A STUDY ON PULMONARY FUNCTION TEST IN DIABETES MELLITUS AND ITS CORRELATION WITH DURATION OF DIABETES MELLITUS

DOCTOR OF MEDICINE

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MADURAI MEDICAL COLLEGE,MADURAI

CERTIFICATE FROM THE DEAN

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CERTIFICATE

This is to certify that the dissertation entitled

"A STUDY ON PULMONARY FUNCTION TEST IN DIABETES MELLITUS AND ITS CORRELATION WITH DURATION OF DIABETES MELLITUS" submitted by **Dr. SREE KUMAR P.S,** to the Tamil Nadu Dr. M.G.R. Medical University, Chennai, in partial fulfillment of the requirement for the award of degree of Doctor Of Medicine (M.D) Branch-I - General Medicine, is a bonafide research work carried out by him under my direct supervision & guidance.

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DECLARATION

I, **Dr. SREE KUMAR P.S,** solemnly declare that, this dissertation "**A STUDY ON PULMONARY FUNCTION TEST IN DIABETES MELLITUS AND ITS CORRELATION WITH DURATION OF DIABETES MELLITUS"** is a bonafide record of work done by me at the Department of General Medicine, Government Rajaji Hospital, Madurai, under the guidance of Professor **Dr.G.BAGIALAKSHMI M.D,** Department of General Medicine, Madurai Medical college, Madurai from June 2016 to September 2016. I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, diploma to any other University, Board either in India or abroad.

This dissertation is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulations for the award of Degree of Doctor of Medicine (M.D.), General Medicine Branch-I, examination to be held in April 2017.

Place: Madurai

Date: **DR.SREE KUMAR P.S**

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CONTENTS

INTRODUCTION

Diabetes mellitus is a leading non communicable disease of the world. As per in International diabetes federation 2013 our country has the second largest diabetic population of about 65.1 million next to China 98.4 million. There are convincing evidences in the literature which show the stead rise in the incidence of this disease in India. With the advancement in the modern science and technology there is a steady decrease in the communicable diseases but there is also increase in the non communicable diseases in developing countries like India.with this advancements in early diagnosis and treatment there is a normal life expectancy of 50-60 years. Though there is a steady increase in life expectancy, the morbidity due to these non communicable diseases remains great economic & social burden to community which leads to evolvement of strategies to control the disease complications.

Diabetes is one of the important non communicable disease of the modern era, which leads to multi system involvement i.e cardiac,nervous,renal,ophthalmic,genito urinal, gastro intestinal,dermatological etc. Although diabetes is a multi systemic disorder its pulmonary involvement is

not extensively studied. Pathological studies in diabetic patients have represented changes in alveolar epithelium and capillaries.

The consequence is development of obstructive or restrictive disorders. Histopathological changes in lungs of diabetic patients are due to collagen and elastin alterations and microangiopathy .These changes become the cause of pulmonary dysfunctions.'' If diabetes is detected early and adequate steps are taken, it may be possible to significantly delay the occurrence of complications and there after their progression.''

'' Although a lot of research is going on the effects of Diabetes Mellitus on pulmonary function tests all over the world, the literature supporting to this is not in abundance in India. Therefore this study was undertaken to find out the correlation between duration of type 2 DM and PFTs in diabetic patients who attended or admitted to medical OPD or wards'' of government rajaji hospital, Madurai.

AIMS AND OBJECTIVES :

“The present study is conducted to find the relation between duration of diabetes and its impairment of pulmonary function tests (PFT) in Type 2 DM patients.”

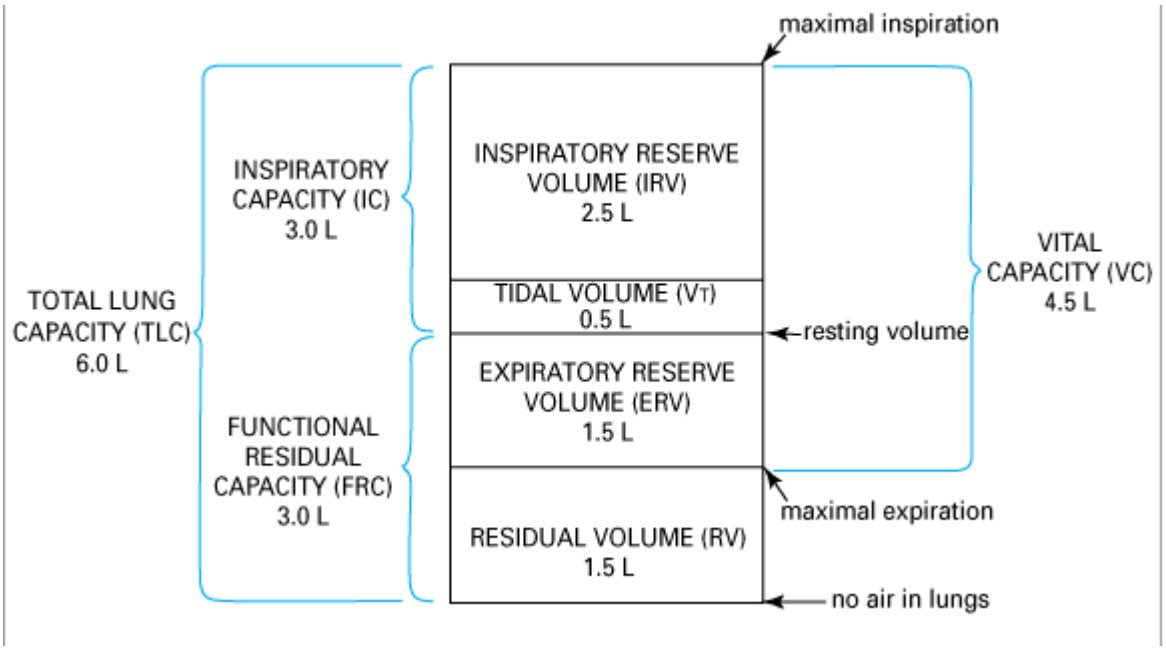
REVIEW OF LITERATURE

“Pulmonary function testing is a useful tool for evaluating the respiratory system, in addition to the history, imaging studies, and invasive investigations such as bronchoscopy and open-lung biopsy. By comparing the measured pulmonary function test values of the patient at any particular point with values derived from population studies is useful in identifying the pathology.”

“The percentage of predicted normal is used to grade the severity of the abnormality. Now a days pulmonary function testing is often used in medicine for evaluating respiratory symptoms, preoperative assessment, and for diagnosing diseases such as asthma and chronic obstructive pulmonary disease.”

“Pulmonary function tests (PFTs) is a term used to indicate a battery of manoeuvres that are performed using standardized instrument to measure lung function. PFTs can include screening spirometry, lung volume measurement, diffusing capacity for carbon monoxide, and arterial blood gases, which may be collectively referred to as a complete pulmonary function survey.”

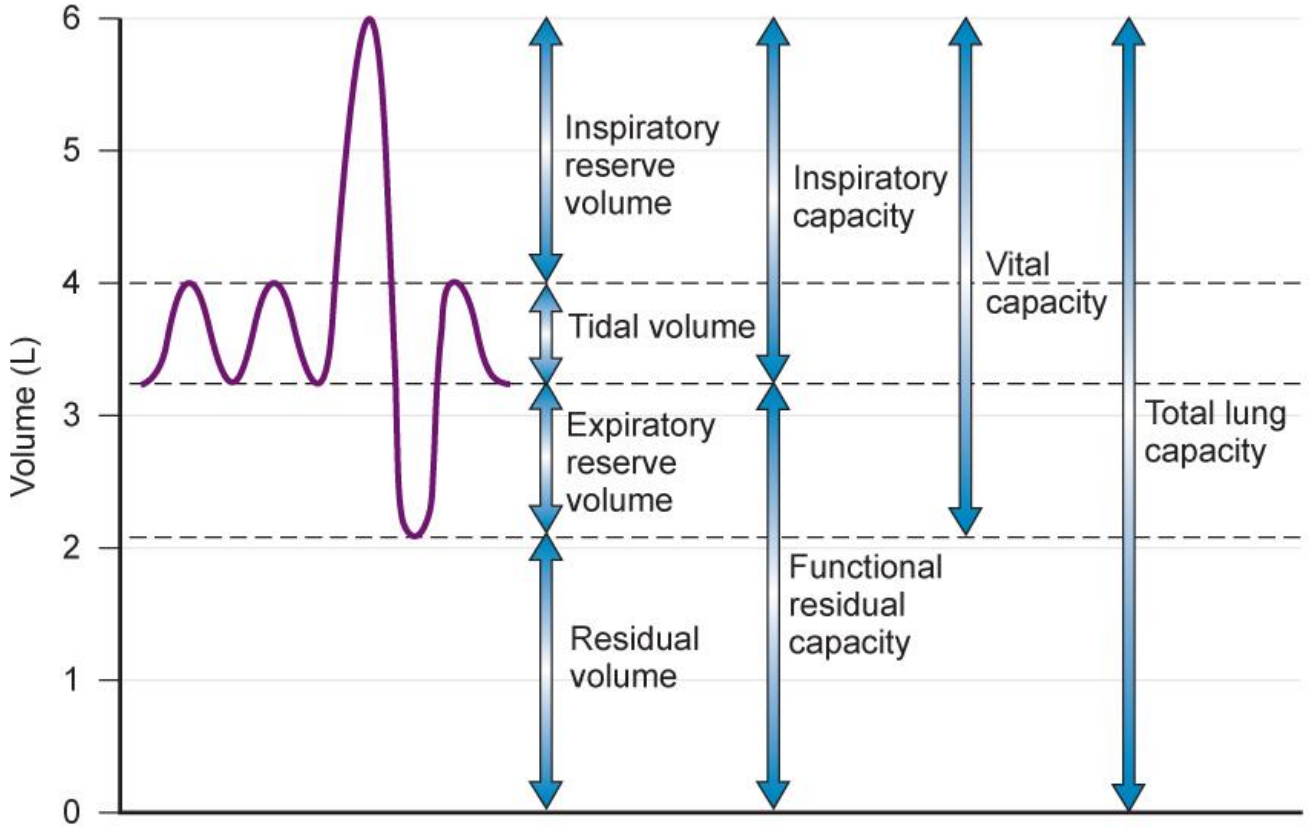
Physiology



The standard lung volumes and capacities. Typical values for a 70-kg adult are shown above

"Alveolar ventilation is the exchange of gas between the alveoli and the external environment. It is the process by which oxygen is brought into the lungs from the atmosphere and by which the carbon dioxide carried into the lungs from the mixed venous blood is expelled from the body. Alveolar ventilation is defined as the volume of fresh air entering the alveoli per minute. It is usually expressed in litres per min."

The Lung Volumes



"The volume of gas in the lungs at any instant depends on the mechanics of the lungs and chest wall and the activity of the muscles of inspiration and expiration. The lung volume under any specified set of conditions can be altered by pathologic and normal physiologic processes. Standardization of the conditions under which lung volumes are measured allows comparisons to be made among subjects or patients. The size of a person's lungs depends on height

and weight or body surface area, age and sex. Therefore, the lung volumes for a patient are usually compared with data of "predicted" lung volumes matched to age, sex, and body size.”

The Tidal Volume

“The tidal volume (TV) is the volume of air entering or leaving the lungs for each respiratory cycle (1). It is determined by the activity of the respiratory control centres in the brain as they affect the respiratory muscles and by the mechanics of the lung and the chest wall. During eupnea (normal, quiet breathing) the TV of a 70-kg adult is about 500 mL per breath, but this volume can increase dramatically during exercise.”

The Residual Volume

“The residual volume (RV) is the volume of air remaining in the lungs after a maximal forced expiration(2). It is determined by the muscles of expiration and the inward elastic recoil of the lungs as they oppose the outward elastic recoil of the chest wall. Dynamic compression of the airways during the forced

expiratory effort may also be an important determinant of the RV as airway collapse occurs, thus trapping gas in the alveoli. The RV of a healthy 70-kg adult is about 1.5 L, but it can be much greater in a disease state such as emphysema, in which inward alveolar elastic recoil is diminished and much airway collapse and gas trapping occur. The RV is important to a healthy person because it prevents the lungs from collapsing at very low lung volumes. Such collapsed alveoli would require great inspiratory efforts to return to normal position .”

The Expiratory Reserve Volume

“The expiratory reserve volume (ERV) is the volume of gas that is expelled from the lungs during a maximal forced expiration that starts at the end of a normal tidal expiration(3). It is therefore determined by the difference between the functional residual capacity (FRC) and the RV. The ERV is about 1.5 L in a healthy 70-kg adult.”

The Inspiratory Reserve Volume

“The inspiratory reserve volume (IRV) is the volume of gas that is inhaled into the lungs during a maximal forced inspiration starting at the end of a normal tidal inspiration(2). It is determined by the strength of contraction of the

inspiratory muscles, the inward elastic recoil of the lung and the chest wall, and the starting point, which is the FRC plus the VT. The IRV of a normal 70-kg adult is about 2.5 L."

The Functional Residual Capacity

"The functional residual capacity (FRC) is the volume of gas remaining in the lungs at the end of a normal tidal expiration(2). Because it was traditionally assumed that no muscles of respiration are contracting at the end of a normal tidal expiration, the FRC is usually considered to represent the balance point between the inward elastic recoil of the lungs and the outward elastic recoil of the chest wall."

"However, the respiratory muscles may have significant tone at the FRC, and in certain circumstances the FRC may be greater than or even less than the lung volume of the totally relaxed respiratory system. Thus, the lung volume at which the inward elastic recoil of the lungs is equal and opposite to the outward elastic recoil of the chest wall is sometimes referred to as the relaxation volume of the respiratory system. The FRC may be greater than the relaxation volume if the next inspiration occurs before the relaxation volume is reached, either because of high breathing rates or high resistance to expiratory airflow in the larynx or peripheral airways; or active contraction of the inspiratory muscles at end expiration. Either or both of these may occur in babies, who have higher

FRCs than would be predicted from the great inward elastic recoil of their lungs and the small outward recoil of their chest walls. During exercise, the FRC may be lower than the relaxation volume because of active contraction of the expiratory muscles."

"The FRC consists of the RV plus the ERV. It is about 3 L in a healthy 70 kilogram adult."

The Inspiratory Capacity

"The inspiratory capacity (IC) is the volume of air that is inhaled into the lungs during a maximal inspiratory effort that begins at the end of a normal tidal expiration (the FRC)(3). It is therefore equal to the VT plus the IRV. The IC of a normal 70-kg adult is about 3 L."

The Total Lung Capacity

"The total lung capacity (TLC) is the volume of air in the lungs after a maximal inspiratory effort(2). It is determined by the strength of contraction of the inspiratory muscles and the inward elastic recoil of the lungs and the chest wall. The TLC consists of all four lung volumes: the RV, the VT, the IRV, and the ERV. The TLC is about 6 L in a healthy 70-kg adult."

The Vital Capacity

“The vital capacity (VC), is the volume of air expelled from the lungs during a maximal forced expiration starting after a maximal forced inspiration(1). The VC is therefore equal to the TLC minus the RV, or about 4.5 L in a healthy 70-kg adult. The VC is also equal to the sum of the VT and the IRV and ERV. It is determined by the factors that determine the TLC and RV.”

Airways Resistance

“Several factors besides the elastic recoil of the lungs and the chest wall must be overcome to move air into or out of the lungs.” These factors include the inertia of the respiratory system, the frictional resistance of the lung and chest wall tissue, and the frictional resistance of the airways to the flow of air. The inertia of the system is negligible. Pulmonary tissue resistance is caused by the friction encountered as the lung tissues move against each other as the lung expands. The airways resistance plus the pulmonary tissue resistance is often referred to as the pulmonary resistance. Pulmonary tissue resistance normally contributes about 20% of the pulmonary resistance, with airways resistance responsible for the other 80%. Pulmonary tissue resistance can be increased in such conditions as pulmonary sarcoidosis and fibrosis. Airway resistance is the major component of the total resistance and because it can increase tremendously both in healthy people and in those suffering from various diseases.

Generally, the relationship among pressure, flow, and resistance is stated as

Pressure Difference = Flow x Resistance

Therefore,

Resistance = Pressure Flow[cm of H20]/ Flow[litres/s]

This means that resistance is a meaningful term only during flow.

Understanding and quantifying the resistance to airflow in the conducting system of the lungs is difficult because of the nature of the airways themselves. It is relatively easy to inspect the resistance to airflow in a single, unbranched, indistensible tube; however, the ever-branching, narrowing, distensible, and compressible system of airways makes analysis of the factors contributing to airways resistance especially complicated. Therefore, equations can only approximate what is really happening clinically.

When a fluid such as air flows through rigid, smooth-bore tubes, its behaviour is governed by Poiseuille's law. The pressure difference is directly proportional to the product of flow and resistance:

$\Delta P \alpha VR$

where Δ P = pressure difference

V= airflow

R = resistance

According to Poiseuille's law, the "resistance is directly proportional to the viscosity of the fluid and the length of the tube and is inversely proportional to the fourth power of the radius of the tube."

$$R = \frac{8\eta l}{\pi r^4}$$

where η = viscosity of fluid

l = length of tube

r = radius of tube

Note that if the radius is halved, the resistance increases by 16 times because the resistance is inversely proportional to the fourth power of radius .

Flow changes from laminar to turbulent when Reynolds' number exceeds 2000. Reynolds' number is equal to the product of density and the velocity of the fluid

and the diameter of the tube divided by the viscosity of the fluid. It does not have unit.

$$\text{Reynolds' number} = \frac{\rho \times Ve \times D}{\eta}$$

where ρ = density of fluid

Ve = linear velocity of fluid

D = diameter of tube

η = viscosity of fluid

During turbulent flow, the relationship among the pressure difference, flow, and resistance changes. Because the pressure difference is proportional to the flow squared, much greater pressure differences are required to generate the same airflow. The resistance term is influenced more by the density than it is by the viscosity during turbulent flow:

$$\Delta P \propto \dot{V}^2 R_2$$

Transitional flow is a mixture of laminar and turbulent flow. This type of flow often occurs at branch points or points distal to partial obstructions.

“Turbulent flow tends to occur if airflow is high, gas density is high, the tube radius is large, or all three conditions exist. True laminar flow probably occurs only in the smallest airways, where the linear velocity of airflow is extremely low”. Linear velocity (cm/s) is equal to the flow (cm^3/s) divided by the cross-sectional area. The total cross-sectional area of the smallest airways is very large, and so the linear velocity of airflow is very low. The airflow in the trachea and larger airways is usually either turbulent or transitional.

Distribution of Airways Resistance

“About 25–40% of the total resistance to airflow is located in the upper airways: the nose, nasal turbinates, oropharynx, nasopharynx, and larynx. Resistance is higher when one breathes through the nose than when one breathes through the mouth.”

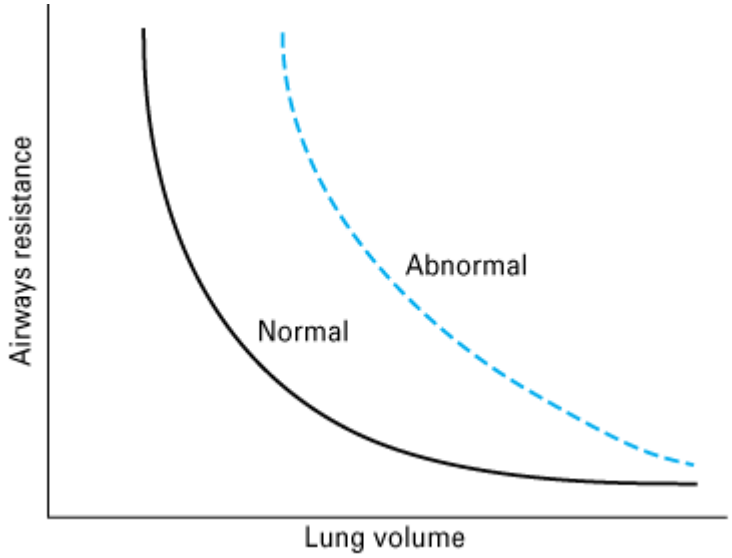
The vocal cords open slightly during normal inspirations and close slightly during expirations. During deep inspirations, they open widely. The muscles of the oropharynx also contract during normal inspirations, which dilates and stabilizes the upper airway. During deep forced inspirations, the development of negative pressure could cause the upper airway to be pulled inward and partly or com-pletely obstruct airflow. Reflex contraction of these pharyngeal dilator muscles normally keeps the airway open.

“As for the tracheobronchial tree, the component with the highest individual resistance is obviously the smallest airway, which has the smallest radius. Nevertheless, because the smallest airways are arranged in parallel, their resistances add as reciprocals, so that the total resistance to airflow offered by the numerous small airways is extremely low during normal, quiet breathing. Therefore, under normal circumstances the greatest resistance to airflow resides in the medium-sized bronchi.”

“Lung Volume & Airways Resistance”

Airways resistance decreases with increasing lung volume, as shown in Figure (normal curve). This relationship is still present in an emphysematous lung,

although in emphysema the resistance is higher than that in a healthy lung, especially at low lung volumes.



“Relationship between lung volume and airways resistance. Total lung capacity” is at right; residual volume is at left.

Solid line = normal lung; dashed line = abnormal (emphysematous) lung

There are two reasons for this relationship; both mainly involve the small airways which, have little or no cartilaginous support. “The small airways are therefore rather distensible and also compressible.” “Thus the transmural pressure gradient across the wall of the small airways is an important

determinant of the radius of the airways. Since resistance is inversely proportional to the fourth power of radius, changes in the radii of small airways can cause dramatic changes in airways resistance, even with so many parallel pathways.” “To increase lung volume, a person breathing normally takes a "deep breath," that is, makes a strong inspiratory effort.” “This effort causes intrapleural pressure to become much more negative than the –7 or –10 cm H_2O seen in a normal, quiet breath. The transmural pressure gradient across the wall becomes much more positive, and small airways are distended.”

“A second reason for the decreased airways resistance seen at higher lung volumes is that the “increase in traction on smaller airways.” The small airways traveling through the lung form attachments to the walls of alveoli. As the alveoli expand during the course of a “deep inspiration, the elastic recoil in their walls increases; this elastic recoil is transmitted to the attachments at the airway, pulling it open.”

Assessment of Airways Resistance

The resistance to airflow cannot be measured directly but must be calculated from the pressure gradient and airflow during a breath:

$$R = \frac{\Delta P}{\dot{V}}$$

This formula is an approximation because it presumes that all airflow is laminar, which is not true. But there is a second problem: How can the pressure gradient be determined?

To know the pressure gradient, the alveolar pressure—which also cannot be measured directly—must be known. Alveolar pressure can be calculated using a body plethysmograph, an expensive piece of equipment, but this procedure is not often done. Instead, airways resistance is usually assessed indirectly. The assessment of airways resistance during expiration will be emphasized because that factor is of interest in patients with emphysema, chronic bronchitis, and asthma.

Measurement of the Lung Volumes

“Measurement of the lung volumes is important clinically because many pathologic states can alter specific lung volumes or their relationships to one another. The lung volumes, however, can also change for normal physiologic

reasons. Changing from a standing to a supine posture decreases the FRC because gravity is no longer pulling the abdominal contents away from the diaphragm. This decreases the outward elastic recoil of the chest wall. The RV and TLC do not change significantly when a person changes from standing to the supine position. If the FRC is decreased, then the ERV will also decrease and the IRV will increase. The VC, RV, and TLC may decrease slightly because some of the venous blood that collects in the lower extremities and the abdomen when a person is standing returns to the thoracic cavity when that person lies down.”

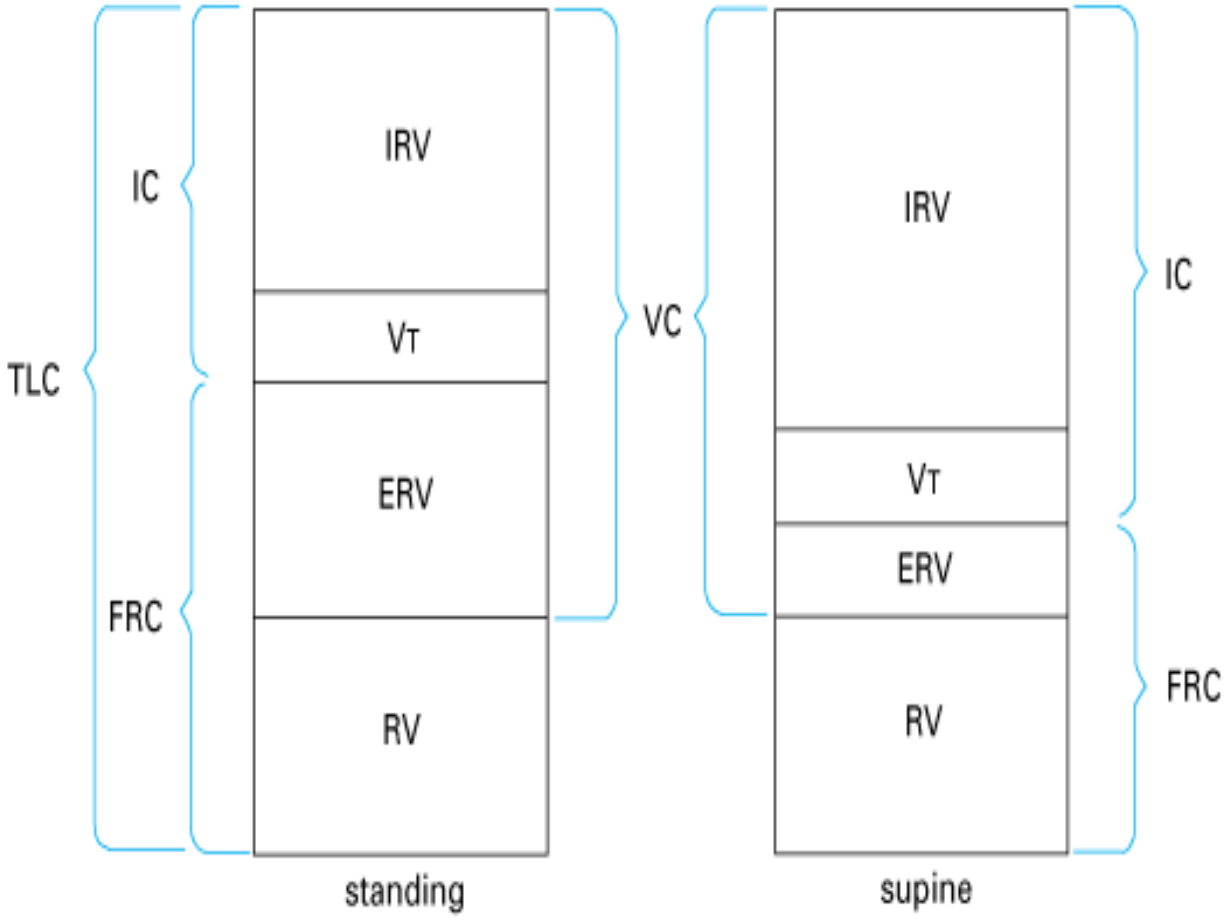


Illustration of alterations in the lung volumes and capacities that occur when a subject changes from the standing to the supine position.

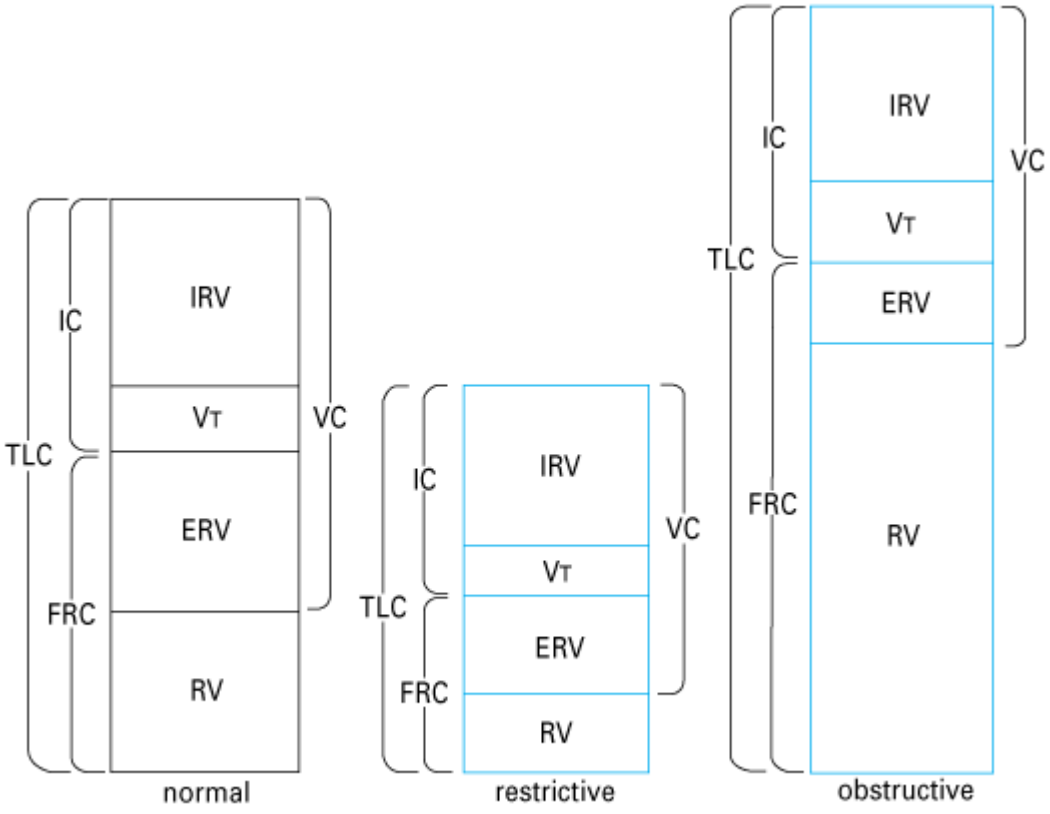


Illustration of typical alterations in the lung volumes and capacities in restrictive and obstructive diseases.

“Battery of manoeuvre’s

Pulmonary function studies use a variety of manoeuvre’s to measure and record the properties of four lung components. These include the

--airways (large and small),

--lung parenchyma (alveoli, interstitium),

--pulmonary vasculature, and

--the bellows-pump mechanism.

Various diseases can affect each of these components.

Spirometry:

Spirometry is the most commonly used lung function screening study. It generally should be the clinician's first option, with other studies being reserved for specific indications. Most patients can easily perform spirometry when coached by an appropriately trained technician or other health care provider. The test can be administered in the ambulatory setting, physician's office, emergency department, or inpatient setting. The indications for spirometry are diverse”

“Indications for Spirometry

Diagnostic

To evaluate symptoms

- Chest pain
- Cough
- Dyspnea
- Orthopnea
- Phlegm production
- Wheezing

To evaluate signs

- Chest deformity
- Cyanosis
- Diminished breath sounds
- Expiratory slowing
- Overinflation
- Unexplained crackles

To evaluate abnormal laboratory tests

- Abnormal chest radiographs
- Hypercapnia
- Hypoxemia
- Polycythemia

To measure the effect of disease on pulmonary function

To screen persons at risk for pulmonary diseases

- Smokers
- Persons in occupations with exposures to injurious substances

Some routine physical examinations

- To assess preoperative risk
- To assess prognosis (lung transplant, etc.)
- To assess health status before enrollment in strenuous physical activity programs

Monitoring

To assess therapeutic interventions

- Bronchodilator therapy
- Steroid treatment for asthma, interstitial lung disease, etc.
- Management of congestive heart failure
- Other (antibiotics in cystic fibrosis, etc.)

To describe the course of diseases affecting lung function

- Pulmonary diseases
- Obstructive small airway diseases
- Interstitial lung diseases
- Cardiac diseases
- Congestive heart failure
- Neuromuscular diseases
- Guillain-Barré syndrome

To monitor persons in occupations with exposure to injurious agents

To monitor for adverse reactions to drugs with known pulmonary toxicity

Evaluation of Disability or Impairment

To assess patients as part of a rehabilitation program

- Medical
- Industrial
- Vocational

To assess risks as part of an insurance evaluation

To assess persons for legal reasons

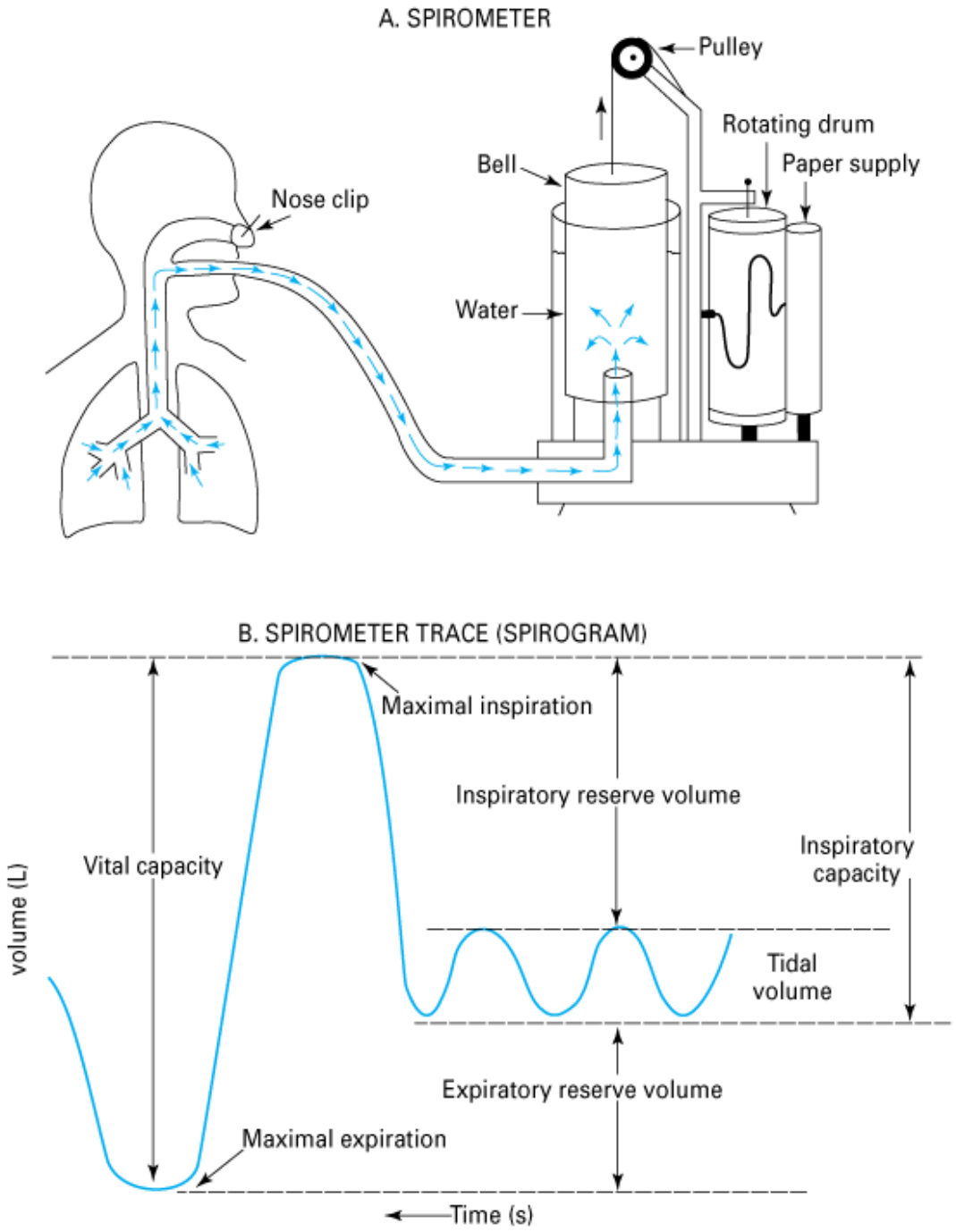
- Social Security or other government compensation programs
- Personal injury lawsuits
- Other

Public Health

- Epidemiologic surveys

- Comparison of health status of populations living in different environments
- Validation of subjective complaints in occupational or environmental settings
- Derivation of reference equations”

“Spirometry requires a voluntary manoeuvre in which a seated patient inhales maximally from tidal respiration to total lung capacity and then rapidly exhales to the fullest extent until no further volume is exhaled at residual volume. The” “manoeuvre may be performed in a forceful manner to generate a forced vital capacity (FVC) or in a more relaxed manner to generate a slow vital capacity (SVC). In normal persons, the inspiratory vital capacity, the expiratory SVC, and expiratory FVC are essentially equal. However, in patients with obstructive small airways disease, the expiratory SVC is generally higher than the FVC. This difference might, however, be due partly to the difficulty in maintaining a maximum expiratory effort for an extended time period without experiencing dizziness or light headedness.”



"A spirometer, including the waterless, rolling seal type, and Stead-Wells water seal type is an instrument that directly measures the volume of air displaced or measures airflow by a flow-sensing device, such as a pneumotachometer or a

tube containing a fixed resistance to flow. Today, most clinical pulmonary function testing laboratories use a microprocessor-driven pneumotachometer to measure air flow directly and then to mathematically derive volume.”

“The frequently used water spirometer, consists of an inverted canister, or "bell," floating in a water-filled space between two concentrically arranged

cylinders. The space inside the inner drum, which is closed off from the atmosphere by the bell, is connected to tubing that extends to a mouthpiece into which the person breathes. As the person breathes in and out, gas enters and leaves the spirometer, and the bell then floats higher (during expiration) and lower (during inspiration). The top of the bell is connected by a pulley to a pen that writes on a rotating drum, thus tracing the person's breathing pattern.”

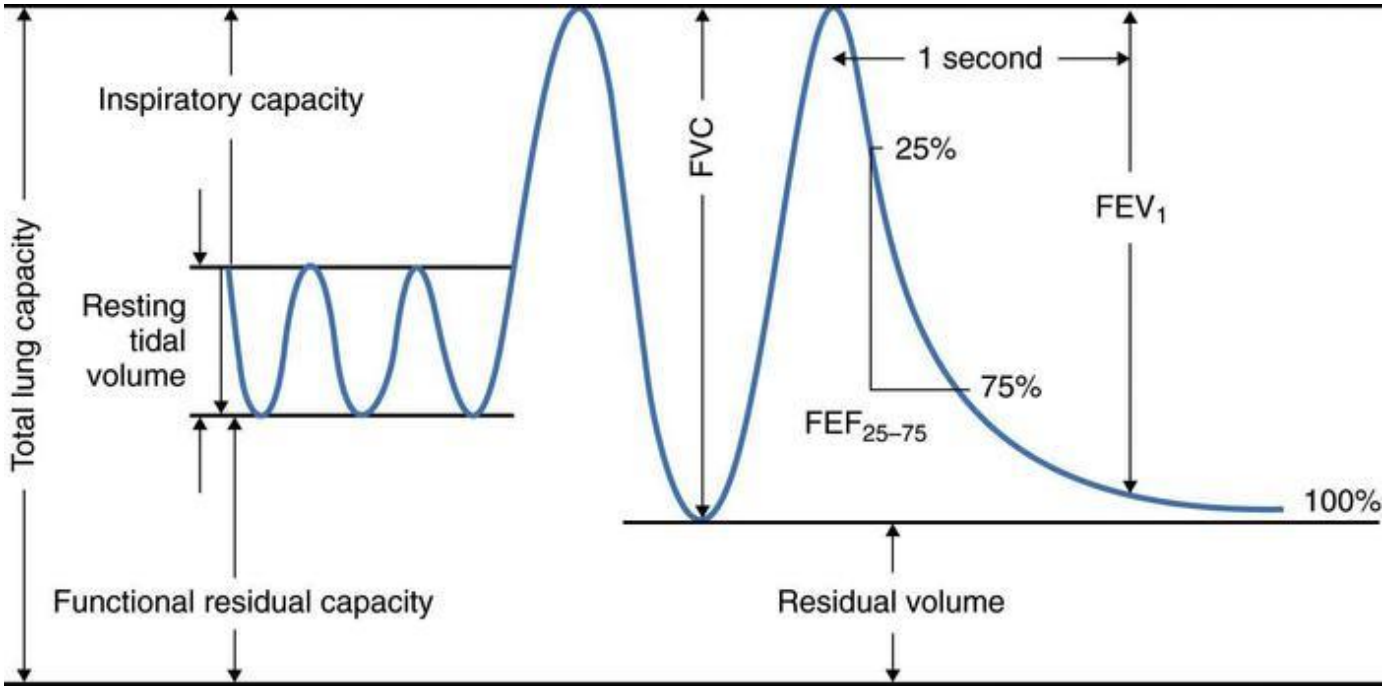
“Types of Spirometers
Volume
• Bellows • Rolling seal • Water • Dry
Flow Sensing (Pneumotach)
• Fleisch • Screen

- Hot-wire
- Turbine”

The spirometer can measure only the lung volumes that the subject can exchange with it. As is the case with many pulmonary function tests, the subject must be conscious and cooperative and understand the instructions for performing the test. The VT, IRV, ERV, IC, and VC can all be measured with a spirometer (as can the forced expiratory volume in 1 second [FEV_1], forced vital capacity [FVC], and forced expiratory flow [$FEF_{25–75\%}$]). The RV, FRC, and the TLC cannot be determined with a spirometer because the subject cannot exhale the lungs completely. The gas in a spirometer is at ambient temperature, pressure, and water vapour saturation, and the volumes of gas collected in a spirometer must be converted to equivalent volumes in the body. Other kinds of spirometers include rolling seal and bellows spirometers. These spirometers are not water-filled and are more portable

“A spirogram is a graphic representation of bulk air movement depicted as a volume-time tracing or as a flow-volume tracing. Values generated from a simple spirogram provide important graphic and numeric data regarding the

mechanical properties of the lungs, including airflow (forced expiratory volume in 1 second [FEV_1] along with other timed volumes) and exhaled lung volume (FVC or SVC). The measurement is typically expressed in liters for volumes or in liters per second for flows and is corrected for body temperature and pressure of gas that is saturated with water vapor. Data from a spirogram provide important clues to help distinguish obstructive pulmonary disorders that typically reduce airflow, such as asthma and emphysema, from restrictive disorders that typically reduce total lung volumes, including pulmonary fibrosis and neuromuscular disease”



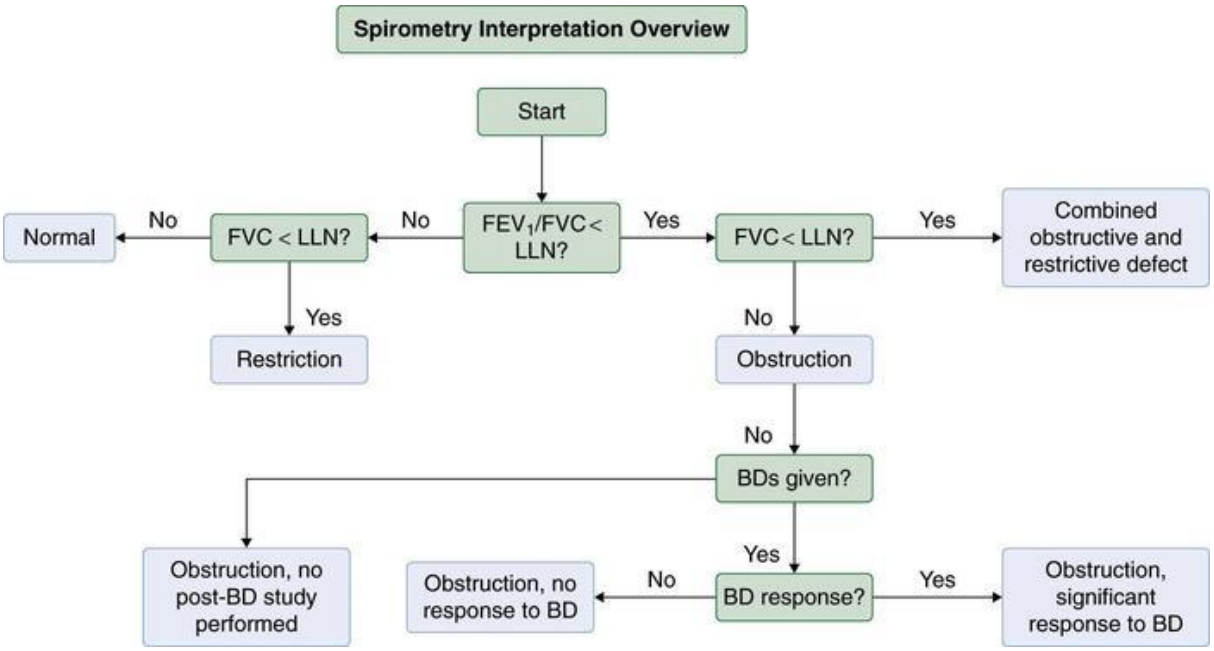
Forced Expiratory Volume in 1 Second

"The FEV_1 is the most widely used parameter to measure the mechanical properties of the lungs. In normal persons, the FEV_1 accounts for the greatest part of the exhaled volume from a spirometric maneuver and reflects mechanical properties of the large and the medium-sized airways. In a normal flow-volume loop, the FEV_1 occurs at about 75% to 85% of the FVC. This parameter is reduced in obstructive and restrictive disorders. In obstructive diseases, FEV_1 is reduced disproportionately to the FVC, reducing the FEV_1/FVC ratio below the lower limit of normal and indicates airflow limitation. In restrictive disorders, the FEV_1, FVC, and total lung capacity are all reduced, and the FEV_1/FVC ratio is normal or even elevated."

Forced Vital Capacity

" FVC is a measure of lung volume and is usually reduced in diseases that cause the lungs to be smaller. Such processes are generally termed restrictive and can include disorders of the lung parenchyma, such as pulmonary fibrosis, or of the bellows, including kyphoscoliosis, neuromuscular disease, and pleural effusion. However, a reduction in FVC is not always due to reduced total volumes and can occur in the setting of large lungs hyperinflated due to severe airflow obstruction and air trapping, as in emphysema. In this setting, the FVC is decreased due to reduced airflow, air trapping, and increased residual volume, a

phenomenon referred to as pseudorestriction. Reduced FVC can occur despite a normal or increased total lung volume. Therefore, FVC is not a reliable indicator of total lung capacity or restriction, especially in the setting of airflow obstruction. The overall accuracy of the FVC for restriction is about 60%”



FEV_1, forced expiratory volume in 1 second;

LLN, lower limit of normal;

TLC,total lung capacity;

VC,vitalcapacity.

“Adapted from American Thoracic Society: Lung function testing: Selection of reference values and interpretative strategies. Am Rev Respir Dis 1991;144:1202-1218”.

Measurement of Lung Volumes Not Measurable with Spirometry

The residual volume (RV), total lung capacity (TLC) and related volumes cannot be measured directly so special techniques are required to record these volumes. There are several accepted methods for determining these volumes, which are frequently referred to as 'static lung volumes'. These methods include helium dilution, nitrogen washout and body plethysmography

The FRC is usually determined, and RV (which is equal to FRC minus ERV) and the TLC (which is equal to VC plus RV) are then calculated from volumes obtained by spirometry.

Nitrogen-Washout Technique

In the nitrogen-washout technique, the person breathes 100% oxygen through a one-way valve so that all the expired gas is collected. The concentration of nitrogen in the expired air is monitored with a nitrogen analyzer until it reaches

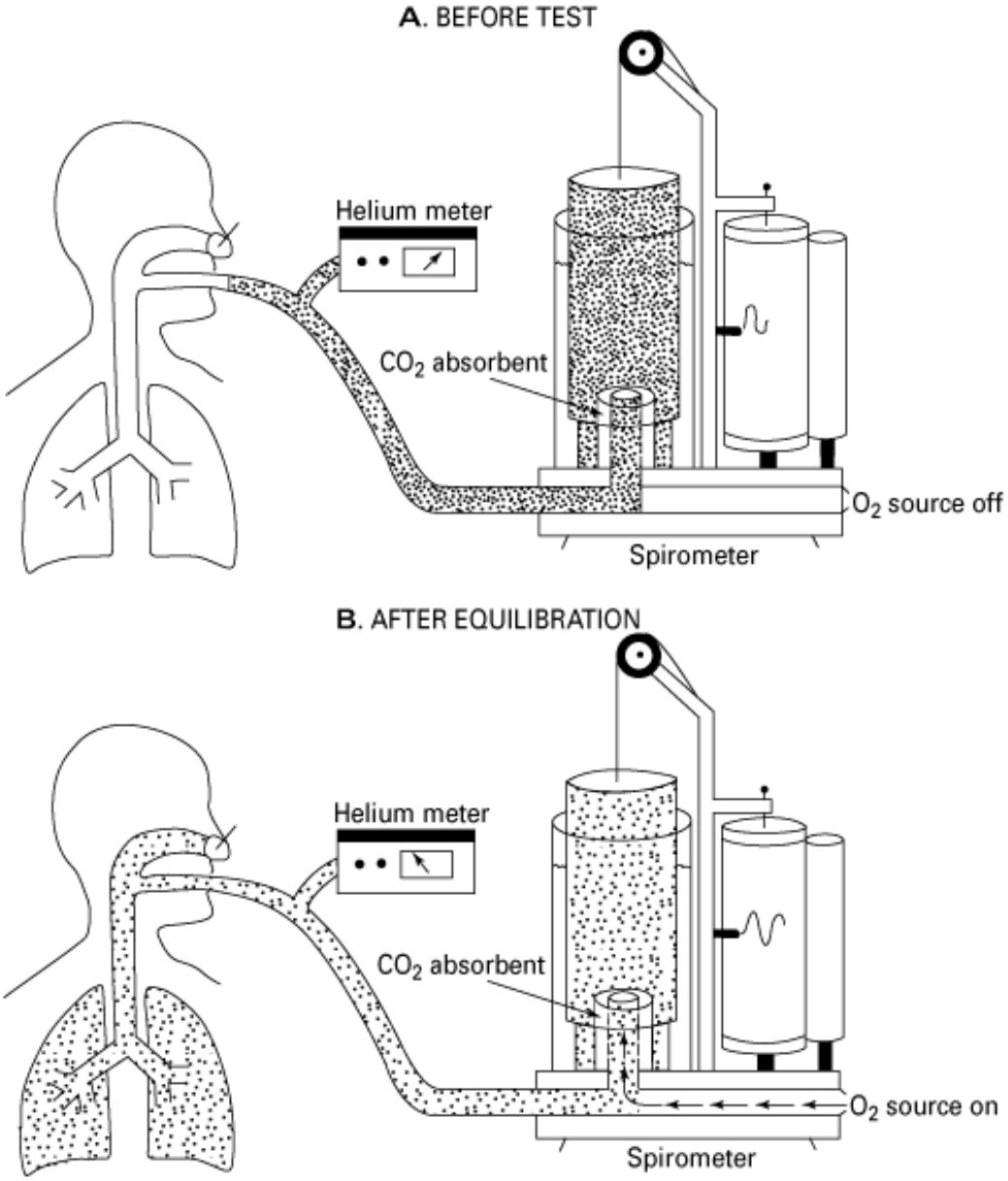
zero. At this point all the nitrogen is washed out of the person's lungs. The total volume of all the gas the person expired is determined, and this amount is multiplied by the percentage of nitrogen in the mixed expired air, which can be determined with the nitrogen analyzer. The total volume of nitrogen in the person's lungs at the beginning of the test can thus be determined. Nitrogen constitutes about 80% of the person's initial lung volume, and so multiplying the initial nitrogen volume by 1.25 gives the person's initial lung volume. If the test is begun at the" end of a normal expiration, "the volume determined is the FRC.

Total Volume expired X %N2 = original volume of N2 in the lungs

original volume of N2 in the lungs X 1.25 = original Lung Volume

Helium Dilution Methods:

Helium (He) is an inert, poorly soluble gas. The principle in helium dilution methods is that if a gas with known He concentration is breathed in, the He will be diluted by the He-free gas within the lungs. If the expired He concentration is monitored the volume of gas within the lungs can then be calculated from the dilution effect.



For example, if a known amount of a solute is dissolved in an unknown volume of solvent, and the concentration of the solute can be determined, then the volume of solvent can be calculated:

Amount of solute (mg) = concentration of solute (mg/mL) X

volume of solvent (mg)

In the helium-dilution technique, helium is dissolved in the gas in the lungs and its concentration is determined with a helium meter, allowing calculation of the lung volume. Helium is used for this test because it is not taken up by the pulmonary capillary blood and because it does not diffuse out of the blood, and so the total amount of helium does not change during the test. The person breathes in and out of a spirometer filled with a mixture of helium and oxygen.

The helium concentration is monitored continuously with a helium meter until its concentration in the inspired air equals its concentration in the person's expired air. At this point, the concentration of helium is the same in the person's lungs as it is in the spirometer, and the test is stopped at the end of a normal expiration.

The FRC can then be determined by the following formula (total amount of He before test = total amount of He at end of test):

$$F_{HE_i} V_{sp_i} = F_{HE_f} (V_{sp_f} + V_{L_f}) \quad 、$$

That is, the total amount of helium in the system initially is equal to its initial fractional concentration (FHE_i) times the initial volume of the spirometer (Vsp_i). This must be equal to the total amount of helium in the lungs and the spirometer at the end of the test, which is equal to the final (lower) fractional concentration

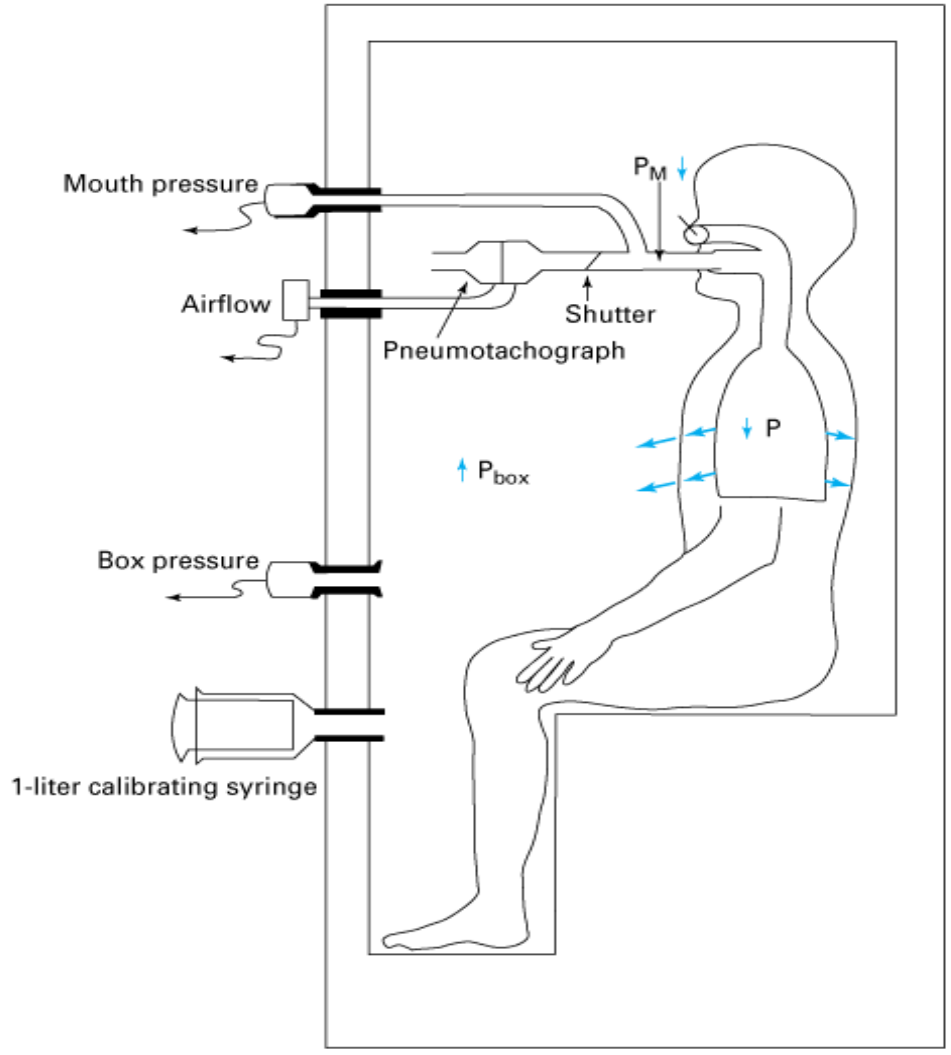
of helium (FHE_f) times the final volume of the spirometer (Vsp_f) and the volume of the lungs at the end of the test (VL_f). Since it may take several minutes for the helium concentration to equilibrate between the lungs and the spirometer, in practice, CO_2 is absorbed from the system and oxygen is added to the spirometer at the rate at which it is used by the person. Both the nitrogen-washout and helium-dilution methods can be used on unconscious patients.

Body Plethysmography:

A problem common to both the nitrogen-washout technique and the helium-dilution technique is that neither can measure trapped gas because nitrogen trapped in alveoli supplied by closed airways cannot be washed out and because the helium cannot enter alveoli supplied by closed airways. Furthermore, if the patient's lungs have many alveoli served by airways with high resistance to airflow , it may take a very long time for all the nitrogen to wash out of the patient's lungs or for the inspired and expired helium concentrations to equilibrate. In such patients, measurements of the lung volumes with a body plethysmograph are much more accurate because they do include trapped gas.

The body plethysmograph works on “Boyle's law, which states that for a closed container at a constant temperature, the pressure times the volume is constant.”

The body plethysmograph, an expensive piece of equipment, is shown schematically in Figure below:



-The subject is seated in the small airtight chamber and breathes through the apparatus shown. By monitoring the subject's airflow with a pneumotachograph, the operator can briefly occlude the subject's airway at end expiration. As the subject makes an inspiratory effort against the closed airway, the pressure in the

chamber (P_{box}) increases and the pressure at the subject's mouth (PM) decreases. The subject's functional residual capacity can then be calculated.

Diffusing Capacity

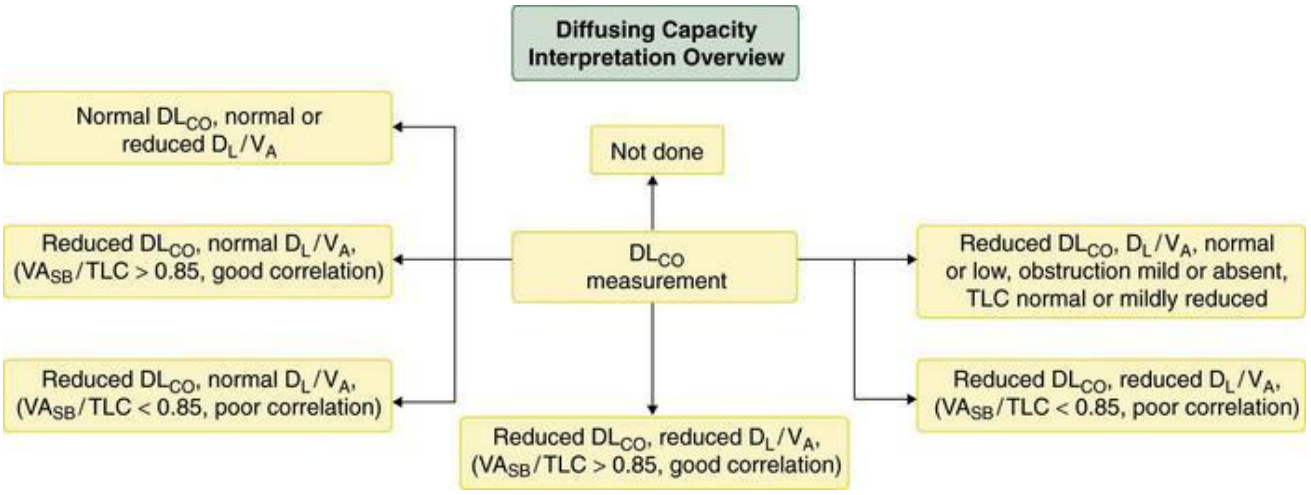
“Understanding gas diffusion through the lungs requires recognizing the basics of the gas exchange interface and of the various forces at work by which oxygen and carbon dioxide move by molecular diffusion. Diffusion is limited by the surface area in which diffusion occurs, capillary blood volume, hemoglobin concentration, and the properties of the lung parenchyma that separate the alveolar gas from the red blood cell with the capillary (alveolar-capillary membrane thickness and/or the presence of excess fluid in the alveoli)”

“Because all lung volume is not exchanged, most gas exchange occurs as a function of diffusion independent of bulk flow”

“The clinical test diffusing capacity of the lung most commonly uses carbon monoxide as the tracer gas for measurement because of its high affinity for binding to the hemoglobin molecule. This property allows a better measurement of pure diffusion, such that the movement of the carbon monoxide in essence only depends on the properties of the diffusion barrier and the amount of hemoglobin.”

"Diffusing capacity of the lung for carbon monoxide (D_LCO) is the measure of carbon monoxide transfer. In Europe, it is often called the transfer factor of carbon monoxide,which describes the process more accurately

A pattern of diffusing capacity reduced proportionate to airflow obstruction (a proportionate reduction in FEV_1 and D_LCO) is typical for emphysema. A D_LCO is reduced proportionately to a reduction in total lung capacity in the context of restrictive abnormalities suggests a parenchymal process such as pulmonary fibrosis. An isolated or disproportionate reduction in diffusing capacity along with either normal or fairly well preserved mechanics suggests predominantly a pulmonary vascular process such as primary pulmonary hypertension or thromboembolic disease."



Diabetes Mellitus

“Diabetes mellitus is a chronic disorder characterized by hyperglycemia and the late development of vascular and neuropathic complications. Regardless of its cause, the disease is associated with a common hormonal defect— namely, insulin deficiency—that may be absolute or relative in the context of coexisting insulin resistance. The effect of insufficient insulin plays a primary role in the metabolic derangements linked to diabetes; hyperglycemia, in turn, plays an important role in disease-related complications.”

Diabetes is the single most important metabolic disease which can affect nearly every organ in the body and is therfore widely recognized as one of the leading causes of death and disability worldwide.

Currently more than **62 million** Indians are diabetic. Nearly 1 million Indians die due to diabetes every year. These statistics have conferred the dubious title of DIABETES CAPITAL to our country.

Etiological Classification of Diabetes:

The vast majority of diabetes cases fall into two broad etiopathogenetic categories:

1.” Type 1 diabetes mellitus (T1DM): Absolute deficiency of insulin secretion

2. Type 2 diabetes mellitus (T2DM): Combination of insulin resistance and inadequate compensatory insulin secretory response (relative insulin deficiency). Diabetes can also develop secondary to other causes like genetic defects in beta cell function, genetic defects in insulin action and diseases of the exocrine pancreas or intake of certain drugs.”

I. Type 1 diabetes mellitus		
A. Immune mediated B. Idiopathic		
II. Type 2 diabetes mellitus		
III. Other specific types		
A. Genetic defects in beta cell function	–	MODY type 1 to type 6 Mitochondrial diabetes
B. Genetic defects in Insulin action	–	Type A Insulin resistance
	–	Lipoatrophic diabetes
C. Pancreatic diseases	–	Fibrocalcific pancreatitis Pancreatectomy Cystic fibrosis
D. Endocrinopathies	–	Acromegaly Cushing's syndrome Pheochromocytoma Hyperthyroidism
E. Drug induced	–	Glucocorticoids Thyroid hormone Diazoxide Thiazides Dilantin Vacor, Pentamidine, Olanzapine, Rifampicin
F. Infections	–	Congenital Rubella Cytomegalovirus Mumps
G. Uncommon forms of immune mediated diabetes	–	"Stiff-man" syndrome Anti-insulin receptor antibodies
H. Genetic syndrome association	–	Down's syndrome Turner's syndrome Klinefelter's syndrome Myotonic dystrophy Prader-Willi syndrome
IV. Gestational Diabetes		

(MODY: Maturity onset diabetes of the young).

DIAGNOSIS OF DIABETES MELLITUS

“Diagnosis of diabetes is based upon plasma glucose levels. Three ways to diagnose diabetes are possible and each, in the absence of unequivocal hyperglycemia, must be confirmed, on a subsequent day. The 75 g oral glucose tolerance test (OGTT) is more sensitive and modestly more specific than fasting plasma glucose (FPG) in the diagnosis of diabetes, but is poorly reproducible. Because of its ease, patient acceptability and lower cost, measurement of FPG is the preferred diagnostic test. The use of the hemoglobin A1c (glycosylated hemoglobin or HbA1c) for the diagnosis of diabetes was previously not recommended due to lack of global standardization and uncertainty about diagnostic thresholds. Presently, because of a worldwide move towards a standardized assay and with increasing evidence about the prognostic significance of HbA1c, it is included as a diagnostic test in the 2011 American Diabetes Association (ADA) guidelines”

- HbA1c ≥ 6.5%. The test should be performed in a laboratory using a method that is NGSP certified and standardized to the DCCT assay

OR

- Fasting ≥ 126 mg/dL. Fasting is defined as no caloric intake for at least 8 hours

OR

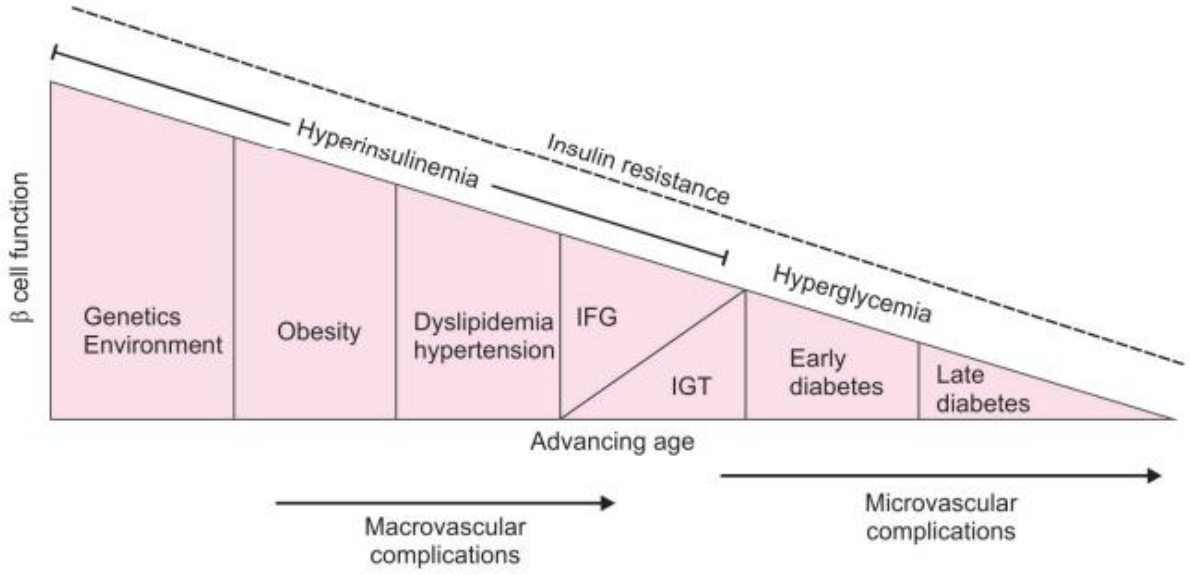
- 2-hr plasma glucose ≥ 200 mg/dL during an OGTT. The test should be performed as described by the World Health Organization, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water*

OR

- Symptoms of hyperglycemia and a casual plasma glucose ≥ 200 mg/dL. Casual is defined as any time of day without regard to time since last meal. The classic symptoms of hyperglycemia include polyuria, polydipsia, and unexplained weight loss

*In the absence of unequivocal hyperglycemia, the first three criteria should be confirmed by repeat testing on a different day.

CONCEPT OF PREDIABETES



The above Figure shows the Natural History of Type 2 Diabetes and its evolution.

Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) are the fore-runners of future T2DM (collectively termed as prediabetes).

The significance of impaired fasting glycemia and IGT

• Increased risk for cardiovascular/cerebrovascular diseases

• Predictor of subsequent diabetes mellitus

• Diabetic range values may be unmasked with stress

Diagnosis of IFG and IGT based on International Diabetes Federation criteria

	Plasma (mg/dL)	*Venous whole blood (mg/dL)*	*Capillary whole blood (mg/dL)*
Impaired fasting glucose			
Fasting glucose	110–125	100–109	100–109
2 hour postglucose load	< 140	< 120	< 140
Impaired glucose tolerance			
Fasting glucose	<126	<110	<110
2 hour postglucose load	140–199	120–179	140–199

CONCEPT OF “THE METABOLIC SYNDROME”

The metabolic syndrome also referred to as syndrome X or insulin resistance syndrome refers to a cluster of cardiovascular disease risk factors and metabolic

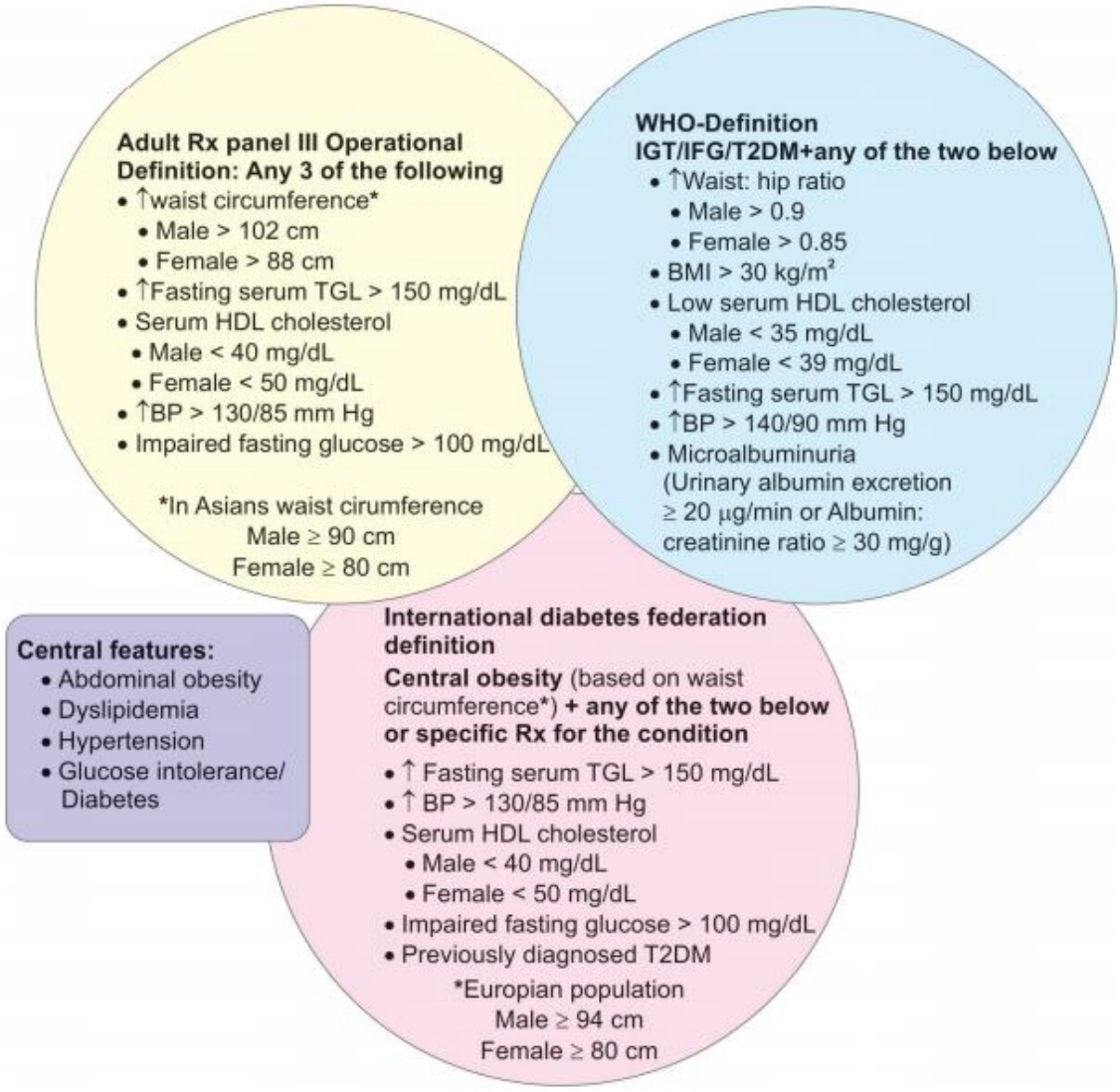
alterations associated with excess body fat. Even though there are different definitions the following are central to the diagnosis abdominal obesity, dyslipidemia, hypertension and glucose intolerance or diabetes.

Insulin resistance and accompanying hyperinsulinemia is said to play a central role in the pathogenesis of the syndrome with a casual relationship to hypertension.This may be due to the effects of insulin in the periphery on vasculature as well as a central action leading to stimulation of sympathetic activity and in turn the renin-angiotensin-aldosterone system.

“Despite the importance of the metabolic syndrome as a risk marker, there remains disagreement regarding the best way to define it. The current scientific statement attempts to clarify the definition of metabolic syndrome and identifies possible future refinements to this definition.”

“The most significant controversy regarding the definition of the metabolic syndrome has been the inclusion of abdominal obesity. It has been required in some recommendations to diagnose the metabolic syndrome, whereas it has served as a nonintegral variable in the diagnosis in other algorithms.”

Different definitions of metabolic syndrome



Criteria for clinical diagnosis of the metabolic syndrome.

Measure	*Categorical cut points*
Elevated waist circumference	Population- and country-specific definitions
Elevated triglycerides (drug treatment for elevated triglycerides is an alternate indicator)	>150 mg/dL
Reduced HDL cholesterol (drug treatment for reduced HDL cholesterol is an alternate indicator)	<40 mg/dL for males and < 50 mg/dL for females
Elevated blood pressure (drug treatment for elevated blood pressure is an alternate indicator)	Systolic >130 mm Hg and/or diastolic >85 mm Hg
Elevated fasting glucose (drug treatment for elevated glucose is an alternate indicator)	>100 mg/dL

SCREENING FOR DIABETES

The following are the ADA guidelines to select asymptomatic adult individuals who will need testing for prediabetes and diabetes

“Testing should be considered in all adults who are overweight [body mass index (BMI) ≥ 25 kg/m2] and have additional risk factors:

A. Physical inactivity

B. First-degree relative with diabetes

C. Members of a high-risk ethnic population (e.g. African American, Latino, Native American, Asian American, Pacific Islander)

D. Women who delivered a baby weighing >4 kg or were diagnosed with gestational diabetes mellitus (GDM)

E. Hypertension (≥140/90 mm Hg or on therapy for hypertension)

F. HDL cholesterol level 250 mg/dL (2.82 mmol/L)

G. Women with polycystic ovarian syndrome (PCOS)

H. IGT or IFG on previous testing

I. Other clinical conditions associated with insulin resistance (e.g. severe obesity, acanthosis nigricans)

J. History of cardiovascular disease.

2. In the absence of the above criteria, testing for prediabetes and diabetes should begin at the age of 45 years.

3. If results are normal, testing should be repeated at least at 3 year intervals, with consideration of more frequent testing depending on initial results and risk status."

GLYCOSYLATED HEMOGLOBIN

Glycation refers to nonenzymatic addition of a sugar residue to an amino group of a protein. Hemoglobin, plasma proteins, membrane proteins, lens protein, etc. may undergo glycosylation. HbA1c forms the major fraction (80%). In HbA1C, the "N-terminal valine residue of each beta chain gets glycated. HbA1c gives a retrospective index of integrated plasma glucose values over a 6–8 weeks period and is not subject to wide fluctuations" in plasma glucose levels.

HbA1c serves as a reliable indicator of diabetes control during the past 90 days, effectiveness of treatment and risk of development of acute or long-term complications. Hence HbA1c should be performed routinely in all patients with diabetes, to assess the degree of glycaemic control at initial visit and then as a part of continuing visits every three months to assess metabolic control.

Normal HbA1c values and interpretation

• Normal nondiabetic range: 4.5–5.8%

• Serious risk of hypoglycemia: < 4.5

• Diabetic range: > 6.5%

• Prediabetic range: 5.8–6.5%

There are some conditions which may lead to a false elevation or reduction in HbA1c levels. Hemoglobinopathies like thalassemia, hereditary persistence of fetal hemoglobin, a low hemoglobin level per se (<7.0 g/dL) and uremia are known to cause altered levels of HbA1c.

Approximate correlation between glycosylated hemoglobin (HbA1c) and mean plasma glucose levels:

HbA1c%	*Mean plasma glucose (mg/dL)*
5	97
6	126
7	154
8	183
9	212
10	240
11	269
12	298

Follow-up of patients and frequency of testing

Tests	*Time to visit*
Blood glucose	- Controlled (HbA1c < 7%)—every 3 months - Uncontrolled—every 2 weeks until target sugars achieved
HbA1c	- Controlled (HbA1c < 7%)—6 months to 1 year - Uncontrolled—every 3 months
Tests for neuropathy	
Monofilament	- Annual
Biothesiometer	- Annual
Foot examination	- Once in 3 months
Test for retinopathy	
Fundus examination	- Annually. If evidence of retinopathy detected at first visit, follow-up every 3–6 months
Tests for nephropathy	
Urinary microalbumin (or 24 hours urinary protein)	- Annual
Serum creatinine	- Annual
Miscellaneous tests	
ECG	- Annual
Treadmill test	- By 5 years after onset of diabetes mellitus, then once in 2 years
Lipid profile	- annual. If abnormal every 6 months
Plain X-ray abdomen	- If BMI < 20 kg/m^2 Or USG abdomen

(BMI: Body mass index; USG: Ultrasonography; ECG: Electrocardiography; HbA1c: Glycosylated hemoglobin).

Diabetes and its Complications

Consequences of disturbed metabolism in diabetes:

Metabolic defect	*Chemical abnormality*	*Clinical abnormalities*
Carbohydrate metabolism		
• ↓↓ Glucose uptake by tissues (muscle, adipose tissue, liver) • ↑↑↑ Glucose production 2° to Glycogenolysis and glyconeo-genesis in liver	Hyperglycemia ↓ Glycosuria ↓ Osmotic diuresis	• Polyuria, Polydipsia, Polyphagia • Blurred vision • Diminished mental alertness • Dehydration (→ death)
Protein metabolism		
• ↓ Uptake of amino acids • ↓ Protein synthesis • ↑ Proteolysis	• Negative nitrogen balance • ↑ Levels of branch chain amino acid • ↑ Blood urea nitrogen level • ↑ K^+ level	• Weakness • Poor resistance to infections • Muscle wasting
Lipid metabolism		
• ↑ Lipolysis • ↓ Lipogenesis • ↑ Triglycerides, FFA production • ↑ Ketone production • ↓ Ketone excretion • ↑ Production of LDL and VLDL	• ↑ Plasma FFA • ↑ Plasma glycerol • Hypertriglyceridemia • ↑ Plasma and urine ketone • ↑ Plasma LDL and VLDL	• Loss of adipose tissue → Weight loss • Pancreatitis • Metabolic acidosis → Hyperventilation → Kussmaul breathing → death • Atherosclerotic vascular disease

“The microvascular complications of both type 1 and type 2 DM result from chronic hyperglycemia. Evidence implicating a causative role for chronic hyperglycemia in the development of macrovascular complications is less conclusive. CHD events and mortality rate are two to four times greater in patients with type 2 DM and correlate with fasting and postprandial plasma glucose levels as well the hemoglobin A1c (HbA1c). Other factors such as dyslipidemia and hypertension also play important roles in macrovascular complications.”

- Microvascular
  - Eye disease
    - Retinopathy (nonproliferative/proliferative)
    - Macular edema
  - Neuropathy
    - Sensory and motor (mono- and polyneuropathy)
    - Autonomic
  - Nephropathy (albuminuria and declining renal function)
- Macrovascular
  - Coronary heart disease
  - Peripheral arterial disease
  - Cerebrovascular disease
- Other
  - Gastrointestinal (gastroparesis, diarrhea)
  - Genitourinary (uropathy/sexual dysfunction)
  - Dermatologic
  - Infectious
  - Cataracts
  - Glaucoma
  - Cheiroarthropathy[a]
  - Periodontal disease
  - Hearing loss
- Other comorbid conditions associated with diabetes (relationship to hyperglycemia is uncertain): depression, obstructive sleep apnea, fatty liver disease, hip fracture, osteoporosis (in type 1 diabetes), cognitive impairment or dementia, low testosterone in men

MECHANISMS OF COMPLICATIONS

“Although chronic hyperglycemia is an important etiologic factor leading to complications of DM, the mechanism(s) by which it leads to such diverse cellular and organ dysfunction is unknown. An emerging hypothesis is that hyperglycemia leads to epigenetic changes that influence gene expression in affected cells.”

Some theories include:

(1) “Increased intracellular glucose leads to the formation of advanced glycosylation end products, which bind to a cell surface receptor, via the nonenzymatic glycosylation of intra- and extracellular proteins, leading to cross-linking of proteins, accelerated atherosclerosis, glomerular dysfunction, endothelial dysfunction, and altered extracellular matrix composition”

(2) “Hyperglycemia increases glucose metabolism via the sorbitol pathway related to the enzyme aldose reductase. However, testing of this theory in humans, using aldose reductase inhibitors, has not demonstrated beneficial effects.”

(3) “Hyperglycemia increases the formation of diacylglycerol, leading to activation of protein kinase C, which alters the transcription of genes for

fibronectin, type IV collagen, contractile proteins, and extracellular matrix proteins in endothelial cells and neurons."

(4) "Hyperglycemia increases the flux through the hexosamine pathway, which generates fructose-6-phosphate, a substrate for O-linked glycosylation and proteoglycan production, leading to altered function by glycosylation of proteins such as endothelial nitric oxide synthase or by changes in gene expression of transforming growth factor β (TGF-β) or plasminogen activator inhibitor-1."

Diabetic Retinopathy:

Diabetic retinopathy is the most common cause of legal blindness between the ages of 20 and 70 years. Blindness usually results from non-resolving vitreous hemorrhage, tractional retinal detachment or diabetic macular edema. However, the 5-year risk of severe visual loss can be reduced if a person with proliferative DR undergoes laser photocoagulation. DR is often asymptomatic in its most treatable stages; hence early detection through regularly scheduled ocular examination is critical.

Risk Factors:

• Duration of diabetes – Most important factor – Longer the duration higher the incidence (after 10 years of DM, incidence of retinopathy is 50% in patients less

than 30 years of age and 90% in patients more than 30 years) – Rare before puberty.

• Poor control of diabetes – Worsens the progression – Tight control does not guarantee prevention, but delays the onset and slows progression.

• Pregnancy – Associated with rapid progression of pre-existent retinopathy especially if prepregnancy control was poor – Postpartum reversal of retinopathy may occur – It is rare for women without retinopathy to develop it during pregnancy – De novo gestational diabetes has no risk of retinopathy.

• Hypertension is associated with worsening

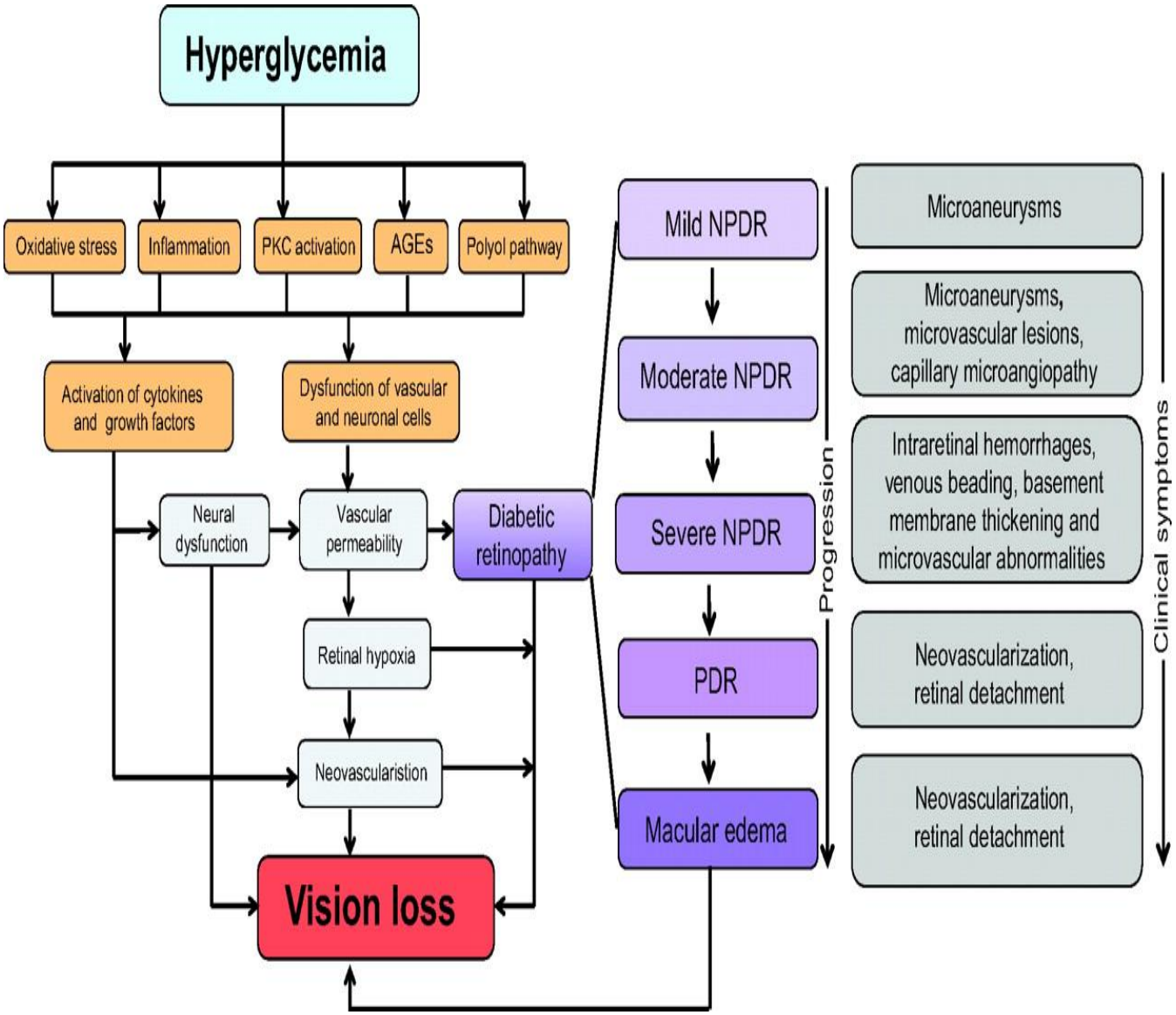
• Nephropathy – Associated with worsening – Treatment as with renal transplantation leads to improvement.

• Obesity

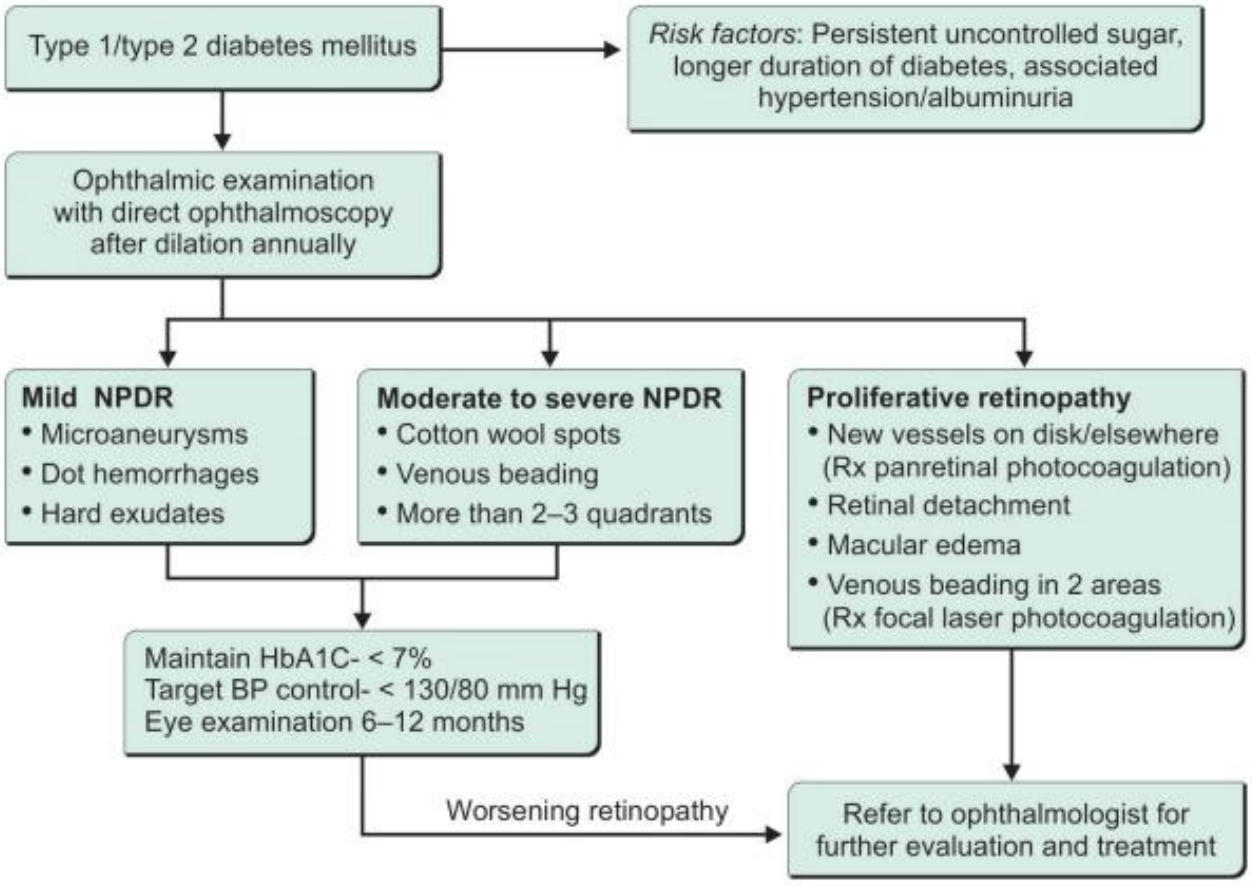
• Hyperlipidemia

• Smoking

PATHOGENESIS OF DIABETIC RETINOPATHY:



Algorithm for management of retinopathy:



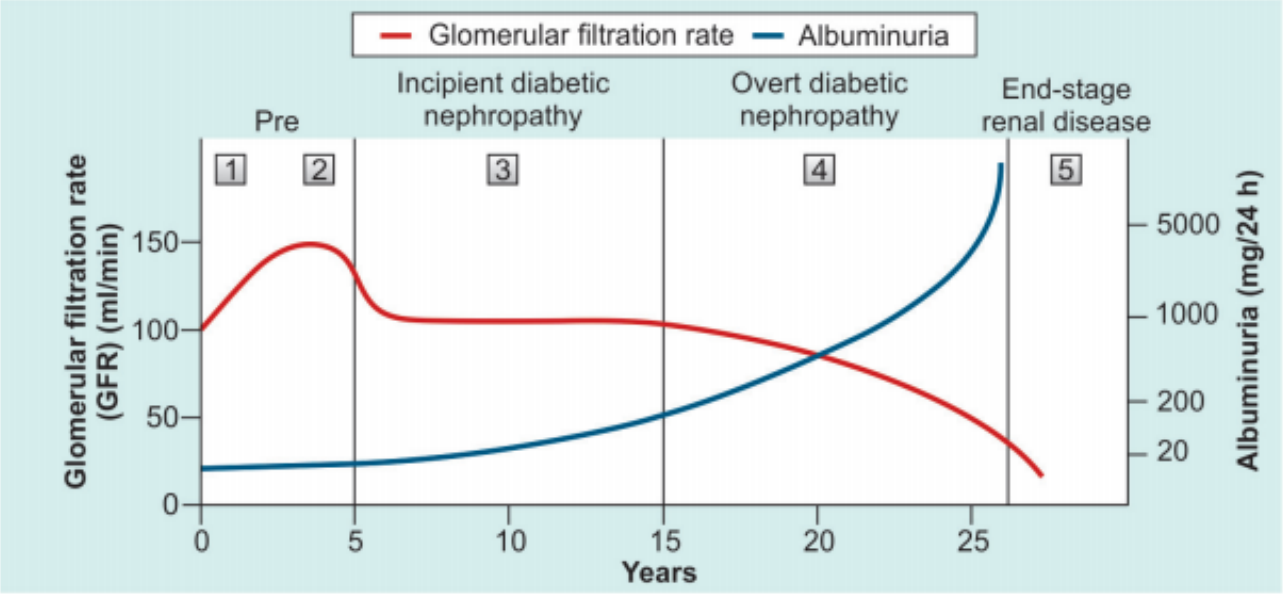
DIABETIC NEPHROPATHY

"Diabetic nephropathy is one of the leading causes of chronic renal failure and end stage renal disease. this is due to the increasing prevalence of type 2 diabetes, longer life span of diabetic patients and improved therapeutic options."

“Diabetic retinopathy is clinically defined as the presence of persistent proteinuria of mre than 500 mg/day in a diabetic patient with concomitant evidence of diabetic retinopathy and hypertension ,in the absence of other kidney or renal tract disease.”

Diabetic patients are 17 times more prone to develop nephropathy than the general population.the peak onset of DN in type 1 diabetes is between 10-15 years after onset of disease.

Stages of diabetic nephropathy



Revised KDIGO CKD classification based on GFR and albuminuria and risk stratification:

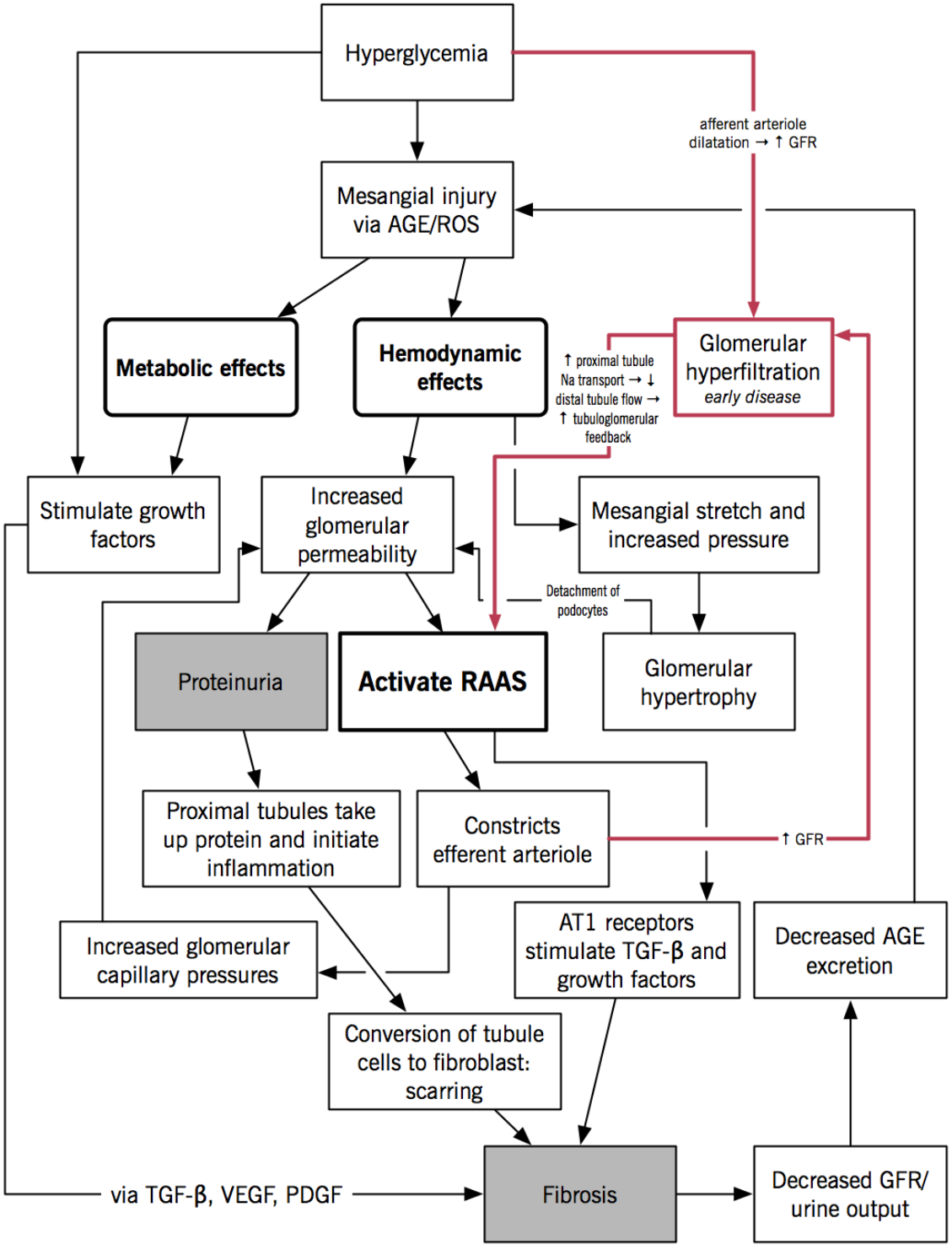
Prognosis of CKD by GFR and albuminuria category

Prognosis of CKD by GFR and albuminuria categories: KDIGO 2012				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
GFR categories (ml/min/1.73 m^2) Description and range	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

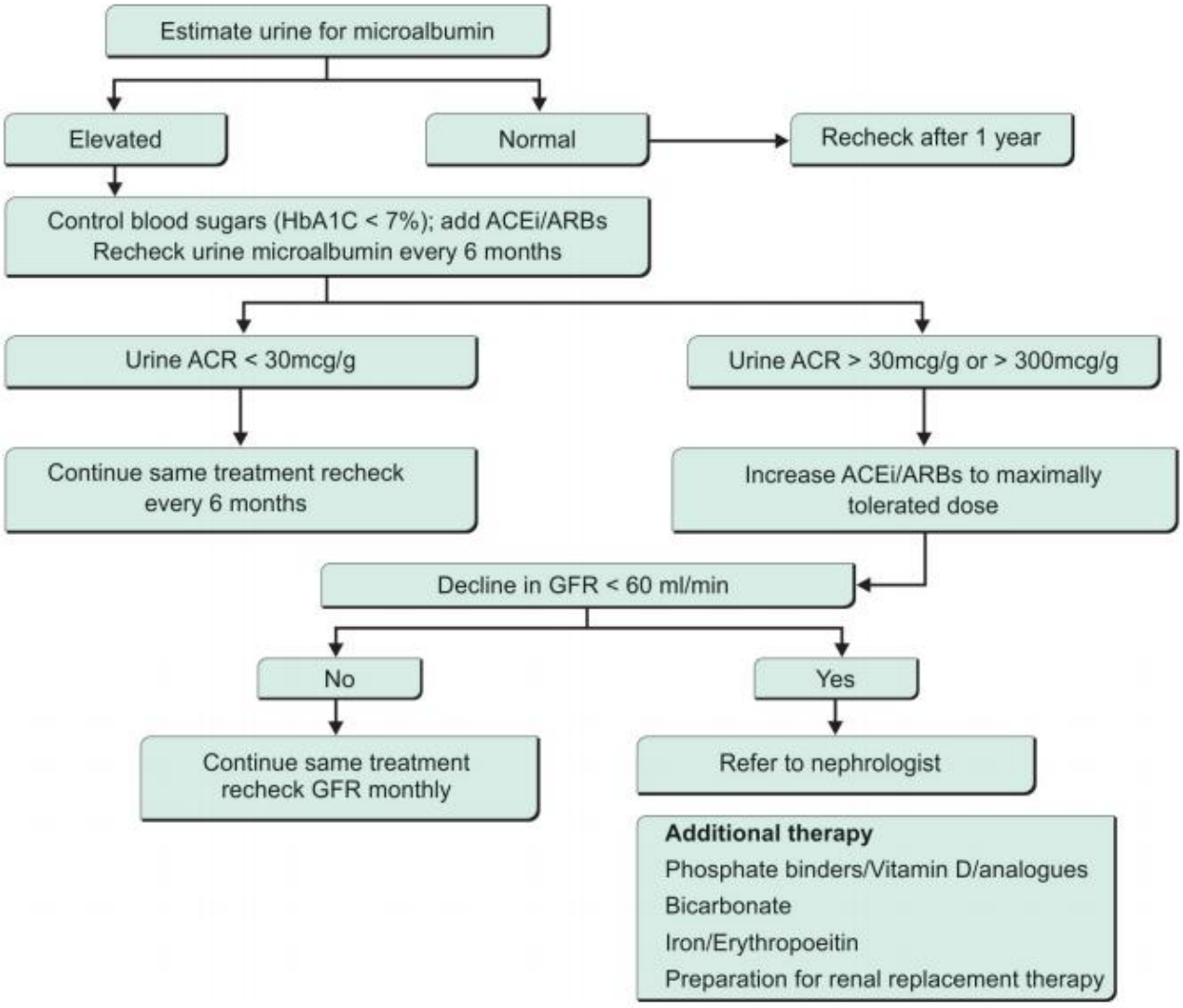
Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red: very high risk

Pathophysiology of diabetic nephropathy

Eric Wong



Algorithm for management of diabetic nephropathy:



(ACE: angiotensin-converting-enzyme; ARB: Angiotensin receptor blocker; ACR: Albumin-creatinine ratio; GFR: Glomerular filtration rate).

DIABETIC NEUROPATHY:

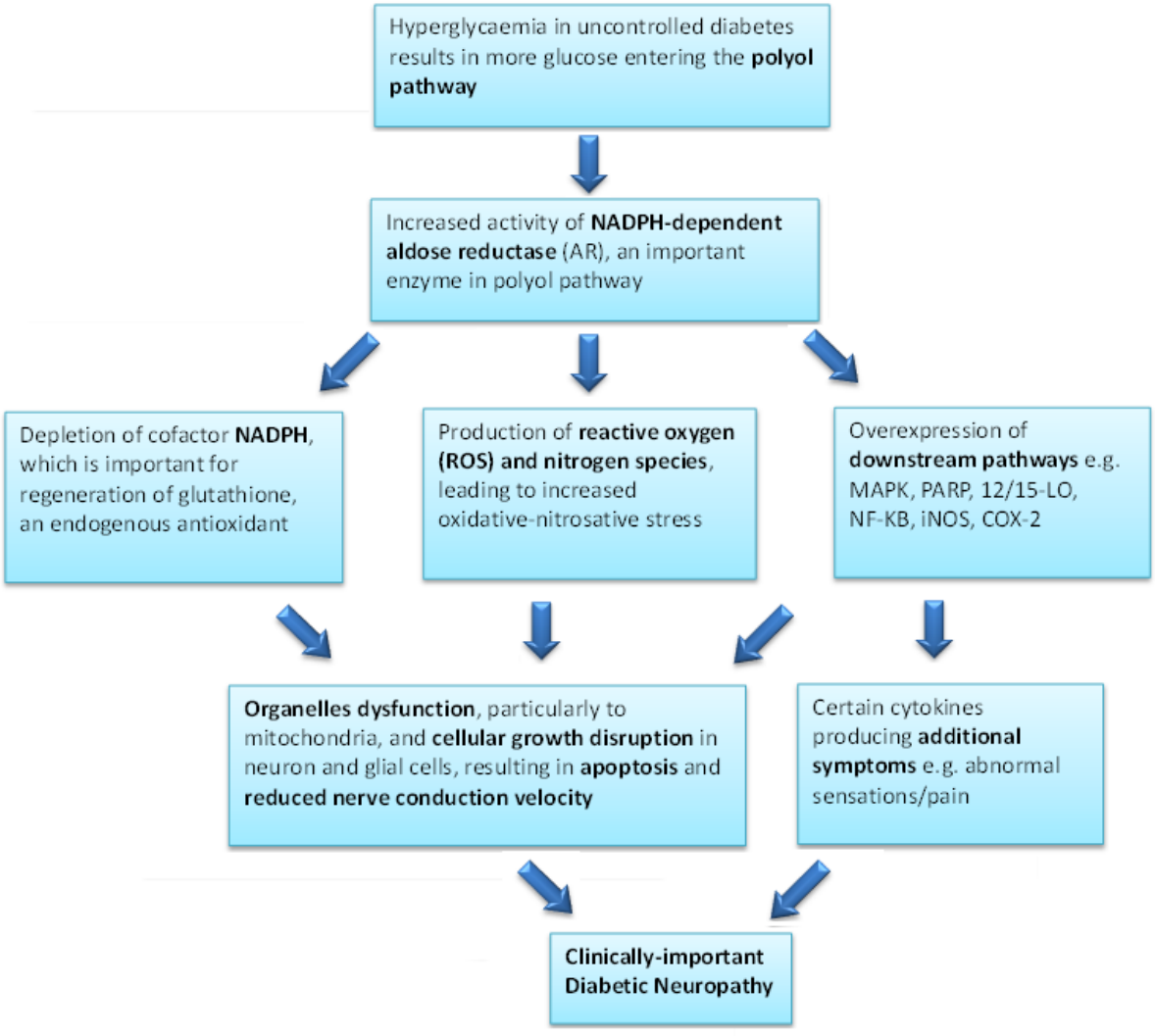
Diabetic neuropathy is a heterogenous condition that encompasses a wide range of peripheral nerve dysfunction and whole development might be attributed to diabetes per se or to factors associated in the disease . It is the most common and most troublesome of all diabetic complications.

Diabetic neuropathy is defined as the presence of symptoms and signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes the neuropathic dysfunction is manifested in the somatic and autonomic nervous system.

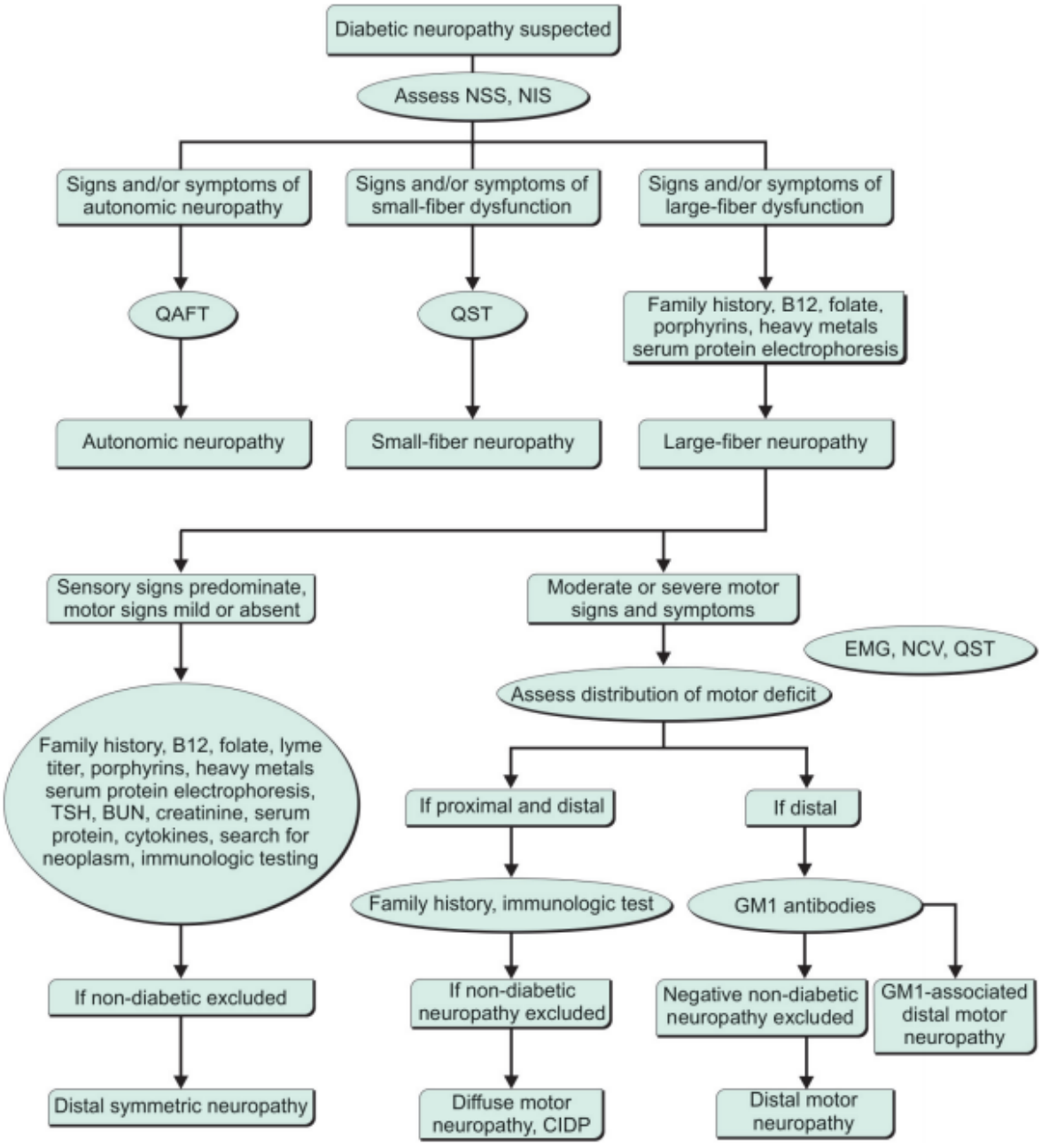
CLASSIFICATION OF DIABETIC NEUROPATHY:

Classifications	**Sub-classifications/Types**
Rapidly reversible	Hyperglycaemic neuropathy
Persistent symmetric polyneuropathy	-Distal symmetric sensory/sensorimotor polyneuropathy -Autonomic neuropathy -Small fibre neuropathy/Acute painful neuropathy
Focal/multifocal neuropathy/Diabetic mononeuropathy	-Cranial neuropathy -Thoracoabdominal radiculopathy/Truncal neuropathy -Focal limb neuropathy -Proximal neuropathy/Amyotrophy -Compression/entrapment neuropathy

PATHOGENESIS OF DIABETIC NEUROPATHY:



Algorithm for management of diabetic peripheral neuropathy



Source: Figure modified from Medscape—endocrine practice, 2007 American association of clinical endocrinologists.

LUNG INVOLVEMENT IN DIABETES:

Despite advancements in understanding the pathogenesis of diabetes and the complications, the pathology of lung involvement is not well established. The PFT might show a restrictive pattern. The probable mechanisms explained are due to the advanced glycation of end products (AGE's). first due to the pro inflammatory effect of AGE's . Second one is functional alteration of lung connection tissue by AGE's.The other proposed mechanisms are micro vascular involvement lead to changes in lung parenchyma. Due to endothelial dysfunction vasodilation does not occur. Insulin resistance may also play role in lung dysfunction. Neuropathy of thoracic nerves leading to respiratory muscle abnormality may have a role.

With these proposed mechanisms it is clear that pulmonary involvement is similar to other micro vascular complications of diabetes and may co exist with other micro and macro vascular complications.

METHODOLOGY

One hundred diabetic patients previously diagnosed, belonging to either sex attending / admitting to OPD/wards of Govt. Rajaji hospital, Madurai medical College Madurai , will be studied.

Patients will be classified into three groups A, B, C depending on the duration of diabetes.

Group A consists of diabetes with duration of up to 3 years.

Group B consists of diabetes with duration of 3to 5 years.

Group C consists of diabetes with duration of 5 to 7 years.

SOURCE OF DATA

"Patients with diabetes mellitus attending OPD in Department of diabetology and admitted in department of general medicine Of Government Rajaji Hospital, Madurai during the study period of june 2016 to august 2016."

SAMPLE SIZE

100 cases

DURATION OF STUDY

June 2016 to August 2016

INCLUSION CRITERIA

"Previously diagnosed Type 2 Diabetic patients for less than 7 years,between age 40-60 years,with regular follow up. One hundred age and sex matched non diabetic were included as the other group. Diabetes was ruled out in non diabetic group with fasting and 2-hr post prandial blood glucose measurement."

EXCLUSION CRITERIA

- Smokers,
- patients with previous/present cardio respiratory diseases
- h/o occupational exposure
- Persons with physical disabilities
- Obese (BMI>30)
- Neuromuscular diseases

METHOD OF COLLECTION OF DATA

"Diabetic patients of different durations were selected carefully using criteria laid down. Their written consent was taken. The history was elicited. Age,

height, weight were recorded. Thorough clinical examination was carried out. The performance of the pulmonary function tests was demonstrated.''

''Patients were made to undergo pulmonary function tests using Medspiror, for 3 times at every 15 minutes interval and best of 3readings was taken.

The Forced Vital Capacity (FVC), Forced Expiratory Volume at the end of one second (FEV1), Peak Expiratory Flow Rate (PEFR),FEV1/ FVC ratio were recorded.''

''Diabetes mellitus was ruled out in non diabetic group by fasting and post prandial blood glucose was analysed by GOD-PAP(glucose oxidase-phenol 4-aminophenazone peroxidase)method.''

Other relevant investigations are done

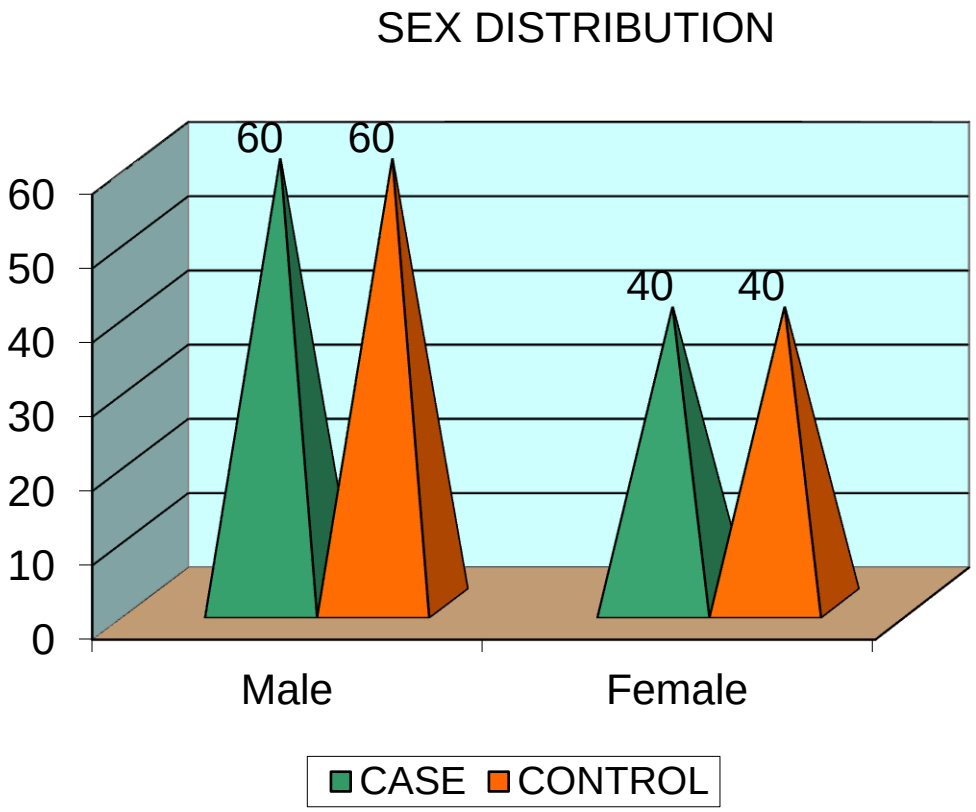
- ECG in all leads
- Echocardiogram
- Fasting and 2 hr blood sugar
- Chest X RAY

STATISTICAL ANALYSIS

Statistical analysis was done by using percentages, mean values, standard deviation, chi-square test, t-test and proportion test. A p-value <0.05 level was considered statistically significant and a p-value >0.05 was considered as not statistically significant.

SEX DISTRIBUTION OF CASES & CONTROLS

Sex	**CASE**	**CONTROL**
Male	60	60
Female	40	40
Total	100	100



Of the total 100 patients 60 are males and 40 females. Among the controls 60 males and 40 females were chosen.

AGE WISE DISTRIBUTION OF CASES

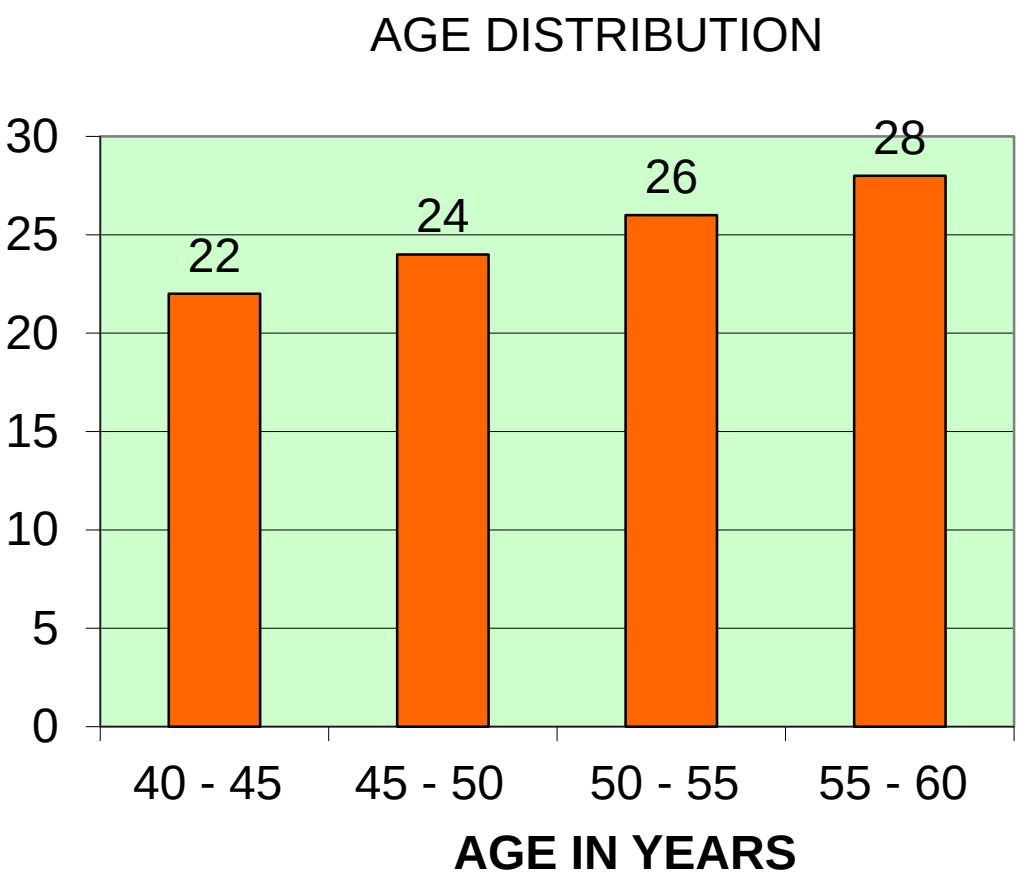
AGE	Total
40 - 45	22
45 - 50	24
50 - 55	26
55 - 60	28

Total 100

In age distribution most of our patients(28%) were in age group of 55-60yrs- 28 patients. Least number of patients(22%) were in 40-45years group-22

This is suggestive that most of the patients have been diagnosed later.`

AGEWISE DISTRIBUTION OF PATIENTS



CLASSIFICATION OF DIABETIC PATIENTS INTO THREE GROUPS BASED ON DUARTION OF DIABETES

DURATION OF DIABETES IN YEARS	GROUP	No.of cases
<3	A	40
3-<5	B	28
>5	C	32
	Total	100

The diabetic patients are classified into three groups A,B,C based on duration of diabetes <3.3-<5,>5 years respectively for the purpose of conducting the study.

Among the three groups group A has maximum number of patients and group B having least number of patients.

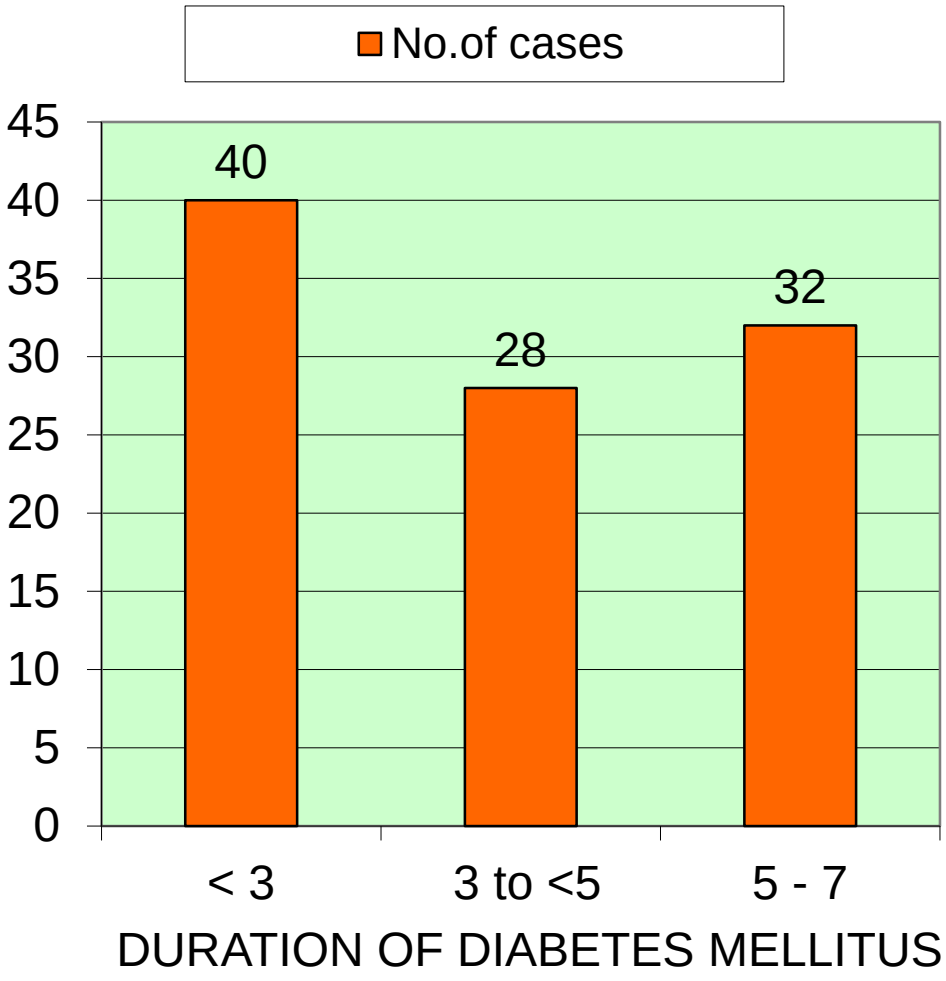

No.of cases
45
40
35
30
25
20
15
10
5
0
40
28
32
< 3
3 to <5
5 - 7
DURATION OF DIABETES MELLITUS

TABLE OF COMPARISON OF DURATION OF DIABETES WITH SEX DISTRIBUTION

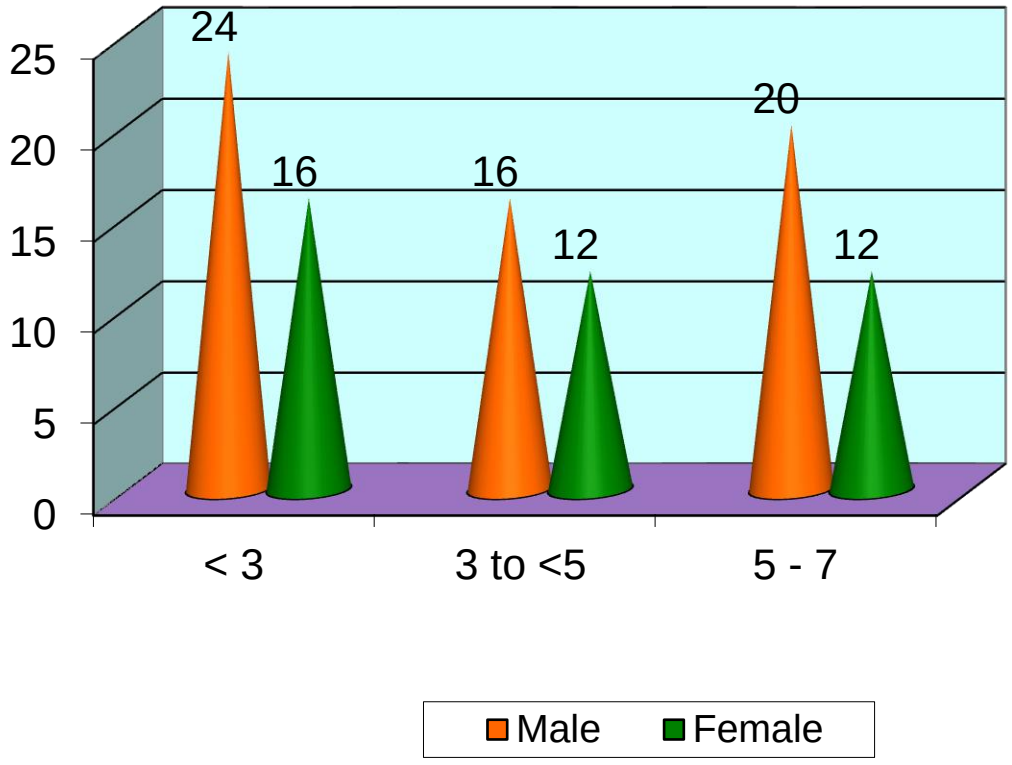
	No.of cases		Duration of DM	Male	Female	Total
< 3	40		**< 3**	24	16	40
3 to <5	28		3 to <5	16	12	28
5 - 7	32		5 - 7	20	12	32
Total	100		Total	60	40	100

Among the patients 60%(60) are males and 40%(40) are females .

Even among the three groups in all the groups males are predominant than females.

Thus males are the predominant population of our study.

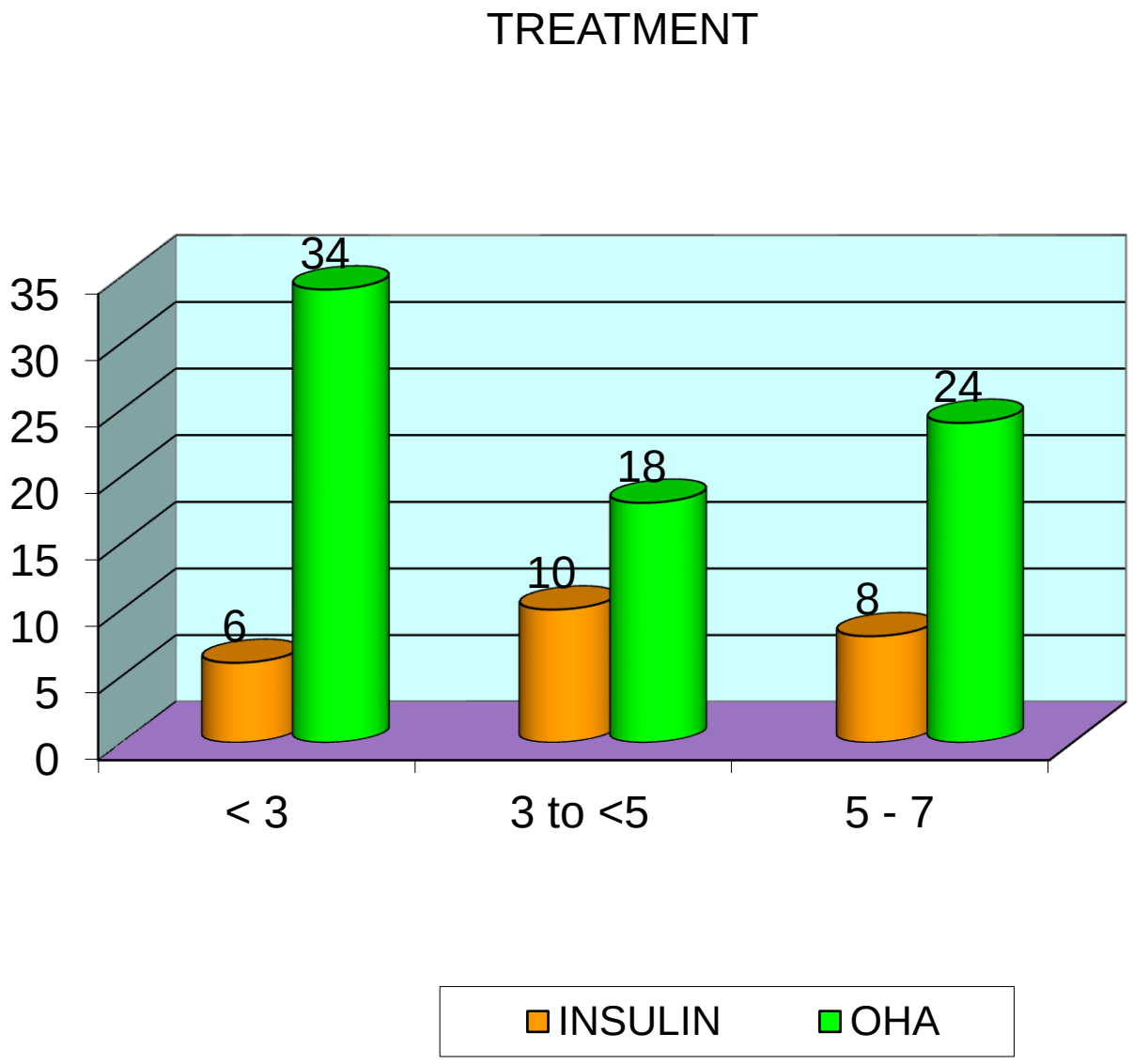
DM VS GENDER



COMPARISON OF DIABETIC PATIENTS BASED ON THEIR TREATMENT(INSULIN OR OHA)

	TREATMENT	
DM	INSULIN	OHA
< 3	6	34
3 to <5	10	18
5 - 7	8	24
Total	24	76

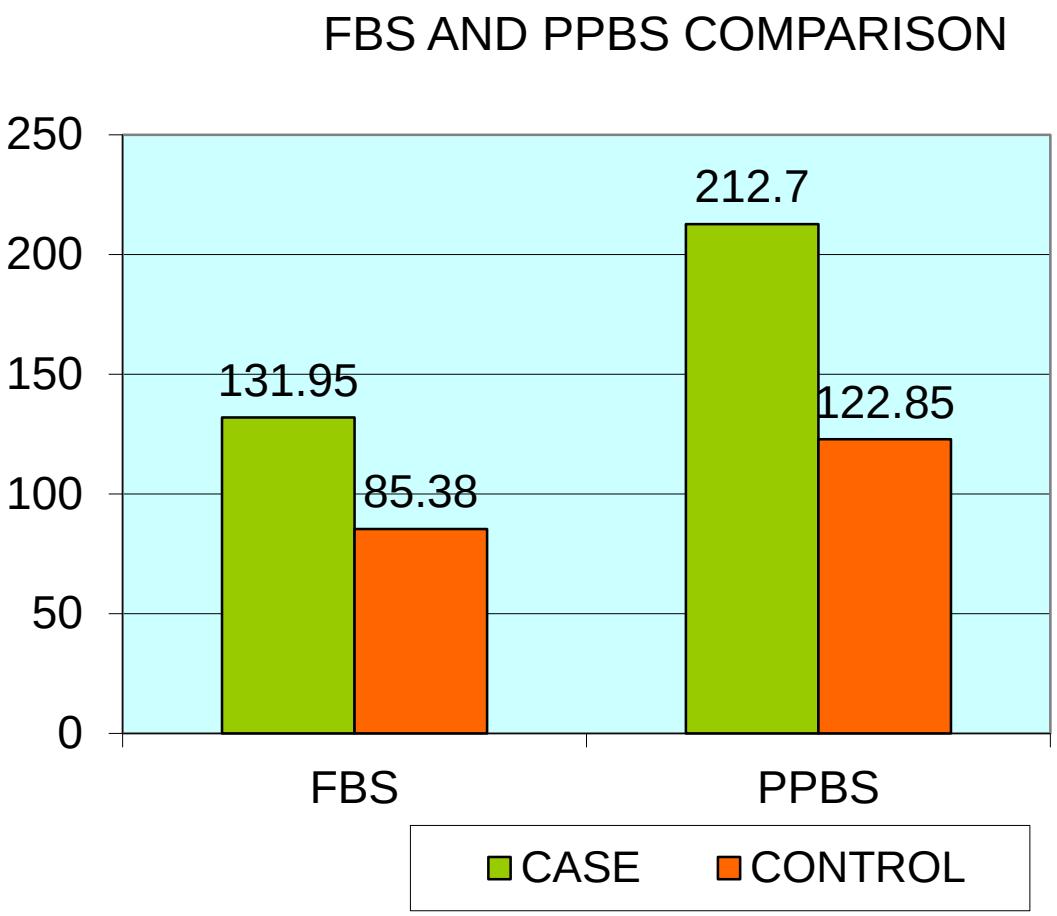
Among the patients most of our patients are OHA treated (76%) when compared to INSULIN treated(24%)


TREATMENT
35
30
25
20
15
10
5
0
34
6
18
10
24
8
< 3
3 to <5
5 - 7
INSULIN
OHA

COMPARISON OF FBS & PPBS AMONG CASES AND CONTROLS

	CASE	CONTROL
FBS	131.95	85.38
PPBS	212.7	122.85

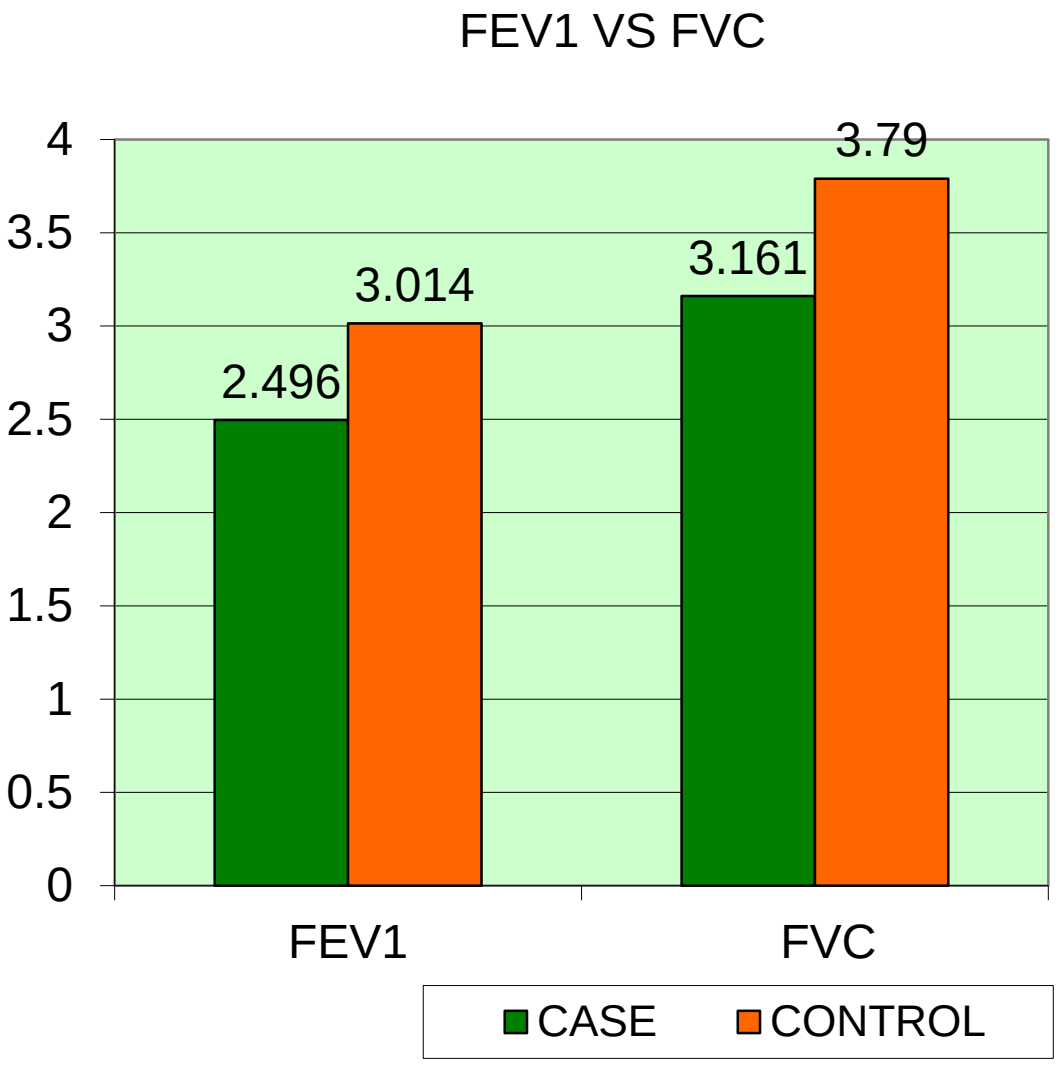
A comparison among the patients and controls were made by using FBS,PPBS was made,which showed our diabetics had sugar values in the range of diabetes as mentioned by American diabetes association. And our controls were healthy individuals with no abnormality in blood sugar values.


FBS AND PPBS COMPARISON
250
200
150
100
50
0
131.95
85.38
212.7
122.85
FBS
PPBS
CASE
CONTROL

COMPARISON OF FEV1 & FVC AMONG CASES AND CONTROLS

	CASE	CONTROL
FEV1	2.496	3.014
FVC	3.161	3.79

After comparing the FEV1 & FVC among the study and controls it was found that FEV1 was 2.496 when compared with 3.014 with controls for which the p value was <0.001 which is significant, FVC was 3.161among cases when compared with controls 3.79 which shows that there is reduction in FEV1 and FVC among diabetics when compared with non diabetics which was statistically significant.


FEV1 VS FVC
4
3.5
3
2.5
2
1.5
1
0.5
0
2.496
3.014
3.161
3.79
FEV1
FVC
CASE
CONTROL

COMPARISON OF FBS,PPBS,FEV1,FVC,FEV1/FVC,PEF AMONG CASES & CONTROLS

Comparison	CASE		CONTROL		P'Value
	Mean	SD	Mean	SD	
FBS	131.95	14.712	85.38	8.098	<0.001
PPBS	212.7	34.735	122.85	15.085	<0.001
FEV1	2.496	0.476	3.014	0.431	<0.001
FVC	3.161	0.568	3.79	0.603	<0.001
FEV1/FVC %	78.901	3.935	79.984	5.43	0.108
PEFR	486.74	73.569	535	72.744	<0.001

When a final comparison is made with all the pulmonary function tests and it is observed that FEV1,FVC,PEFR had significant reduction among diabetic patients and this was found to be statistically significant ($p<0.001$) . but FEV1/FVC was not significant ($p=0.108$) which needs to evaluated further .

COMPARISON OF FBS,PPBS,FEV1,FVC,FEV1/FVC,PEF AMONG DIFFERENT GROUPS OF DIABETIC PATIENTS

Duration of DM in years	<3		3 to <5		5 - 7		P	
	Mean	SD	Mean	SD	Mean	SD		
FBS	122.80	11.43	129.00	10.93	145.97	10.21	<0.001	Sig
PPBS	198.88	26.22	216.79	45.51	226.41	27.00	0.002	Sig
FEV1	2.65	0.48	2.65	0.39	2.17	0.39	<0.001	Sig
FVC	3.33	0.568	3.329	0.474	2.802	0.481	<0.001	Sig
FEV1/FVC %	79.531	4.174	79.563	3.789	77.533	3.494	0.057	Not Sig
PEF	509.9	75.681	480.679	75.683	463.094	61.543	0.022	Sig

On observing all the pulmonary function tests among three groups and it is observed that FEV1,FVC,PEFR had significant reduction among diabetic patients and this was found to be statistically significant ($p<0.001$). . but FEV1/FVC was not significant ($p=0.057$).

DISCUSSION

Diabetes is a multisystem disease . involvement of cardiac,renal,ocular systems are more extensively studied when compared to lung involvement. The cause of lung function has not been studied. There are no detailed proposed mechanisms for it .

Possible mechanisms are microvascular changes in lung tissue will lead to impairement in pulmonary functions. Few studies have shown that T2DM with microangiopathies show reduced diffusion capacity for carbon monoxide (DLCO).The study further suggested that hyperglycaemia and dyslipidaemia might have a contributory role in its pathogenesis.

In this study we found that diabetics had decreased lung volumes compared to normoglycemic subjects. FVC, FEV1,FVC/FEV1 & PEFR were statististically significantly lower in diabetic patients than in normal controls ($p<0.05$):

In the present study, two hundred patients with type 2 diabetes mellitus were taken, of which 100 patients are diabetic and 100 patients non diabetic. Pulmonary function tests was compared between these two groups, along with comparison of other parameters.

On analysing results, patients had significant impairment in FEV1 (2.496 in patients when compared with 3.014 with controls) for which the p value was <0.001 which is statistically significant.

This concludes have a significant reduction in the FEV1 when compared with the controls.

Also FVC was 3.161among cases when compared with controls 3.79 which also showed a statistically significant reduction.

Our results showed a similar results with schanek et al,ljubic et al.

Similar to our study Gregory L. Kinney et al have observed a moderate reduction in FVC,FEV1 and diffusing capacity for carbon monoxide of the lung in patients with type 1 and type 2 diabetes**.**

YehHC et al have suggested that pulmonary function test in middle aged non diabetic adult showed a restrictive pattern of lung pathology which is predictive of subsequent type 2 diabetes.

David et al studied 495 diabetic patients and recorded baseline values. A subset of 125 patients were studied after 7 years, who showed a significant reduction in the FEV1,FVC,PEFR .

Irfan et al studied 64 diabetic and 64 non diabetic patients and showed that diabetic patients had reductions in FEV1,FVC when compared with non diabetic controls. This result concurred with our result.

The FEV1/FVC % in our study was lower than normal and was found to have restrictive pattern. This is in concordance Boulbou et al ,Sultan et al, Sreeja et al, Fimognari et al, and Nakagima et al,

Studies of klein OL stated diabetics have reduced FVC more consistent than reduced FEV1 and our study had given similar results.

PEFR was also reduced in our study which was similar to Sreeja et al.

Among the groups A,B,C the pattern of restrictive PFT is more prominent as the duration advances FEV1(A=2.65 B=2.65 C=2.17) , FVC(A=3.33 B=3.33 =3.17) PEFR (A=509 B=480 C=463). So which gives the impression that restriction is more prominent as the disease duration advances.

Despite the reduction in FEV1&FVC, FEV1/FVC%(A=79.53 B=79.56 C=77.53) ratio declines but which is more than the predicted value. Davis et al had reported that FEV1% declines approximately about 1.5 % for each year of diabetes.

Kanya Kumari et al studied 125 patients and showed that type 2 diabetes patients have a restrictive pattern of PFT. And the restriction is more prominent as the duration of diabetes is prolonged which concurs with our study.

Anuradha et al, Kapoor et al also had similar results in their results.

Also patients had higher mean FBS(131),PPBS(212) than healthy controls FBS(85),PPBS(122). Interestingly patients with higher FBS,PPBS had more decrease in PFT values when compared with lower FBS,PPBS which was also statistically significant.

SUMMARY

- Mean FEV1 in our study is 2.496 litres/min which is reduced significantly than control ($p<0.001$)
- Mean FVC in our study is 3.161 which is reduced significantly ($p<0.001$)
- There is a restrictive pattern in diabetics when compared with the non diabetic controls of same age.
- FEV1,FVC,FEV1/FVC,PEFR are low in type -2 diabetic patients when compared to non diabetic patients.
- FEV1,FVC,PEFR reductions are statistically significant.
- FEV1/FVC% reduction is not statistically significant.
- The reductions of FEV1,FVC,PEFR are more as the duration of diabetes advances and these reductions are statistically significant($p<0.001$)
- The reduction in FEV1,FVC,PEFR are inversely co related to glycaemic control. Poor glycaemic control results in increased impairment of these parameters.

LIMITATIONS

- It is a single centre study so results are needed to be evaluated further.
- DLCO is not studied in this study,which is also an iimportant parameter in PFT
- Type 1 diabetics are not included.
- Period of study is short.

CONCLUSIONS

- Type-2 diabetic patients have reduced FEV1,FVC,PEFR when compared with non diabetics of same age .
- Type 2 diabetic patients have a restrictive pattern of pulmonary function tests even in the absence of any symptoms.
- This restrictive pattern is more prominent as the duration of diabetes is increased.
- Thus spirometry can be used as a simple investigation to study the pulmonary morbidity among the diabetics and to plan for an effective aggressive strategy in management of diabetes.
- Periodic monitoring of lung functions is nessacary in diabetics as spirometry is a cost effective, non-invasive tool.

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29. Assessment of pulmonary function in patients with type 2 diabetes mellitus: a case-control study

Dhiraj Kapoor1, Pankaj Kumar1*, Asha Ranjan1, Kailash Nath Sharma1, Varun Deep Dogra1, Rekha Bansal2, K. K. Sharma3, Dinesh Kumar4

30.A study of pulmonary function test in type-2 diabetes – A case control study Dr. Anuradha Yadav, Dr.A.k.Saxena, Dr.Kusum Gaur, Dr. Poonam Punjabi, Dr.Goverdhan Meena,

PROFORMA:

Name:

Age / Sex:

IP no:

Occupation:

Presenting complaints:

Past History:

H/o DM, HT, CVD,CAD,DRUG INTAKE, Thyroid disorders, malignancies pulmonary or extra pulmonary tuberculosis , CLD, COPD.

Duration of diabetes- (completed years)

Personal history

smoker/ nonsmoker

alcoholic/ non alcoholic

Family H/o COPD,Bronchial asthma

Treatment history

Oral hypoglycemic agents/ insulin

Clinical Examination:

General Examination

Consciousness, Pallor, jaundice, Clubbing, Lymphadenopathy,

Vitals:

PR

BP

RR

SpO2

Systemic examination:

CVS:

RS:

ABDOMEN:

CNS:

Laboratory investigations:

Complete hemogram

Renal function test

Liver function test

Sputum AFB, gram stain & culture

Chest x-ray PA view

Urine routine

FBS,PPBS

PULMONARY FUNCTION TESTS:

FEV1

FVC

FEV1/FVC%

PEFR

TREATMENT:

ABBREVATIONS

FBS	FASTING BLOOD SUGAR
PPBS	POST PRANDIAL BLOOD SUGAR
FEV1	FORCED EXPIRATORY VOLUME IN 1 SECOND
FVC	FORCED VITAL CAPACITY
PEFR	PEAK EXPIRATORY FLOW RATE
OHA	ORAL HYPOGLYCEMIC AGENTS
TLC	TOTAL LUNG CAPACITY;
VC	VITAL CAPACITY.
RV	RESIDUAL VOLUME
FRC	FUNCTIONAL RESIDUAL CAPACITY
IC	INSPIRATORY CAPACITY
EC	EXPIRATOY CAPACITY

					CONTROL			
S.NO	AGE	sex	FBS	PPBS	FEV1	FVC	FEV1/FVC	PEF
1	40	male	94	130	3.66	4.46	82.06	620
2	42	male	88	118	3.62	4.62	78.35	616
3	41	male	85	106	3.64	4.59	79.30	618
4	44	male	91	104	3.57	4.42	80.77	614
5	43	male	93	116	3.58	4.43	80.81	615
6	45	male	76	118	3.54	4.39	80.64	613
7	47	male	88	128	3.47	4.12	84.22	609
8	48	male	75	110	3.44	4.22	81.52	607
9	47	male	82	130	3.47	4.35	79.77	610
10	49	male	80	115	3.35	4.23	79.20	605
11	49	male	84	128	3.34	4.19	79.71	604
12	47	male	83	135	3.45	4.36	79.13	609
13	50	male	82	129	3.37	4.21	80.05	602
14	53	male	96	136	3.35	4.2	79.76	595
15	55	female	91	130	2.35	2.56	91.80	442
16	51	female	92	129	2.45	3.56	68.82	444
17	52	female	90	114	2.42	2.65	91.32	451
18	53	female	80	136	2.4	2.72	88.24	450
19	51	female	81	136	2.45	2.72	90.07	451
20	55	male	70	120	3.23	4.21	76.72	442
21	53	male	71	99	3.3	4.12	80.10	448
22	55	male	76	100	3.23	4.22	76.54	442
23	54	male	95	125	3.22	4.05	79.51	591
24	54	male	88	128	3.21	4.21	76.25	590
25	55	female	82	134	2.35	2.7	87.04	443
26	50	male	84	130	3.37	4.31	78.19	603
27	59	male	86	120	3.08	4.1	75.12	574
28	58	male	94	138	3.11	4.12	75.49	578
29	59	male	99	136	3.06	4.1	74.63	576
30	47	female	95	135	2.44	2.7	90.37	460
31	59	male	92	128	3.08	4.12	74.76	577
32	46	female	94	130	2.49	3.52	70.74	459
33	48	female	97	135	2.54	3.36	75.60	457
34	58	male	98	128	3.11	4.11	75.67	536
35	57	male	95	129	3.14	4	78.50	580
36	48	female	96	18	2.57	3.39	75.81	609
37	46	female	91	130	2.6	3.5	74.29	460
38	59	male	88	112	3.06	4.09	74.82	576
39	59	male	84	127	3.05	3.96	77.02	575
40	56	male	86	120	3.26	4.25	76.71	590
41	40	female	82	135	2.72	3.46	78.61	469
42	59	female	83	136	2.25	3	75.00	434

43	41	female	81	130	2.71	3.2	84.69	466
44	58	female	89	140	2.26	2.96	76.35	436
45	42	female	87	125	2.7	3.62	74.59	464
46	57	female	74	118	2.31	2.56	90.23	439
47	43	female	76	114	2.66	3.39	78.47	465
48	56	female	75	100	2.32	2.9	80.00	440
49	45	female	81	120	2.62	3.54	74.01	463
50	58	male	86	117	2.27	2.99	75.92	578
51	45	male	79	104	3.54	4.4	80.45	613
52	40	female	83	131	2.73	3.6	75.83	467
53	44	male	70	121	3.52	4.45	79.10	615
54	41	female	79	124	2.69	3.45	77.97	465
55	43	male	88	122	3.6	4.62	77.92	615
56	42	female	91	129	2.67	3.32	80.42	463
57	44	male	94	138	3.51	4.29	81.82	610
58	43	female	96	135	2.67	3.39	78.76	464
59	45	male	81	125	3.53	4.41	80.05	613
60	45	female	72	135	2.63	3.32	79.22	463
61	41	male	86	119	3.65	4.45	82.02	619
62	50	male	75	105	3.39	4.12	82.28	603
63	46	female	99	139	2.49	3.41	73.02	459
64	49	male	92	129	3.35	4.09	81.91	605
65	47	female	78	100	2.46	2.56	96.09	459
66	48	male	84	130	3.44	4.21	81.71	603
67	48	female	83	120	2.53	3.42	73.98	459
68	47	male	91	115	3.46	4.16	83.17	610
69	49	female	72	105	2.49	3.35	74.33	456
70	46	male	77	120	3.49	4.26	81.92	610
71	48	female	76	115	2.41	2.59	93.05	458
72	47	male	95	129	3.46	4.2	82.38	609
73	51	male	91	130	3.35	4.12	81.31	600
74	52	female	98	136	2.42	2.56	94.53	451
75	52	male	87	134	3.33	4.12	80.83	597
76	54	female	86	125	2.33	2.56	91.02	446
77	55	male	84	120	3.23	4.12	78.40	588
78	53	female	95	135	3.3	4.12	80.10	448
79	51	male	76	114	3.36	4.1	81.95	600
80	52	female	77	112	2.42	2.56	94.53	451
81	52	male	71	111	3.33	4.2	79.29	597
82	54	female	96	136	2.37	2.96	80.07	444
83	55	male	94	139	3.23	4.05	79.75	589
84	51	male	96	136	3.36	4.21	79.81	599
85	53	female	93	124	2.41	2.54	94.88	446
86	55	male	82	122	3.23	3.96	81.57	587
87	56	female	88	125	3.2	4.2	76.19	441

88	57	female	84	121	3.16	4.09	77.26	439
89	58	female	86	124	3.13	4.05	77.28	436
90	60	female	65	129	3.06	4	76.50	431
91	56	male	84	135	3.21	4.12	77.91	585
92	56	male	95	140	3.3	4.12	80.10	584
93	57	male	92	130	3.15	4.09	77.02	579
94	57	male	76	103	3.16	4.12	76.70	580
95	58	male	69	124	3.1	4.12	75.24	577
96	58	male	84	110	3.09	3.96	78.03	579
97	59	male	75	100	3.07	4.1	74.88	576
98	59	male	84	120	3.05	3.98	76.63	571
99	60	male	89	132	3.04	3.96	76.77	572
100	60	male	94	123	3.05	4.06	75.12	574

					CASE						
S.NO	AGE	sex	Duration of DM	group	FBS	PPBS	FEV1	FVC	FEV1/FVC	PEF	TREATMENT
1	40	male	1	A	104	165	3.36	3.96	84.85	590	INSULIN
2	42	male	2	A	112	185	3.26	3.99	81.70	583	OHA
3	41	male	1	A	125	199	3.35	3.59	93.31	588	INSULIN
4	44	male	2	A	116	155	3.21	4.02	79.85	579	OHA
5	43	male	1	A	120	187	3.3	4.12	80.10	584	OHA
6	45	male	1	A	125	199	3.24	4.08	79.41	585	OHA
7	47	male	2	A	136	212	3.16	4.26	74.18	575	OHA
8	48	male	2	A	133	222	3.12	4.02	77.61	572	OHA
9	47	male	1	A	125	200	3.15	3.96	79.55	579	INSULIN
10	49	male	2	A	138	240	3.03	3.78	80.16	570	OHA
11	49	male	1	A	139	210	3.08	3.85	80.00	575	OHA
12	47	male	2	A	126	188	3.12	3.95	78.99	574	INSULIN
13	50	male	4	B	145	255	2.72	3.4	80.00	548	OHA
14	53	male	4	B	135	198	2.61	3.36	77.68	540	OHA
15	55	female	1	A	140	177	2.05	2.54	80.71	412	INSULIN
16	51	female	1	A	128	195	2.15	2.62	82.06	421	OHA
17	52	female	2	A	130	210	2.07	2.45	84.49	414	OHA

18	53	female	2	A	132	200	2.05	2.5	82.00	413	OHA
19	51	female	2	A	140	231	2.09	2.9	72.07	416	OHA
20	55	male	4	B	138	210	2.88	3.65	78.90	387	OHA
21	53	male	4	B	136	236	2.95	3.45	85.51	540	OHA
22	55	male	3	B	140	289	2.88	3.66	78.69	538	OHA
23	54	male	3	B	133	298	2.92	3.49	83.67	541	INSULIN
24	54	male	3	B	136	312	2.92	3.42	85.38	541	OHA
25	55	female	2	A	128	200	3.05	3.76	81.12	407	OHA
26	50	male	3	B	132	165	3.02	3.85	78.44	552	OHA
27	59	male	7	C	144	254	2.42	3.02	80.13	505	OHA
28	58	male	6	C	140	203	2.47	3.35	73.73	508	OHA
29	59	male	6	C	142	266	2.42	3.11	77.81	504	OHA
30	47	female	1	A	124	188	2.34	2.95	79.32	430	OHA
31	59	male	5	C	135	250	2.43	2.98	81.54	515	OHA
32	46	female	2	A	130	199	2.3	2.86	80.42	575	OHA
33	48	female	3	B	130	210	2.18	2.66	81.95	407	OHA
34	58	male	6	C	135	165	2.48	3.15	78.73	508	INSULIN
35	57	male	6	C	140	200	2.47	2.99	82.61	510	OHA
36	48	female	4	B	120	185	2.18	2.85	76.49	402	INSULIN
37	46	female	3	B	112	174	2.25	2.85	78.95	414	INSULIN
38	59	male	7	C	145	220	1.68	2.11	79.62	500	OHA
39	59	male	7	C	140	210	1.69	2.15	78.60	500	OHA
40	56	male	7	C	150	265	1.66	2.15	77.21	515	OHA
41	40	female	4	B	125	186	2.37	2.92	81.16	419	INSULIN
42	59	female	3	B	120	188	2.63	3.28	80.18	383	OHA
43	41	female	4	B	130	200	2.34	2.87	81.53	410	INSULIN
44	58	female	5	C	135	210	1.62	2.09	77.51	371	OHA
45	42	female	6	C	140	230	2.02	2.64	76.52	401	INSULIN
46	57	female	7	C	142	245	1.64	2.11	77.73	372	OHA
47	43	female	5	C	132	205	2.01	2.59	77.61	399	OHA
48	56	female	7	C	146	210	1.67	2.12	78.77	370	OHA
49	45	female	6	C	150	225	2.03	2.46	82.52	402	OHA

50	58	male	7	C	135	215	2.38	3.2	74.38	508	OHA
51	45	male	1	A	100	166	2.32	2.9	80.00	585	OHA
52	40	female	2	A	110	175	2.42	3.02	80.13	436	OHA
53	44	male	2	A	115	180	3.25	4.08	79.66	425	OHA
54	41	female	2	A	112	195	2.39	3.26	73.31	430	INSULIN
55	43	male	3	B	90	150	3.25	4.13	78.69	564	OHA
56	42	female	2	A	124	175	2.39	3.36	71.13	430	OHA
57	44	male	4	B	115	175	3.16	4	79.00	559	OHA
58	43	female	1	A	120	195	2.37	3.12	75.96	430	OHA
59	45	male	3	B	130	300	3.19	4.32	73.84	563	OHA
60	45	female	1	A	112	201	2.32	3.12	74.36	432	OHA
61	41	male	4	B	120	192	2.35	3.2	73.44	563	INSULIN
62	50	male	4	B	140	230	2.12	2.9	73.10	548	OHA
63	46	female	1	A	130	215	2.3	3.12	73.72	431	OHA
64	49	male	1	A	115	195	2.19	2.95	74.24	424	OHA
65	47	female	2	A	125	205	2.28	3	76.00	424	OHA
66	48	male	2	A	122	199	2.24	2.8	80.00	572	OHA
67	48	female	1	A	110	185	2.24	2.72	82.35	427	OHA
68	47	male	2	A	115	196	2.27	2.7	84.07	574	OHA
69	49	female	3	B	125	186	2.14	2.7	79.26	420	OHA
70	46	male	2	A	126	305	2.3	2.95	77.97	575	OHA
71	48	female	4	B	135	145	2.19	2.92	75.00	402	INSULIN
72	47	male	4	B	136	255	2.22	2.85	77.89	554	INSULIN
73	51	male	2	A	120	195	2.15	2.75	78.18	565	OHA
74	52	female	3	B	126	245	2.07	2.6	79.62	400	OHA
75	52	male	2	A	120	215	3.08	3.8	81.05	563	OHA
76	54	female	4	B	135	210	2.61	3.3	79.09	389	INSULIN
77	55	male	2	A	110	220	2.93	3.45	84.93	553	OHA
78	53	female	4	B	128	180	2.96	3.36	88.10	393	OHA
79	51	male	4	B	136	236	3.03	3.75	80.80	545	OHA
80	52	female	4	B	130	250	2.98	3.46	86.13	395	OHA
81	52	male	4	B	134	210	3.01	4	75.25	542	INSULIN
82	54	female	6	C	160	240	1.68	2.2	76.36	374	OHA

83	55	male	6	C	155	221	2.58	3.36	76.79	518	OHA
84	51	male	2	A	135	201	3.06	3.98	76.88	565	OHA
85	53	female	5	C	144	225	2.66	3.55	74.93	383	OHA
86	55	male	1	A	145	230	2.93	3.45	84.93	558	OHA
87	56	female	5	C	152	245	2.6	3.41	76.25	375	OHA
88	57	female	6	C	160	275	1.64	2.31	71.00	373	OHA
89	58	female	7	C	165	246	1.6	2.41	66.39	466	INSULIN
90	60	female	7	C	180	275	1.57	2.12	74.06	370	OHA
91	56	male	1	A	95	145	2.02	2.51	80.48	555	OHA
92	56	male	5	C	140	196	2.55	3.12	81.73	520	INSULIN
93	57	male	6	C	150	220	2.51	3.02	83.11	515	OHA
94	57	male	7	C	156	230	2.5	3.16	79.11	510	INSULIN
95	58	male	5	C	145	199	2.48	3.02	82.12	513	INSULIN
96	58	male	6	C	140	210	2.45	3.12	78.53	508	INSULIN
97	59	male	7	C	138	205	2.42	3.12	77.56	504	INSULIN
98	59	male	5	C	140	185	2.43	3.23	75.23	498	OHA
99	60	male	7	C	145	235	2.4	3.12	76.92	502	OHA
100	60	male	7	C	150	265	2.4	3.16	75.95	502	OHA

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Chennai, Tamil Nadu)

ETHICS COMMITTEE CERTIFICATE

Name of the Candidate	:	Dr.Sreekumar . P.S
Course	:	PG in MD., General Medicine
Period of Study	:	2014-2017
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	A study on pulmonary function test in diabetes mellitus and its correlation with duration of diabetes mellitus
Ethical Committee as on	:	27.07.2016

The Ethics Committee, Madurai Medical College has decided to inform that your Research proposal is accepted.

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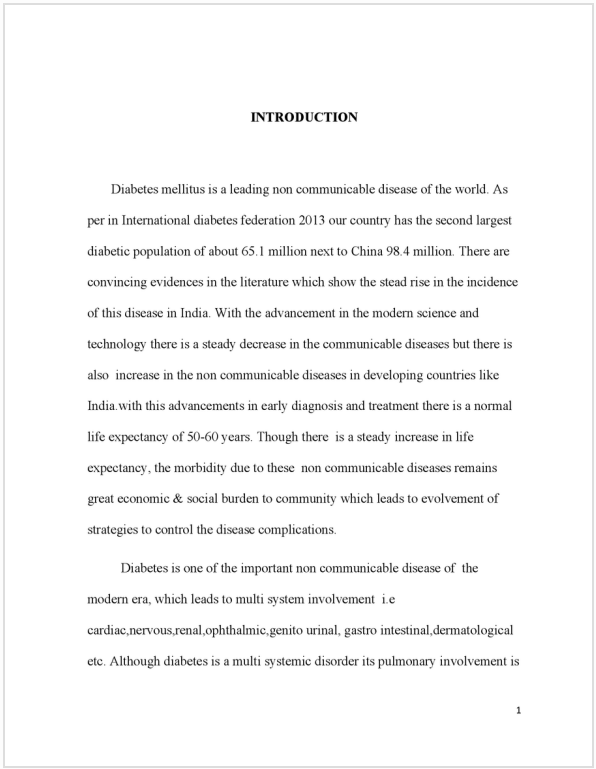

INTRODUCTION

Diabetes mellitus is a leading non communicable disease of the world. As per in International diabetes federation 2013 our country has the second largest diabetic population of about 65.1 million next to China 98.4 million. There are convincing evidences in the literature which show the stead rise in the incidence of this disease in India. With the advancement in the modern science and technology there is a steady decrease in the communicable diseases but there is also increase in the non communicable diseases in developing countries like India.with this advancements in early diagnosis and treatment there is a normal life expectancy of 50-60 years. Though there is a steady increase in life expectancy, the morbidity due to these non communicable diseases remains great economic & social burden to community which leads to evolvement of strategies to control the disease complications.

Diabetes is one of the important non communicable disease of the modern era, which leads to multi system involvement i.e cardiac,nervous,renal,ophthalmic,genito urinal, gastro intestinal,dermatological etc. Although diabetes is a multi systemic disorder its pulmonary involvement is

1

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