
PEFR	-0.3055	0.055	NS
$FEF_{25-75\%}$	-0.2935	0.066	NS
MVV	-0.4843	0.001	S

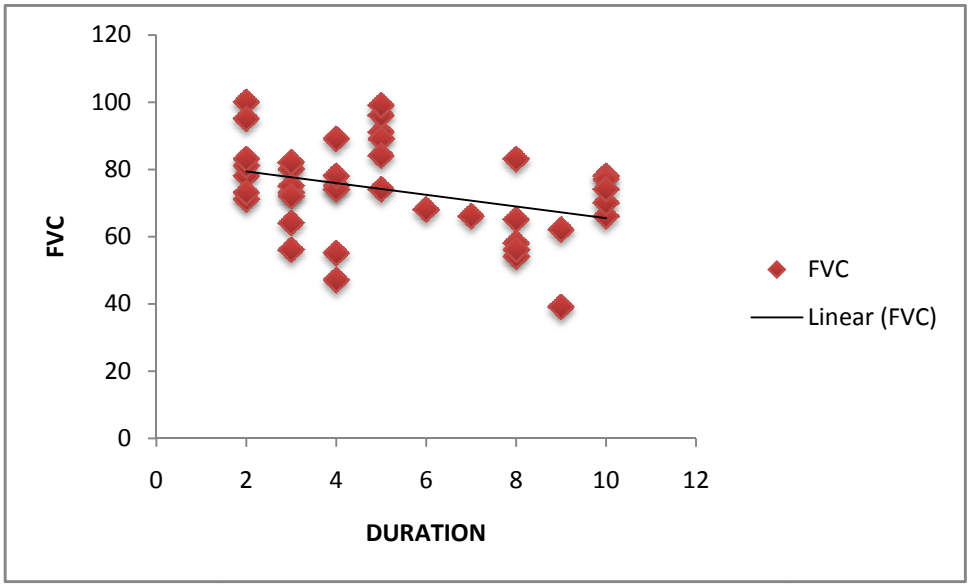
The lung function parameters FEV_1, FVC and MVV showed a significant negative correlation with the duration of diabetes whereas FEV_1/FVC %, PEFR, $FEF_{25-75\%}$ showed negative correlation but not significantly.

Figure 9: Correlation between duration of diabetes and FEV_1



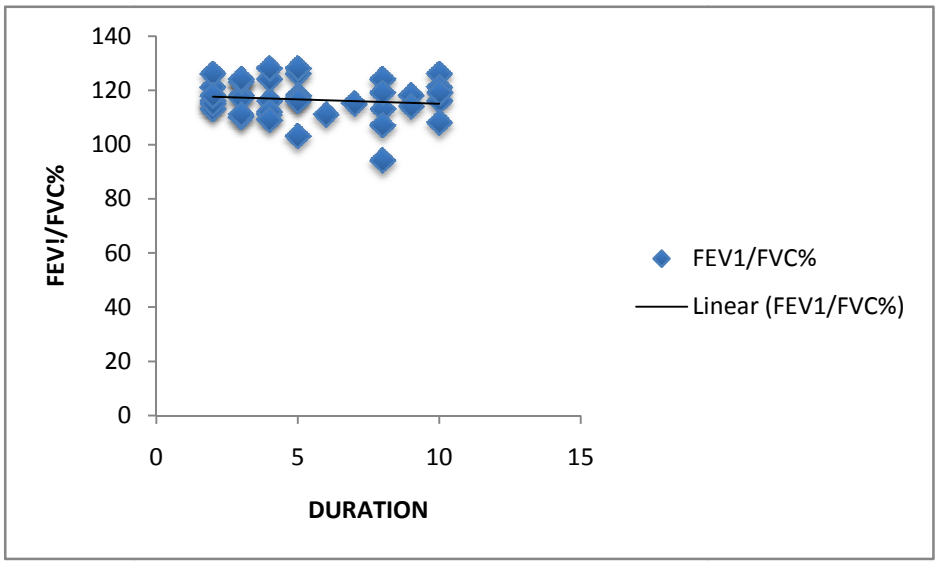
Graph shows Negative correlation of FEV_1 (r = -0.0368) with duration of diabetes. It is found to be statistically significant.

Figure 10: Correlation between duration of diabetes and FVC



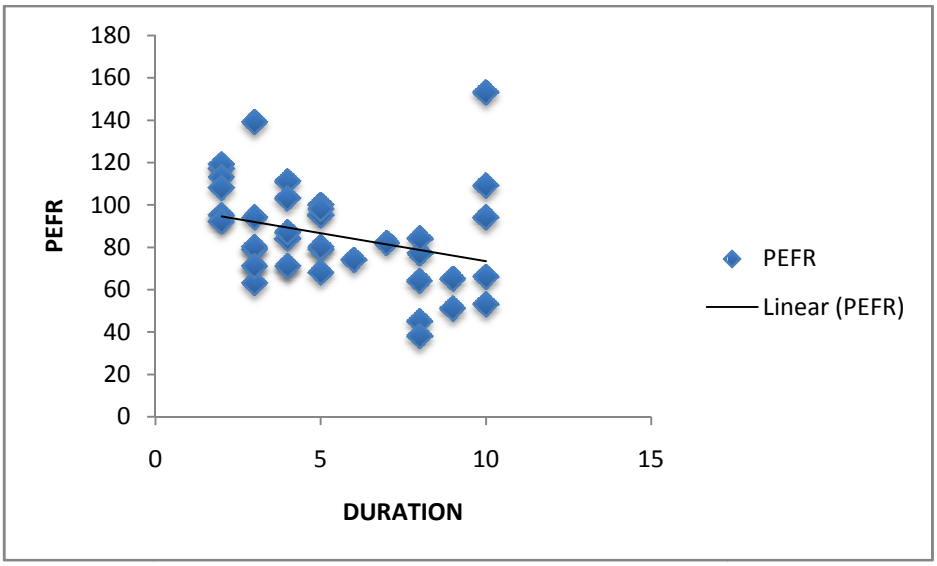
Graph shows Negative correlation of FVC (r = -0.3478) with duration of diabetes and is correlated significantly.

Figure 11: Correlation between duration of diabetes and FEV_1/FVC



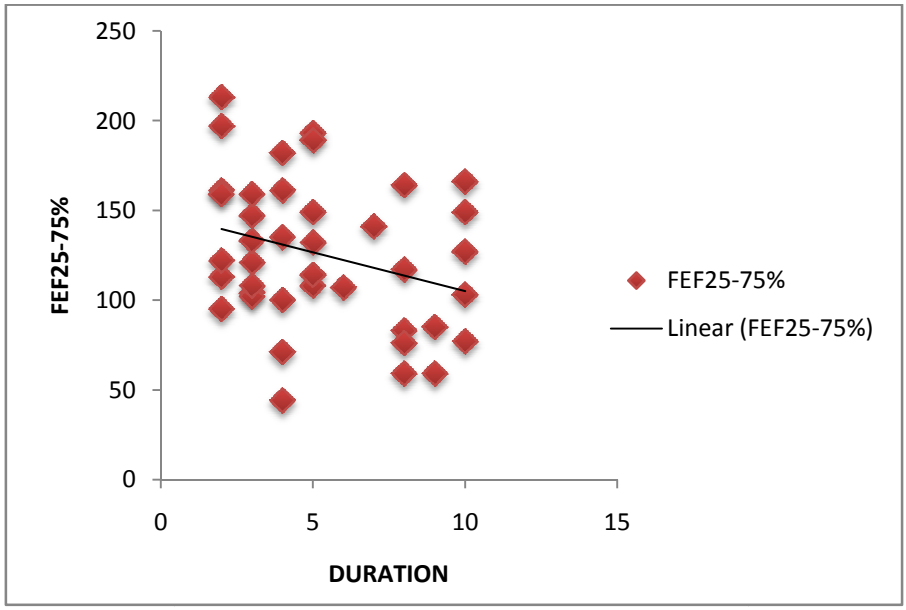
Graph shows Negative correlation of FEVI/FVC % (r = -0.1301) with duration of diabetes but not significantly.

Figure 12: Correlation between duration of diabetes and PEFR



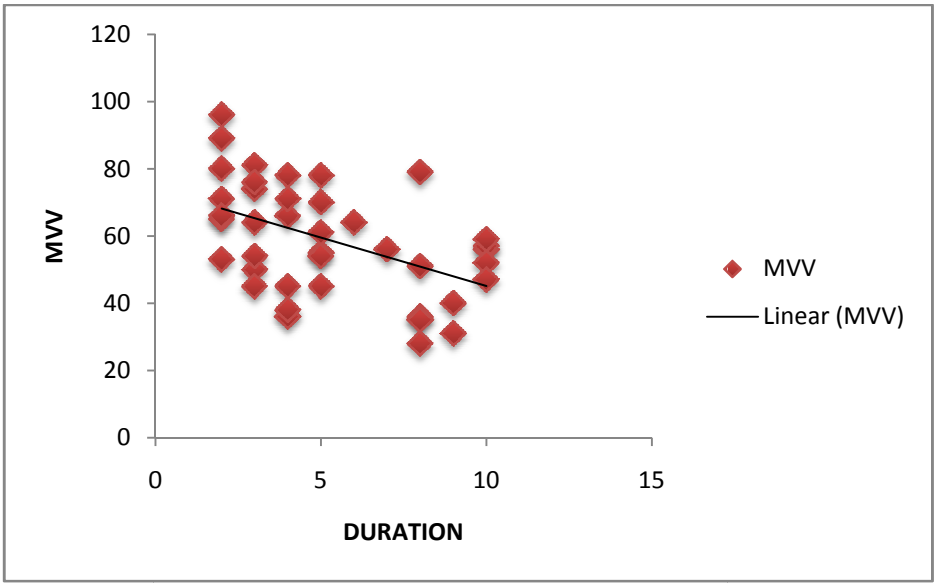
Graph shows Negative correlation of PEFR (r = -0.3055) with duration of diabetes but not significantly.

Figure 13: Correlation between duration of diabetes and $FEF_{25-75\%}$



Graph shows Negative correlation of FEF 25-75% (r = -0.2935) with duration of diabetes but not significantly.

Figure 14: Correlation between duration of diabetes and MVV



Graph shows Negative correlation of MVV (r = -0.4843) with duration of diabetes and there is significant correlation.

TABLE IX

Number of subjects with abnormal pulmonary function in the diabetes group and control group

	Control group (n = 40)	Diabetic group (n = 40)
Number of subjects with abnormal pulmonary function	9	30
Number of subjects with restrictive pulmonary function	8	17
Number of subjects with obstructive pulmonary function	1	13

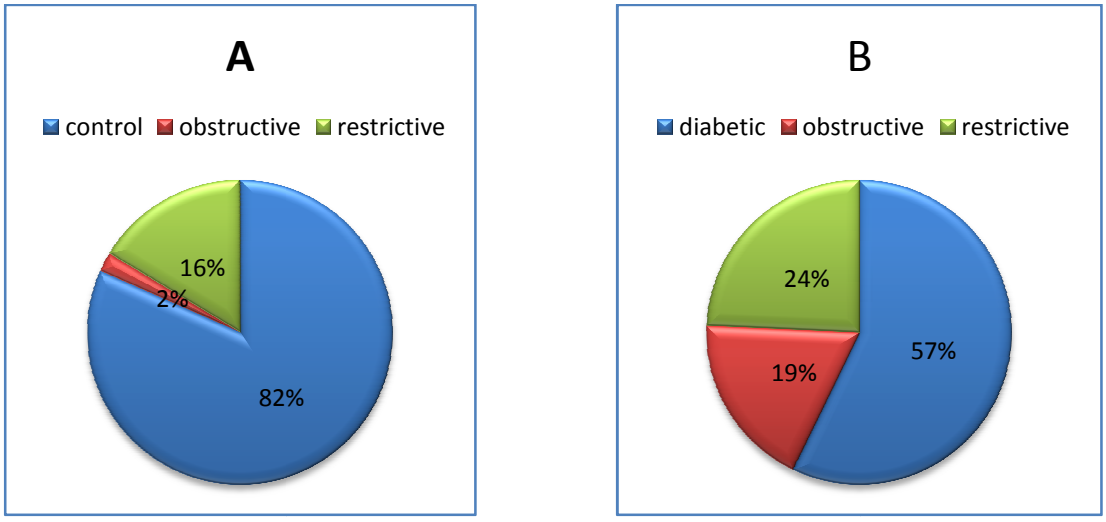


Figure 15: Chart A and Chart B shows the distribution of abnormal respiratory function in control and diabetic group.

Compared with the % predicted values, 10 of type II diabetes had normal pulmonary function compared with 31 of control subjects with normal

pulmonary function. 17 subjects with type II diabetes had restrictive lung disease and 13 had obstructive lung disease while 8 of the controls had restrictive lung disease and 1 had obstructive lung disease.

DISCUSSION

DISCUSSION

Type II diabetes mellitus is the most common form of diabetes. It is one of the major causes of morbidity and mortality [47].

Diabetes is a systemic disease that produces changes in the structure and function of several tissues, particularly of the connective tissues due to microvascular and macrovascular damage that include cardiovascular disease, nephropathy, retinopathy and neuropathy. Since the lungs have abundant connective tissue, it raises the possibility that lung is also a target organ in diabetes [42].

Histological evidence of pulmonary abnormalities has included alterations in the ultra structure of granular pneumocytes in the interalveolar septum of non-ciliated bronchiolar epithelial cells and of collagen and elastin in the alveolar wall.

Post-mortem studies on diabetic patients have shown the thickening of alveolar epithelial and pulmonary capillary basal laminae, centrilobular emphysema and pulmonary angiopathy [34].

The pulmonary function tests are important to assess the respiratory function of a person. The association of reduced lung function and diabetes has been described many years [32].

In this study, the pulmonary function of type II diabetic patients are compared with healthy subjects.

In the present study the age group of the subjects was between 35-55 years. The mean values of anthropometric parameters – height, weight and BMI were not compared between the control and diabetic group. Sreeja et al reported that there was no statistically significant difference in the anthropometric profiles of patients [27]. Similarly Asanuma et al also observed that there was no significant difference in the anthropometric profiles between male diabetics and controls.

In the present study,the Mean (±SD) of HbA1c of controls is 3.16 ± 0.482 and for the study group is 5.38 ± 1.174. This shows that the controls and study group with good glycemic control are selected for the study. HbA1c reflects the glycemic control only for the past 2-3 months, a duration which may not be long enough to impact an effect on lung function [35].

In their study Davis Timothy ME et al explained that HbA1c is relatively short term marker of glycemic control and the impaired lung function could still be present in diabetes. But the duration of glycemic exposure is more important than its magnitude [38].

Effect of type II diabetes on$FEV_1$and FVC:

In the present study the values of $FEV_1$and FVC are significantly reduced in type II diabetic patients when compared to healthy controls. These findings were consistent with findings of T.M.E Davis et al [38] and Davis et al [26] study.

Meo et al also supported our findings, that in normal healthy non smokers after the age of 35 years, the expected decline in lung function (FEV_1) is 25-30 ml/yr, whereas in diabetics, the decline is 71 ml/yr.

The reduced FVC was due to increase in the cross-linkage formation between polypeptides of collagen in pulmonary connective tissue. This is responsible for the restrictive pattern of pulmonary function [49]. The results of this study were in agreement with those of Sanjeev et al [2] and Maurizio et al [5] study.

The results of our study agreed with that of Yeh et al [45]. They reported that adults with impaired FVC (% predicted) had various features of insulin resistance. The main suggestion of their study was that impaired lung function (FEV_1 and FVC) deserves high attention as an emerging novel risk factor for type II diabetes.

Effect of type II diabetes onFEV_1/ FVC%:

FEVI/FVC ratio is a more sensitive indicator of airway obstruction than FVC or FEV_1 alone. In the present study, the FEV_1/FVC ratio did not show any significant change in diabetics when compared with controls. This shows restrictive type of pulmonary impairment as evidenced by significant reduction in FEV_1, FVC and normal FEV_1/FVC ratio. Similar results were observed with the study of Agarwal et al [22], Nakajima et al [41] and Ozoh et al in their cross-sectional study [35].

Similar results in Sanjeev et al [2] study showed that there was no significant change in FEV_1/FVC %. But FVC or FEV_1 were reduced show restrictive type of pulmonary impairment.

Our findings were consistent with Wannamethee and Associates study [47] and showed restrictive lung function with reduced FVC, FEV1and normal FEV_1/FVC %.

In the prospective analyses, Heianza et al [53] found restrictive lung dysfunction and the possible explanations would be hypoxia induced insulin resistance, chronic inflammation and low birth weight in early life

The explanation for restrictive type of pulmonary dysfunction was partially explained by inflammation, traditional and metabolic risk factors or by obesity and inflammation. In these individuals FEV_1, FVC and total lung capacity are reduced, but FEV_1/FVC % are usually normal [50] and this study results were similar to the findings in large population studies in Australia, Denmark and the United States [38], [33], [28].

But Gupta et al [54] and Sreeja et al [27] observed obstructive pattern of lung dysfunction and it may be early change or subclinical.

Effect of type II diabetes on PEFR:

In this study, the PEFR values were reduced significantly in diabetics (P value - 0.014) when compared with non-diabetics. The possible explanation is the decrease in the force generating capacity of the expiratory

muscle and the reduced elastic recoiling of the lungs. These findings were consistent with findings of Davis et al [26] and Agarwal et al [22] study.

Meo et al also observed reduced PEFR in their study and stated that the PEFR reflects not only the lung volume and the state of airways, but it also shows the expiratory muscle force and persistently low PEFR represents the collapsing of large airways [23].

Effect of type II diabetes on $FEV_{25-75\%}$:

In this study $FEF_{25-75\%}$ values were reduced among diabetics when compared to non-diabetics but not significantly. $FEF_{25-75\%}$ reflects the flow rate during middle 50% of FVC. It also indicates patency of the small airways. Reduced $FEF_{25-75\%}$ results from increased amounts of collagen and elastin in basal lamina of alveolar wall. However, low $FEF_{25-75\%}$ represents the involvement of peripheral bronchioles [23].

Sreeja et al [27] observed significant reduction in $FEF_{25-75\%}$ and stated that this reduction is due to a lower airway caliber and high airway resistance [27].

Effect of type II diabetes on MVV:

In the present study the mean MVV values were lower in diabetics than controls but not significantly. MVV is the maximum breathing capacity which is decreased in diabetics due to poor respiratory muscle strength as a result of increased protein catabolism. A study conducted by Meo et al [23]

and Keerthi et al [49] showed similar results. The reason for reduced respiratory muscle function may be due to neuropathy, myopathy or both [32].

The explanation for reduced lung functions in diabetics are due to biochemical alterations in the connective tissue of the lung, particularly collagen and elastin, as well as microangiopathy. This is due to non-enzymatic glycosylation of proteins induced by chronic hyperglycemia.

The functional abnormalities from these changes are thickening of the pulmonary capillary basal lamina and the alveolar epithelium, reduction in elastic recoil of the lung, lung volumes, and also reduced pulmonary capacity for the diffusion of carbon monoxide [25].

Effect of duration of diabetes on lung function:

In the present study, there is no significant reduction in lung function parameters of diabetic subjects of duration 2-5 years when compared with controls. But there is a significant reduction in FEV_1, FVC, $FEF_{25-75\%,}$ PEFR and MVV of diabetics of duration 6-10years when compared with non-diabetics. Whereas no significant change was observed in FEV_1/FVC % of diabetics of 6-10 years duration shows a restrictive type of pulmonary impairment.

Thus this study shows a strong association between the duration of disease and decreased pulmonary function impairment in diabetic patients. Our findings were also supported by Nandhini et al [42].

Similar observation in Kanya Kumari et al [39] study showed a progressive decrease in mean FVC, FEV_1 and PEFR values but FEV_1/FVC % was increased suggestive of restrictive pattern of respiratory abnormality.

Similarly Meo et al [23] observed that type II diabetics with longer than 10years showed a significant reduction in FVC, FEV_1, $FEF_{25-75\%,}$ and PEFR relative to their controls but the FEV_1/FVC % is normal or increased. This impairment shows a restrictive pattern of airway disease.

In the Ozoh et al study, showed similar result that the effect of diabetes increases on ventilatory function increases with duration of diabetes. The underlying mechanism of reduced ventilator function in diabetes may be related to inflammation. As the duration of diabetes increases the inflammatory process also increases leading to progressive decrease in lung function [35].

Correlation of duration of diabetes with pulmonary function

In our study lung function parameters were negatively correlated with the duration of diabetes mellitus. FEV_1 (r = - 0.0368), FVC (r = -0.3478) and MVV (r = -0.4843) were significantly and negatively correlated with the duration of diabetes mellitus. These findings were consistent with findings of Davis et al [26] and Timothy et al [38] study. They also suggested that the reduced lung volumes and air flow are due to chronic complications of type II diabetes.

Similar findings were observed by Banu et al [32] Mahadeva murthy et al [52] that respiratory parameters were negatively correlated with the duration of diabetes.

In Framingham heart study by Walter et al [51] demonstrated the reduced lung function with duration of diabetes. In a cross-sectional study Sandler et al [37] found that the degree of pulmonary dysfunction was negatively correlated with the duration of diabetes. Similar results are observed in the present study.

CONCLUSION

The result of the present study shows that there is a decrease in the pulmonary function in type II diabetics when compared with healthy controls.

In this study there is a restrictive type of pulmonary impairment in type II diabetics and as the duration of diabetes increases the restrictive lung impairment becomes more prominent.

Pulmonary function parameters are negatively correlated with the duration of diabetes. These findings are of importance in that they demonstrate the need for prevention of lung damage.

The pulmonary dysfunction may be one of the earliest and easily measurable non-metabolic alterations in diabetes. Therefore the patients with diabetes are suggested to undergo pulmonary function testing periodically.

As spirometry is much more reliable, valid and simple test, it is time to include the spirometer as a tool for monitoring diabetes.

Strict glycemic control and regular breathing exercises to strengthen respiratory muscles is necessary to improve the pulmonary function in type II diabetics.

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ANNEXURES

CONSENT FORM

Dr.S.Suguna post graduate student in the Department of physiology, Thanjavur Medical College, Thanjavur is doing a study on pulmonary functions tests in Type II Diabetes Mellitus. The procedures have been explained to me clearly. I understand that there are no risks involved in the above procedure. I hereby give my consent to participate in this study. The data obtained here may be used for research and publication.

Signature:

Name:

Place:

PROFORMA

TOPIC: A study of pulmonary function test in type II diabetes mellitus

-Spirometry based – by Dr.S.Suguna.

NAME OF THE PATIENT / CONTROL:

AGE: **SEX:**

ADDRESS: **OCCUPATION:**

PRESENT HISTORY:

H/o cough with expectoration/hemoptysis/ recent surgery & MI.

PAST HISTORY:

H/o asthma, hypertension, myocardial infarction, tuberculosis.

PERSONAL HISTORY:

H/o smoking, alcoholic, tobacco & betel nut chewer

FAMILY HISTORY :

H/o asthma , tuberculosis , hypertension , diabetes.

OCCUPATIONAL HISTORY:

H/o exposure to cotton dust, smokes.

DIABETIC HISTORY:

Duration –

Taking oral hypoglycemic drugs -

GENERAL EXAMINATION:

Height: Weight: BMI:

Anemia: clubbing: pedal edema:

Cyanosis: jaundice: lymphadenopathy:

Skeletal deformity:

VITAL SIGNS:

Pulse rate: Respiratory rate:

Blood pressure: Temperature:

Examination of cardiovascular system:

Examination of respiratory system:

Examination of abdomen:

Examination of nervous system:

BLOOD INVESTIGATION :

Hb: Serum creatinine:

Blood sugar – fasting: Blood urea:

Blood sugar–postprandial: Urine sugar:

HbA1c: Urine albumin

PULMONARY FUNCTION TEST

PARAMETERS	PREDICTED VALUE	SUBJECT'S BEST VALUE	PREDICTED %
FVC			
FEV_1			
FEV_1/FVC			
$FEV_{(25\%-75\%)}$			
$FEV_{25\%}$			
$FEV_{50\%}$			
$FEV_{75\%}$			
PEFR			
MVV			
V_T			
SVC			

ABBREVIATIONS

DM	- Diabetes Mellitus.
HbA1c	- Glycated Hemoglobin.
AGEs	- Advanced Glycation End Products.
PFT	- Pulmonary Function Test.
VC	- Vital Capacity.
FVC	- Forced Vital Capacity.
FEV1	- Forced Expiratory Volume in First Second.
PEFR	- Peak Expiratory Flow Rate.
MEFV	- Maximum Expiratory flow volume.
MVV	- Maximum Voluntary Ventilation.
TLC	- Total Lung Capacity.
RV	- Residual Volume.

PULMONARY FUNCTION PARAMETERS FOR CONTROL GROUP

S.no	AGE (yrs)	SEX	HEIGHT (cm)	WEIGHT (kg)	BMI	HbA1C %	FEV_1	FVC	FEV1/FVC%	PEFR	FEF 25-75%	MVV
1	35	F	160	54	21.09	3.5	80	83	101	92	85	66
2	38	F	152	53	22.94	3.8	93	88	110	118	113	55
3	41	F	162	77	29.34	4.1	94	81	124	73	124	76
4	35	F	164	58	21.56	2.5	72	62	122	70	115	42
5	54	M	166	65	23.59	2.7	64	73	91	84	125	46
6	47	M	166	58	21.05	3.4	106	94	118	107	168	98
7	43	M	158	74	29.64	2.9	104	92	119	93	152	58
8	44	M	164	60	22.31	3	89	82	113	104	139	52
9	40	M	161	69	26.62	2.7	93	80	121	129	212	58
10	40	M	165	58	21.30	2.5	88	85	108	80	101	68
11	35	F	168	60	21.26	3.1	97	98	104	106	122	68
12	38	F	158	46	18.43	3.6	99	87	120	98	148	48
13	35	M	169	74	25.91	2.8	91	86	110	87	133	45
14	44	M	167	76	27.25	3.5	91	76	125	103	170	68
15	35	M	158	41	16.42	3.1	77	67	121	83	130	53
16	51	M	160	42	16.41	3.8	100	83	126	110	170	90
17	35	M	161	55	21.22	2.9	76	71	114	59	89	42
18	35	M	161	52	20.06	2.3	95	81	123	74	117	75
19	36	F	158	65	26.04	3.4	110	95	121	95	138	43
20	35	M	165	52	19.10	2.8	96	82	122	117	171	87

S.no	AGE (yrs)	SEX	HEIGHT (cm)	WEIGHT (kg)	BMI	HbA1C %	FEV_1	FVC	FEV1/FVC%	PEFR	FEF 25-75%	MVV
21	38	F	163	60	22.58	4.3	88	80	116	101	129	70
22	39	M	163	56	21.08	3.2	105	90	123	102	170	50
23	37	M	163	81	30.49	2.6	90	77	122	83	151	76
24	44	F	161	63	24.30	2.4	88	82	114	99	118	49
25	39	F	158	46	18.43	2.9	86	81	112	81	112	61
26	45	F	155	56	23.31	3.6	105	92	122	118	135	74
27	38	F	162	76	28.96	2.5	101	87	122	143	145	61
28	44	M	165	51	18.73	2.8	71	59	126	81	138	65
29	40	F	158	58	23.23	3.2	89	82	115	111	94	79
30	51	F	162	52	19.81	3.7	92	85	115	82	117	77
31	35	F	160	67	26.17	3.1	94	83	119	137	132	65
32	44	M	161	45	17.36	3.4	115	100	119	137	132	65
33	36	F	159	66	26.11	3.1	94	81	121	168	141	78
34	38	M	164	58	21.56	2.9	85	71	124	99	159	60
35	54	M	167	91	32.63	3	100	85	122	91	160	93
36	38	M	166	69	25.04	3.5	97	85	119	94	152	74
37	35	M	166	60	21.77	3.8	80	74	111	91	125	44
38	40	M	165	69	25.34	3.2	79	73	112	76	114	66
39	37	M	166	66	23.95	2.7	78	68	119	90	164	89
40	51	M	168	88	31.18	3.6	104	93	116	88	159	74

PULMONARY FUNCTION PARAMETERS FOR DIABETIC GROUP

S.no	AGE (yrs)	SEX	HEIGHT (cms)	WEIGHT (kg)	BMI	HbA_{1C} %	DURATION (yrs)	FEV1	FVC	FEV1/ FVC%	PEFR	FEF 25-75%	MVV
1	46	M	167	70	25.10	6.1	10	94	78	126	109	166	56
2	45	M	169	62	21.71	6.5	5	110	91	126	95	193	55
3	40	M	163	66	24.84	6.8	6	72	68	111	74	107	64
4	54	M	164	66	24.54	6.5	9	44	39	118	51	59	31
5	47	F	163	48	18.07	4.5	5	98	89	118	100	108	45
6	55	F	157	47	19.07	4.86	8	61	58	113	64	83	28
7	48	F	162	56	21.34	5.86	8	73	83	94	77	117	51
8	46	F	158	57	22.83	5.4	4	57	55	111	111	71	45
9	52	M	164	71	26.40	5.12	5	103	84	128	98	189	61
10	55	M	164	59	21.94	6.01	8	78	65	124	84	164	79
11	36	F	158	53	21.23	6.1	10	89	77	121	153	149	57
12	52	M	164	62	23.05	5	3	82	73	118	79	121	50
13	50	F	160	62	24.22	4.57	10	75	66	116	66	103	52
14	50	M	164	59	21.94	5.67	5	86	96	117	79	132	70
15	35	F	159	61	24.13	5.67	2	78	71	115	117	113	65
16	49	M	165	75	27.55	5.2	5	97	99	103	80	149	78
17	42	M	167	56	20.08	2.4	2	111	100	116	119	161	80
18	37	M	168	78	27.64	4.33	3	90	80	117	94	147	81
19	40	M	167	68	24.38	2.94	2	91	78	121	113	197	71
20	36	F	163	81	30.49	6.69	3	79	75	110	71	104	74

S.no	AGE (yrs)	SEX	HEIGHT (cms)	WEIGHT (kg)	BMI	HbA_{1C} %	DURATION (yrs)	FEV1	FVC	FEV1/ FVC%	PEFR	FEF 25-75%	MVV
21	47	M	166	75	27.22	6.43	3	97	82	123	80	159	64
22	55	F	161	56	21.60	5.83	10	71	70	108	53	77	47
23	55	F	159	49	19.38	3.8	4	95	89	116	84	135	66
24	47	M	163	55	20.70	6.67	2	88	81	113	95	122	66
25	55	F	159	42	16.61	6.17	8	66	54	119	45	76	36
26	50	F	162	72	27.43	6.49	5	80	74	116	68	114	54
27	48	F	161	63	24.30	6.31	3	63	56	123	63	102	76
28	43	F	166	62	22.50	4	3	73	64	124	139	133	45
29	51	M	166	64	23.23	4.26	2	115	95	126	108	213	89
30	50	M	165	56	20.57	3	2	80	73	115	95	95	53
31	46	M	163	55	20.70	4.83	4	88	75	124	103	182	78
32	46	M	167	66	23.67	4.76	2	93	83	118	92	159	96
33	52	F	159	43	17.01	3.7	4	77	74	112	71	100	36
34	50	F	159	52	20.57	4.61	3	75	72	111	71	108	54
35	49	F	161	48	18.52	6.7	4	47	47	109	71	44	38
36	46	M	164	72	26.77	6.39	4	95	78	128	87	161	38
37	55	F	159	48	18.99	5.71	8	56	56	107	38	59	35
38	48	F	162	56	21.34	6.68	7	71	66	115	82	141	56
39	52	F	161	57	21.99	6	10	81	74	119	94	127	59
40	40	F	161	53	20.45	6.7	9	67	62	114	65	85	40