TO STUDY THE PREVALENCE OF RENAL FUNCTION DEFECTS IN COPD PATIENTS USING CREATININE CLEARANCE AND URINE PROTEIN ANALYSIS

Dissertation submitted to The Tamil Nadu Dr. M.G.R. Medical University in partial fulfilment of the requirements for the degree of

Doctor of Medicine (M.D) in Tuberculosis and Respiratory Diseases Branch – XVII

GOVERNMENT KILPAUK MEDICAL COLLEGE & HOSPITAL.
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BONAFIDE CERTIFICATE

This is to certify that the dissertation “To study the prevalence of renal function defects in COPD patients using creatinine clearance and urine protein analysis” is the Bonafide work done by **Dr.R.Vignesshkanth** during his **MD (Tuberculosis and Respiratory Diseases)** course from May 2017 to May 2020 at Government Kilpauk Medical College, Chennai.

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I**, Dr. R.Vignesshkanth ,** solemnly declare that the dissertation titled " To study the prevalence of renal function defects in COPD patients using creatinine clearance and urine protein analysis **"** has been prepared by me. This is submitted to "**The Tamil Nadu Dr. M.G.R. Medical University, Chennai"** in partial fulfilment of the requirement for the award of M.D degree examination branch XVII **Tuberculosis and Respiratory Diseases** from May 2017 to May 2020 .

Place: CHENNAI **(**Dr. R.VIGNESSHKANTH)

Date: Signature of the candidate

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INTRODUCTION

DEFINITION :

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

• The most common respiratory symptoms include dyspnea, cough and/or sputum production. These symptoms may be under-reported by patients.

• The main risk factor for COPD is tobacco smoking but other environmental exposures such as biomass fuel exposure and air pollution may contribute. Besides exposures, host factors predispose individuals to develop COPD. These include genetic abnormalities, abnormal lung development and accelerated aging .

• COPD may be punctuated by periods of acute worsening of respiratory symptoms, called exacerbations.

• In most patients, COPD is associated with significant concomitant chronic diseases, which increase its morbidity and mortality.

The chronic airflow limitation that is characteristic of COPD is caused by a mixture of small airways disease (e.g., obstructive bronchiolitis) and parenchymal destruction (emphysema), the relative contributions of which vary from person to person (. These changes do not always occur together, but evolve at different rates over time. Chronic inflammation causes structural

changes, narrowing of the small airways and destruction of the lung parenchyma that leads to the loss of alveolar attachments to the small airways and decreases lung elastic recoil. In turn, these changes diminish the ability of the airways to remain open during expiration. A loss of small airways may also contribute to airflow limitation and mucociliary dysfunction is a characteristic feature of the disease. Airflow limitation is usually measured by spirometry as this is the most widely available and reproducible test of lung function. Many previous definitions of COPD have emphasized the terms “emphysema” and “chronic bronchitis”, which are not included in the definition used in this or earlier GOLD reports. Emphysema, or destruction of the gas-exchanging surfaces of the lung (alveoli), is a pathological term that is often (but incorrectly) used clinically and describes only one of several structural abnormalities present in patients with COPD. Chronic bronchitis, or the presence of cough and sputum production for at least 3 months in each of two consecutive years, remains a clinically and epidemiologically useful term, but is present in only a minority of subjects when this definition is used. However, when alternative definitions are used to define chronic bronchitis, or older populations with greater levels of smoke or occupational inhalant exposure are queried, the prevalence of chronic bronchitis is greater.1,2 It is important to recognize that chronic respiratory symptoms may precede the development of airflow limitation and may be associated with the development of acute respiratory events.3 Chronic respiratory symptoms also exist in individuals with normal spirometry3,4 and a significant number of smokers without

airflow limitation have structural evidence of lung disease manifested by the varying presence of emphysema, airway wall thickening and gas trapping.

SYMPTOMS OF COPD :

Shortness of breath

Cough with expectoration

Wheeze

Chest tightness

Fatigue, weight loss and anorexia

Cough syncope

Rib fractures

Depression / anxiety

Ankle swelling – Cor Pulmonale

All symptoms mentioned above are common manifesting symptoms of COPD .

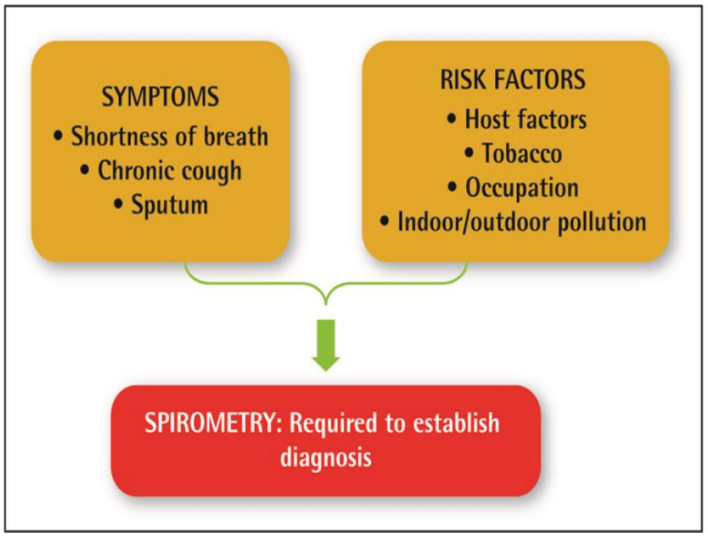
BURDEN OF COPD :

COPD is a leading cause of morbidity and mortality worldwide that induces an economic and social burden that is both substantial and increasing.(5,6) COPD prevalence, morbidity and mortality vary across countries and across different groups within countries. COPD is the result of a complex interplay of long-term cumulative exposure to noxious gases and particles, combined with a variety of host factors including genetics, airway hyper-responsiveness and poor lung growth during childhood.(7-9) Often, the prevalence of COPD is

directly related to the prevalence of tobacco smoking, although in many countries outdoor, occupational and indoor air pollution (resulting from the burning of wood and other biomass fuels) are major COPD risk factors.(10,11) The prevalence and burden of COPD are projected to increase over the coming decades due to continued exposure to COPD risk factors and aging of the world's population; as longevity increases more people will express the long-term effects of exposure to COPD risk factors.(12) Information on the burden of COPD can be found on international websites, for example the:

- World Health Organization (WHO)(13)
- World Bank/WHO Global Burden of Disease Study(14)

Figure 2.1. Pathways to the diagnosis of COPD



A detailed medical history of a new patient who is known, or suspected, to have COPD should include:

• Patient's exposure to risk factors, such as smoking and occupational or environmental exposures.

• Past medical history, including asthma, allergy, sinusitis, or nasal polyps; respiratory infections in childhood; other chronic respiratory and non-respiratory diseases.

• Family history of COPD or other chronic respiratory disease.

• Pattern of symptom development: COPD typically develops in adult life and most patients are conscious of increased breathlessness, more frequent or prolonged "winter colds," and some social restriction for a number of years before seeking medical help.

• History of exacerbations or previous hospitalizations for respiratory disorder. Patients may be aware of periodic worsening of symptoms even if these episodes have not been identified as exacerbations of COPD.

• Presence of comorbidities, such as heart disease, osteoporosis, musculoskeletal disorders, and malignancies that may also contribute to restriction of activity.

• Impact of disease on patient's life, including limitation of activity, missed work and economic impact, effect on family routines, feelings of depression or anxiety, well-being and sexual activity.

• Social and family support available to the patient.

• Possibilities for reducing risk factors, especially smoking cessation.

Figure 2.2A. Spirometry - Normal Trace

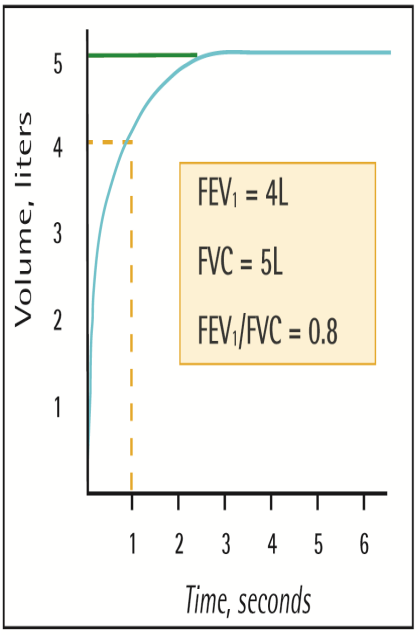
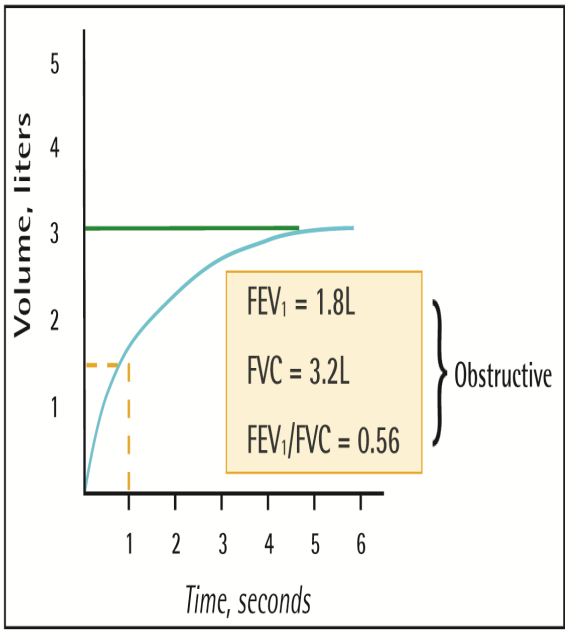


Figure 2.2B. Spirometry - Obstructive Disease



FVC =

FEV_1 =

Table 2.4. Classification of airflow limitation severity in COPD (Based on post-bronchodilator FEV_1)		
In patients with $FEV_1/FVC < 0.70$:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

RISK FACTORS OF COPD:

COPD results from a complex interaction between genes and environment. Though cigarette smoking is the commonest risk factor, there are evidences that non-smokers may also develop COPD.

Exposure to Particles:

Cigarette smoking is the commonest risk factor for COPD. Other types of tobacco such as pipe, cigar [15] are also risk factors of COPD. Passive exposure to cigarette smoke is also known an Environmental Tobacco Smoke (ETS), is also a known risk factor for COPD. Occupational exposure, indoor and outdoor air pollution are other risk factors of COPD.

A Swedish cohort study [16] reported that population attributable risk for development of COPD in smokers is 76.2% . In India most of the smokers are using bidi for smoking than cigarette [17]. Ventilatory function deterioration is common among smokers than non-smokers.

In males, the average decline in FEV1 is around 9 ml per year for each pack-year of smoking. In females the average decline in FEV1 is approximately around 6 ml per year for each pack-year of smoking. Eventhough tobacco content is low in bidi, bidi smokers are more vulnerable to develop COPD than cigarette smokers [18].

Risk of COPD is proportional to the number of cigarettes or bidis smoked per day. Risk also increases with the duration of smoking. The risks are lower at a lower dose and lesser duration of smoking .The Lung Health Study, stated that there is an accelerated decline in FEV1 in COPD patients if they continue smoking.

Chronic inhalation of particles and the gases carry a greater risk for developing COPD. But we are not able to estimate the correct prevalence of COPD among workers because most of the workers are also smokers and those with COPD drop out from work. The American Thoracic Society states that 15% of COPD cases are due to occupational exposure.

People working in rubber industry, plastic industry and leather industry are at increased risk of COPD[19] Also, people who work in textile mills and food product manufacturing unit are also at increased risk[20].

In developing countries like India, especially in an urban population, outdoor air pollution has been implicated as a cause for COPD and various other respiratory diseases [21]. It is due to the pollutants from industries and motor vehicles causing pathological changes in the lung and airway. A prior study observed that higher traffic density is associated with increased risk of COPD in women population. These pollutants are known to cause bronchial hyperactivity, airway oxidative stress, pulmonary and systemic inflammation [22].

Biomass fuel is obtained from the combustion of wood, dried dung, and crop residue. Exposure to biomass fuel is an important source of indoor air pollution. It is an important cause of COPD among the women population, especially in rural India. Combustion of biomass fuel especially in closed spaces results in the inhalation of the toxic gases which contributes to the development of COPD. The risk of COPD among women in urban population is less when compared to women in rural areas. This is because women in rural areas frequently use biomass fuel whereas women in urban areas use LPG as fuel for cooking purposes.

Genetic factors:

The genetic factor that is documented is a hereditary deficiency of alpha 1 antitrypsin (AATD) [23], a major inhibitor of serine proteases. It illustrates the interaction between the gene and the environmental exposures that

predispose an individual to Chronic Obstructive Pulmonary Disease.

Gene encoding for the matrix metalloproteinase 12 (MMP12) was related to decline in lung function . AATD accounts for approximately 1-2% of total cases of COPD. Conditions suggesting alpha 1 anti-trypsin deficiency are:

- Early onset emphysema (age less than 45 years).
- Emphysema in a non-smoker.
- Emphysema predominantly in lung bases.
- Family history of early onset emphysema or non-smoking related emphysema.
- Bronchiectasis without any other etiology [2]

Age and Gender :

Age is often listed as a risk factor for development of COPD. Aging of the airway and lung parenchyma may resemble some of the changes associated with COPD.

In earlier days, COPD prevalence and mortality were greater in men, but recent data from developed countries has reported that the prevalence of COPD is almost equal among both the sexes, this could be due to changing trends in tobacco smoking.

Childhood lower respiratory tract infection:

Ventilatory function in an adult depends upon the lung function in their childhood. Hence, the respiratory tract infections that occurred during childhood can affect the lung development and tend to increase the risk of developing COPD later [24].

Airway Hyperresponsiveness:

In COPD, airway hyper-responsiveness is often associated with an accelerated decline in FEV1.However airway hyper-responsiveness does not predict bronchodilator responsiveness.

Socioeconomic status:

Lower socioeconomic status is one of the factor associated with increased risk of COPD. This is because, an increased amount of smoking is seen in people with low socioeconomic status.

PATHOGENESIS:

Inflammation:

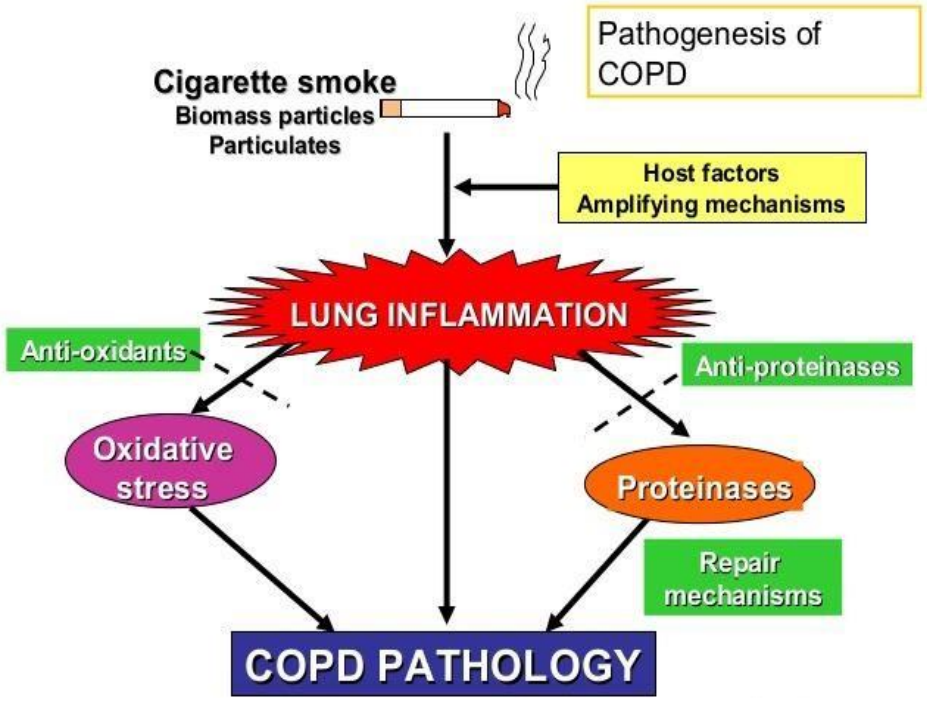
Inflammation of the lower respiratory tract has an important role in the pathogenesis of COPD. Following the exposure to tobacco smoke and other inhaled particles, there is a recruitment of inflammatory cells in the lungs and airways. Inflammatory cells seen are neutrophils, macrophages, eosinophils and lymphocytes. They cause lung injury and disrupt the normal mechanism of

lung repair. Bronchoalveolar lavage (BAL) fluid collected from smokers show more macrophages when compared to non-smokers[15]

Proteinase and Antiprotease Imbalance:

In COPD, there is an imbalance between the production of proteinase and antiproteinase. Major proteinase that affects the lung parenchyma are neutrophil elastase, Proteinase 3, cathepsin B, cathepsin S, cathepsin L, MMP (Matrix Metalloproteinase).Some of the antiproteinases are alpha 1 antitrypsin, Matrix metalloproteinase inhibitors, alpha 2 macroglobulin, Secretory leukocyte protease inhibitor(SLPI), Elafin and cystatin C. Neutrophil elastase causes parenchymal destruction, hyperplasia of mucous glands and induces mucus hypersecretion.

Fig: Overview of COPD pathology



Oxidative Stress :

Cigarette smoke contains many chemicals that are reactive oxidant species. Also, the inflammation caused itself generates oxygen-free radicals leading to tissue destruction. In vitro study done by Schaberg et al showed that alveolar macrophages and airway neutrophils generate more oxygen free radicals such as hydrogen peroxide, hydroxyl radicals, and superoxide radicals in smokers than non-smokers.

Oxidative stress causes the damage of the extracellular matrix and inactivation of key anti-oxidant defences. Antioxidants generally protects against oxidative injury. Superoxide dismutase, Catalase, and glutathione peroxidase are some of the antioxidants that protects against oxidation injury. Copper and zinc dependent superoxide dismutase are found in cytoplasm and manganese dependent superoxide dismutase is found in mitochondria.

There can also be reduction of endogenous antioxidants in COPD, due to reduction in the levels of the transcription factor Nrf2 regulates many of the antioxidant genes.

Vitamin A and Vitamin E are present in epithelial lining fluid and act as antioxidants[15].

COPD AND IT'S COMORBIDITIES:

COPD is a multisystem disorder with inflammation at its peak leading on to high mortality. The extent of the inflammation directly correlates with the severity of the disease.

Extrapulmonary comorbidities has additional influence on the prognostic outcomes of the patients with COPD. Smoking is a common risk factor for many other associated comorbidities including coronary heart disease, heart failure and lung cancer(25).

Various comorbidities associated with COPD include Pulmonary hypertension , Malnutrition , Coronary artery disease , Heart failure, Lung cancer ,Systemic venous thromboembolism ,Peripheral muscle wasting, Anxiety & depression, Osteoporosis , Metabolic syndrome , Diabetes and hypertension, Sleep disturbances , OSA Peripheral vascular diseases and Cognitive impairment .

Renal dysfunctions associated with COPD is mostly under studied. It could be a part of systemic inflammation or it could be due to the common risk factors associated with both the conditions such as age and tobacco use.

The probable mechanisms involved in the pathogenesis may include vascular cause , persistent hypercapnia and chronic hypoxia that drives the development of renal dysfunction.

INFLAMMATORY RESPONSES IN COPD :

Chronic obstructive pulmonary disease is characterised by chronic inflammation involving the large airways , small airways and the alveolar wall . The extent of the inflammation correlates directly to the severity of the disease.

The increase in inflammatory mediators in COPD has been thought be a part of "spill over" of the inflammatory mediators from the pulmonary compartment which is mainly responsible for the inflammation present in the systemic circulation. The role of the spill over hypothesis has been further emphasized in many other researches by observing the association between the inflammatory mediators and pulmonary tissue-derived proteins.

The probable mechanism proposed in spill over hypothesis are(27) :

The production of of reactive oxygen species and stress induced cytokines and their leakage into systemic circulation. Already activated peripheral blood leukocytes that can result in aberrant recruitment and activation of inflammatory cells. Liberation of proinflammatory cytokines by parenchymal cells and leucocytes present in the pulmonary tissues during the course of the disease.

The intensity of the inflammation in the systemic circulation is directly proportional to the decreased quality of life, degree of airflow obstruction and exercise limitation observed in COPD.(16) COPD can lead to low grade

systemic inflammation due to hypoxia and various other mechanisms and systemic inflammation in turn show response that adversely affect the clinical and functional outcomes of COPD.

The various counterparts that take part in systemic inflammation are:

Cytokines :

Interleukin-6:

Interleukin (IL)-6 is an important cytokine that increases in the systemic circulation of patients with COPD during exacerbations and it mainly account for the increase in acute phase reactants such as C-reactive protein (CRP) found in patients with COPD as it induces the release of acute phase proteins from the liver [32]. The effects of circulating IL-6, apart from increasing acute phase proteins, are not certain but there is evidence that it is associated with weakness of the skeletal muscles.

In an elderly population with or without airway obstruction, plasma IL-6 levels are directly related to decreased muscle strength as measured by quadriceps strength and exercise capacity [33]. In rats, infusion of IL-6 can cause both cardiac failure and skeletal muscle weakness [34]. Increased levels of IL-6 concentrations are found in several other comorbid diseases.

Tumour necrosis factor -α:

Plasma tumour necrosis factor (TNF)-alpha along with its soluble receptor are increased in COPD patients [35-37] and is more commonly seen in COPD patients with cachexia[38]. Circulating TNF-alpha in part appears to be related to hypoxia [39]. Increased systemic TNF- alpha has been identified as a mechanism of cachexia, skeletal muscle atrophy and weakness in COPD patients. Chronic administration of TNF-alpha in animals results in anemia , leukocytosis , weight loss and organ infiltration of neutrophils into the heart, liver and spleen[40].

IL-1 β:

Although there is an association between COPD and a polymorphism of the IL-1b gene [37], increased plasma levels or decreased levels of its endogenous antagonist IL-1 receptor antagonist have not been found in COPD . IL-1Beta is said to be associated with cachexia , but lacks evidence in COPD .

Chemokines:

In COPD patients , CXCL8 (IL-8) and CXC chemokines play an important role in neutrophil and monocyte recruitment . CXCL8 concentrations are found to be high in COPD patients which contributes to skeletal muscle weakness [41].

Adipokines:

Leptin is an adipokine derived from adipose cells that plays a vital role in energy homeostasis . In COPD patients, plasma concentrations of adipokines tend to be lower and diurnal variation is lost [37], but its role in cachexia is not clear. In contrast , circulating levels of ghrelin, a GHRP (growth hormone-releasing peptide) that is involved in improving appetite , is elevated in cachectic COPD patients

ACUTE PHASE PROTEINS :

CRP:

CRP is an acute phase reactant , which is increased in the systemic circulation of patients with COPD along with IL-6 , mainly during exacerbations. In stable COPD patients, plasma concentrations of CRP are related to mortality in mild to moderate patients, which is not a case in severe and very severe COPD patients . Increased CRP is also related to functional performance and exercise tolerance and is an important predictor of body mass index (BMI)[35].Though CRP is said to be related to forced expiratory volume in one second (FEV1) in cross-sectional studies, there lies no association with the gradual decline of FEV1 and CRP in longitudinal studies . CRP is increased in COPD acute exacerbations due to viral or bacterial causes and a increased concentration of CRP measured 2 weeks post exacerbation predicts the likelihood of further exacerbation [42].

Increased C-Reactive Protein levels and the incidence of cardiovascular risk associated with it has suggested that there could be an association between COPD and the increased prevalence of cardiovascular disease among COPD patients , but this relationship is confounded by some common risk factors, such as smoking. The functional role of CRP is uncertain. CRP leads to activation of the complement, resulting in endothelial damage and further tissue inflammation. 1, 6-bis(phosphocholine)- hexane, a pentameric protein , an inhibitor of CRP neutralises the effects of CRP in animal models and therefore considered cardioprotective . A recent study in mice shown that transgenic overexpression of human CRP was neither pro-inflammatory nor pro-atherogenic , making the role of CRP as an inflammatory agent questionable . But some other studies present with evidence to suggest that CRP may play a vital role in innate immunity against Streptococcal pneumoniae, so that inhibiting CRP could have detrimental effects, since this organism colonises the lower airways of these most COPD patients [43].

Fibrinogen:

Fibrinogen levels were increased in patients with recurrent exacerbations. Elevated plasma fibrinogen levels in a population is associated with low FEV1 and an increased risk of further episodes of exacerbation in COPD [44] patients .

Serum amyloid A:

Circulating pro-inflammatory cytokines from the liver are the main sources secreting SAA . But unlike CRP, it is also secreted from inflamed tissue. SAA concentrations are proportionate with the severity of COPD and are predictors of further exacerbations. SA-A acts as a part of the innate immune system by binding with gram negative organisms and iniating immune responses against bacterial infections, but it also has pro inflammatory action like activation of monocytes, neutrophils and T-helper cell (Th) type . It has recently been discovered that SA-A is an activates Toll-like receptor (TLR)2 and resulting in activation of the transcription factor nuclear factor (NF)-kB [45].

Surfactant protein D:

Surfactant protein (SP)-D is a glycoprotein that belongs to collectin family and is secreted by type II pneumocytes and plays a significant role in innate immune response against microorganisms. Serum Surfactant protein (SP)-D levels are raised in COPD patients . They are related to severity of the disease and symptoms and are more sensitive than C-Reactive Protein [46]. As Surfactant protein -D is secreted mainly from peripheral lung tissue, it provides a significant evidence that pulmonary inflammation can lead on to inflammatory changes in the systemic circulation rather than vice versa.

COPD AND ITS IMPACT ON RENAL FUNCTION :

It is largely unexplored to which extent COPD has its effect on renal functions.

COPD patients present with low muscular mass , which are the sources of creatinine . hence creatinine values measured may be low . In such patients , in case of CRF chronic renal failure the estimated creatinine levels may be low or normal , a condition referred as concealed renal failure .

The relationship between COPD and CRF may be explained by the various factors as follows :

- Increase in adrenergic discharge secondary to CO2 retention
- Increased adrenergic discharge leading to increased renal arteriolar resistance
- Increased PaCO2 is inversely related to renal blood flow , hence in COPD with increased co2 , renal blood flow is reduced
- Increased PaCO2 is related to sodium and water retention
- Direct and indirect effect (sympathetic stimulation) of co2 causing constriction of renal blood vessels (77-78).
- Nicotine induced nephropathy (79)
- Other heavy metals like cadmium and lead contributing to renal dysfunction

COPD is no more a disease confined to the respiratory system alone . The systemic inflammatory mediators released contribute various other comorbidities such as coronary artery disease , Heart failure, Lung cancer , Systemic venous thromboembolism ,Peripheral muscle wasting, Anxiety & depression, Osteoporosis , Metabolic syndrome , Diabetes hypertension, Sleep disturbances , OSA Peripheral vascular diseases and Cognitive impairment . These inflammatory mediators may also contribute to the association between CRF AND COPD (80) .

Pulmonary hypertension developing secondary to COPD is involved in the progression of kidney disease .

Coronary artery disease associated with vascular dysfunction may lead to the development of chronic kidney disease .

HYPOXIC RESPONSE MECHANISMS IN RENAL TISSUE :

About 20% of cardiac output goes to the kidney , but o2 tension measured were low and in narrow range 5mmHg (47) , because most o2 is consumed by Na+K+Atpase pump . Renal o2 consumption increases with increased RBF . Hence renal PO2 cannot be raised by increasing RBF and it always lie in a narrow range . PO2 in renal vessels is maintained by A-V O2 shunt resulting from exchange of o2 between arterial and venous circulation before entry into microcirculation (48).

Because of narrow range of PO2 , susceptibility to hypoxic injury is more in renal tissues particularly renal medulla . To compensate renal cells have a variety of molecular mechanisms that help in adapting to varying oxygenation levels both under physiological and pathological conditions . HIF pathway is one of the most important area of interest under research as far as renal mechanisms of hypoxia is concerned . It plays vital roles in hypoxic adaptation , cytoprotection , cancer , wound healing and treatment of anaemia .

O2 sensors in kidney :

- Fe (11) and 2 oxy glutarate dependent oxygenase control hypoxic signalling by specific hydroxylation of proline with O2 dependent domain of HIF under normoxia . Under hypoxia , hydroxylation is inhibited and HIF signalling is activated .
- HIFs :

  Hypoxia Inducible Factors – they are pleotrophic , O2 sensitive heterodimeric transcription factors that act in response to hypoxia .
- HIFs also play a role in erythropoiesis , iron metabolism , anaerobic glucose metabolism , angiogenesis , growth and proliferation .
- 3 major hydroxylase domains determine the activation of HIF pathway :

  PHD 1 OR EGLN 1

  PHD 2 OR EGLN 2

  PHD 3 OR EGLN 3

  PHD – PROLYL 4 HYDROXYLASE DOMAIN

PHD 2 is the main enzyme involved in targeting HIF under normoxia (50) . All are expressed in kidney and control HIF (52) .

P4HTM - 4th potential HIF prolyl hydroxylase

- Hydroxylate HIF- 1a derived peptides
- Recent studies suggest their role in humans is unknown (53) .

- The second switch :

  FIH – Factor inhibiting HIF , a 20 G oxygenase , that catalyse the hydroxylation of HIFa by inhibiting CREB binding proteins and P300 binding to HIF transitional complex .

  FIH inactivation leads to CREB binding protein and P300 recruitment which increases HIF expression under hypoxia (50).

  FIH are located in the podocytes of kidney (54).

  Another regulatory factor is O2 dependant micro RNA expression (55).

- Other non- HIF regulators of renal hypoxia :
- Epigenetic changes by non -HIF 20G oxygenases
- Jumanji – domain containing oxygenases

  Both are involved in acute and chronic alteration in PO2 levels , metabolism and gene expression (58). They also aid in demehylation of methylated histones (49) .

- Multiple signalling molecules involved in renal hypoxia :
  - ROS – reactive oxygen species
  - Nitric oxide acting through NO synthase or Angiotensin 2 receptors

(50,59).

- Plays a significant role in Diabetic , Aging and Inflammatory nephropathy .
- Mutation in Krebs cycle involving fumarate dehydrogenase in Hereditary leiomyomatosis , renal cell cancer syndrome – fumarate accumulation .
- Competitive inhibition of 20 G oxygenase , degradation of NF- like 2 , NRF 2 transcription factors regulating anti oxidant response (60) . but their role is little known in non malignant kidney disease .

- **KIDNEY AND O2 CARRYING CAPACITY :**
  - Hypoxia induces erythropoietin (EPO) synthesis in the kidneys
  - Renal EPO synthesis is carried out by HIF – 2 , which is proven by genetic and immunohistochemistry studies (61).
  - Peritubular interstitial fibroblasts produce erythropoietin (62,63).
  - Activity of HIF -2 in renal EPO producing cells (REPC) controlled by PHD-2. PHD 1 and PHD 3 have role in regulating REPC cells (61).
  - EPO transcription is the most sensitive hypoxic response in kidney . It increases O2 delivery through increase in O2 carrying capacity by erythropoietin increase .
  - EPO output is controlled by number of REPC and not by in cellular m RNA coding EPO . In CKD , decreased EPO secretion leads to

anemia .

- Transcription of REPC to myofibroblast phenotype results in decrease in the number of cells to get recruited for the synthesis of EPO , when PO2 is low (62).
- HIF induces EPO , also enhances iron uptake and helps erythroid progenitor maturation , PHD inhibitors are being tried in the treatment of anaemia in CKD (61,64) .

O2 AND METABOLIC REPROGRAMMING :

- Under low PO2 , PHD/HIF plays important role in metabolic reprogramming to conserve o2 for Na+K+Atp ase pump function .
- HIF regulates energy and glucose metabolism at various levels . It shifts oxidative phosphorylation to anaerobic glycolysis (65, 66).
- Suppress mitochondrial respiration and ROS generation .
- It inhibits conversion of pyruvate to Acetyl co-A
- Increases anaerobic glycolysis , but at the same time it decreases lactic acidification by expression of Na+-H+ exchanger and mono carboxylic acid transporter 4 – excretes H+ and lactate (67) .
- HIF in tumor cells , keeps the PH alkaline by conversion of CO2 to HCO3- by carbonic anhydrase expression (67).

THERAPEUTIC OPPURTUNITIES BEYOND RENAL ANAEMIA :

- Acute changes in renal PO2 results in acute AKI which does not require renal replacement therapy .
- The effects of sub acute / chronic hypoxia have been studied in people living in high altitude (68) .
- Renal tumours caused by mutation in O2 sensing machinery like Von Hippel Lindau Tumor Suppressor gene causes HIF activation .
- In non malignant kidney condition , HIF-a stabilisation is seen in both acute and chronic condition (69) .
- In DM nephropathy , degree of HIF activation is proportionate to severity of renal injury .

Causes of HIF activation :

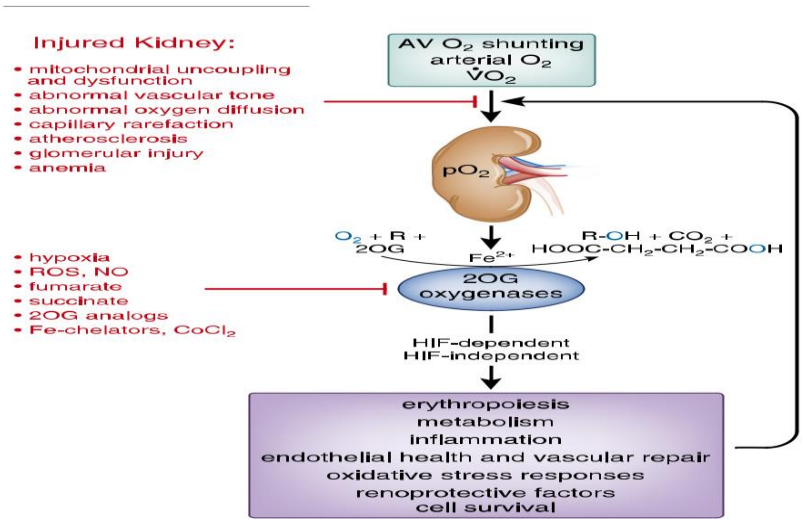
- Chronic hypoxia
- O2 dependant PHD inhibitors (69)
- Decreased renal perfusion
- Glomerular injury
- Altered vascular tone
- Anemia
- Impaired O2 diffusion – fibrosis (71)
- Increased VO2 , decreased Renal PO2– mitochondrial dysfunction (72)
- HIF activation protects from reperfusion injury , evidence from animal models of Acute Renal Failure (73). Role in CKD is under debate .

- Recent studies suggest that renoprotection is dependant on timing of HIF activation (74) .

<u>To summarise HIF activation has :</u>

- Renoprotective roles
- Cytoprotective gene expression
- Glucose , energy , adenosine metabolism reprogramming
- Mitochondrial O2 utilisation
- Mitochondrial ROS production
- ROS scavenging
- Suppression of renal inflammation
- Maintainance of vascular integrity (69,73,75,76) .
- Regulation of PHD / HIF axis is cell type dependant and involves multiple loops , but the mechanism differs between acute and chronic hypoxia .

<u>Fig. Overview of renal hypoxia mechanisms and selected 2OG oxygenase - regulated processes that affect renal physiology and pathophysiology</u>.



AIMS AND OBJECTIVES

AIM OF THE STUDY:

1. To study the prevalence of Renal Function defects in COPD patients

OBJECTIVES OF THE STUDY:

1. To asses renal function using Creatinine clearance & urine proteins
2. To estimate the Creatinine clearance using Cockroft gault equation

REVIEW OF LITERATURE

The prevalence of renal dysfunction in various studies are as follows :

- **Ibrahim l.Elmahallawy et al [82]** reported an increased incidence of 46% of renal dysfunction among them prevalence of overt renal failure was 20% and prevalence of concealed renal failure was 26%.
- **Raffaele Antonelli Incalzi et all [83]** reported an incidence of 43% of renal dysfunction among them prevalence of overt renal failure was 22.2% and prevalence of concealed renal failure was 20.8%.
- **Takayuki Yoshizawa et all [84**] found that 31% of the study population developed renal dysfunction.
- **Sharanya et al [85]** reported an incidence of 37% of renal dysfunction among COPD patients.
- **Bjarte Gjerde et all** [86] had a prevalence of 9.6% in Female COPD patients and 5.1% in male COPD patients .
- **Study by Yvette R. B. M. van Gestel, Michel Chonchol, Sanne E. Hoeks , Gijs M. J. M. Welten, Henk Stam, Frans W. Mertens, Ron T. van Domburg and Don Poldermans -** . COPD was independently associated with CKD (OR 1.22; 95% CI 1.03– 1.44; P = 0.03). This association was strongest in patients with moderate COPD (OR 1.33; 95% CI 1.07–1.65; P = 0.01). Both moderate and severe COPD were associated with increased long-term mortality in patients with CKD (HR 1.27; 95% CI 1.03–1.56; P = 0.03 and HR 1.61; 95% CI 1.10–2.35; P = 0.01, respectively), compared to patients without COPD.

Relation between microalbuminuria and COPD in previous studies :

- **In a study by Mehmet polatli , Aysel Çakir , Orhan Cildag , A. Zahit Bolaman , Cigdem Yenisey , Yavuz Yenicerioglu** - The level of microalbuminuria was found to increase significantly in COPD - AE group, compared to that of the controls .
- **Study by A. Kömürcüog˘lu , S. Kalenci , D. Kalenci, B. Kömürcüog˘lu , G. Tibet** - Microalbuminuria was detected in 14 (56%) subjects at admission and in 7 (28%) subjects at discharge in the COPD group and in 1 (4%) subject in the control group . In a quite large number of patients with COPD in whom no proteinuria were determined by conventional methods, especially at the time of exacerbation, microalbuminuria could be seen. Microalbuminuria was related with hypoxemia but has no predictive role on mortality .
- **Solfrid Romundstad , Thor Naustdal , Pal Richard Romundstad , Hanne Sorger and Arnulf Langhammer** , a 12-year follow-up study of 3129 participants - Compared to those with COPD without microalbuminuria, the adjusted hazard ratio for all-cause mortality in those with COPD and microalbuminuria was 1.54, 95% CI (1.16–2.04) . Microalbuminuria is associated with all-cause mortality in individuals with COPD and could be a relevant tool in identification of patients with poor prognosis.

- **A work by Ciro Casanova, Juan P. de Torres , Juan Navarro , Armando Aguirre-Jaı´me , Pablo Toledo, Elizabeth Cordoba2, Rebeca Baz , and Bartolome´ R Celli** : MAB (microalbuminuria) was higher in patients with COPD than in control smokers (8 [5th295th percentile (P5–95), 2.9– 113] vs. 4.2 [P5–95, 1.8–22.7] mg/g, P , 0.001]). : MAB is frequent in patients with COPD and is associated with hypoxemia independent of other cardiovascular risk factors. Further studies are necessary to investigate whether MAB could be an early simple biomarker of cardiovascular compromise in patients with COPD
- **Study by Khalid Mehmood* and Fayaz Ahmad Sofi** - Microalbuminuria was more frequent in COPD patients compared to smokers without obstruction (20.6% versus 7.4%respectively); p=0.007. There was an inverse association of the PO2 and MAB in patients with COPD (r=-0.35, p<0.001) . MAB is frequent in patients with COPD and is associated with hypoxemia independent of other cardiovascular risk factors .

MATERIALS AND METHODS

Study design : Cross sectional study

Place of Study : Govt Thiruvoteeswarar Hospital of Thoracic Medicine Chennai

Duration of study : 1 YEAR

Sample size : 146

Sampling method : Simple random sampling

Conflict of interest : Nil

Hazards of study : Nil

METHODOLOGY:

Sample size –

Allowable alpha error is 8% with a confidence level of 95% and desired accuracy of 10% .

INCLUSION CRITERIA	EXCLUSION CRITERIA
Patients who are already diagnosed as COPD / newly diagnosed COPD as per GOLD guidelines	COPD patients who are known CKD patients Patients not willing to participate in the study Patients on long term nephrotoxic drug theraphy

DATA COLLECTION :

The data of each patient will be collected on a proforma which includes the following:

- Name
- Age
- Gender
- Anthropometry

Detailed clinical history was collected which included

- Presenting illness
- Smoking
- Alcohol history
- Comorbid illness
- Previous treatment details
- Drug intake history

PFT, chest X ray, RBS , Blood pressure analysis , B.urea , S.creatinine , Urine protein and Creatinine clearance data were collected and compiled in the profoma.

Calculation of eGFR:

The Cockcroft and Gault formula (1973)

Cockcroft-Gault Formula for Estimating Creatinine Clearance

$$\text{CrCl (mL/min)} = \frac{(140\text{-age}) \times \text{Lean Body Weight (kg)}}{\text{Serum Creatinine (mg/dL)} \times 72} \quad (\times 0.85 \text{ if female})$$

Abbreviations/ Units

CCr (creatinine clearance) = mL/minute

Age = years

Weight = kg

SCr (serum creatinine) = mg/dL

Pulmonary Function Test:

Pulmonary function test was done for all patients who were enrolled. The test was performed in accordance with the criteria set by American Thoracic Society using Easyone Spirometer. The instrument was calibrated daily as recommended. The procedure was explained to all the patients clearly before the test is done. Any recent history of smoking, illness, medications

were enquired and the height and weight of the patient was recorded. All participants were kept in the sitting posture for the procedure.

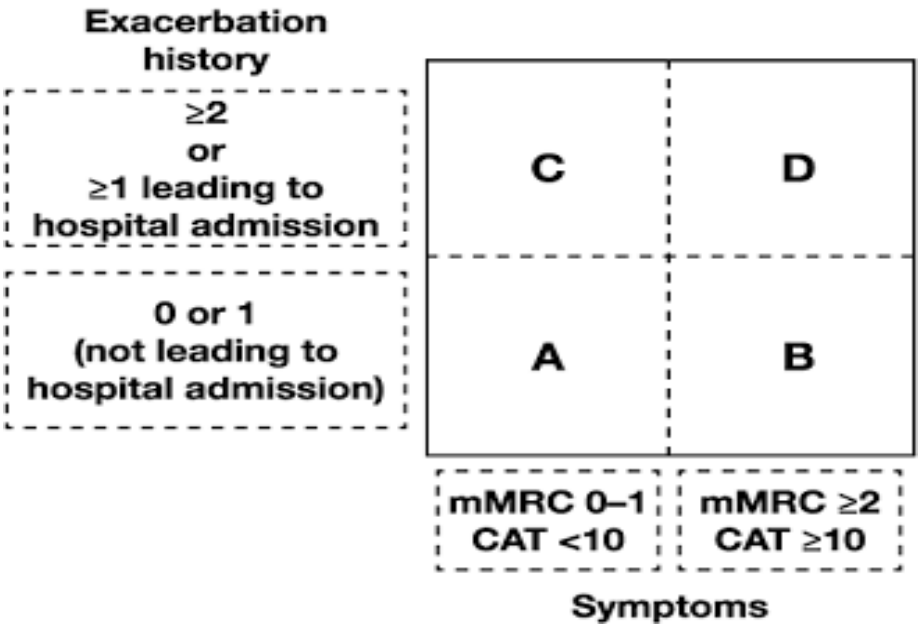
All participants were instructed and demonstrated to hold the head in slightly elevated manner, position the mouthpiece and close the lips, inhale completely and rapidly and then exhale maximally until no more air can be expelled out.

Instructions were repeated as necessary. Throughout the manoeuvre, subjects were encouraged to blast out and exhale using appropriate body languages and phrases. The test was stopped whenever they complained of distress or dizziness. The test was repeated till at least three trials with two acceptable and reproducible tests for both FEV1 and FVC were obtained. Measurements were made before and after at least 15 minutes of two puffs of salbutamol (200 microgram) administered using metered dose inhaler with a volumetric spacer. The degree of airflow obstruction was assessed using GOLD guidelines.

Table : Severity of airflow limitation as per GOLD guidelines

GOLD 1	Mild	FEV1≥ 80% PREDICTED
GOLD 2	Moderate	50%≤ FEV1 <80% PREDICTED
GOLD 3	Severe	30%≤ FEV1 < 50% PREDICTED
GOLD 4	Very severe	FEV1 < 30% PREDICTED

Table : GOLD Category



Urine albumin dipstick test:

Albumin, the major protein in the blood is usually not filtered in the urine unless there is underlying abnormality in the glomerular basement membrane. Normal urinary proteins values are less than 150 mg/d and are undetectable using urinary dipstick. The urinary dipstick only detects the presence of albumin and no other proteins. When urinary protein values exceed 300-500 mg/d, the dipstick test result becomes positive. Thus, it is a very specific, but not sensitive, test for proteinuria

It is measured in this study using dipstick method.

Dipstick result interpretation:

Trace proteinuria - Approximately 10-30 mg/dL, as follows:

1+ - Approximately 30 mg/dL

2+ - Approximately 100 mg/dL

3+ - Approximately 300 mg/dL

4+ - 1000 mg/dL or more

Spot Protein Creatinine Ratio:

Normal: less than 30 micrograms (mcg) per milligram (mg) of creatinine

Microalbuminuria: 300 mcg per mg of creatinine

Clinical albuminuria: More than 300 mcg/mg creatinine

24-Hour Test

Normal: Less than 30 mg

Microalbuminuria: 30-300 mg

Clinical albuminuria: More than 300 mg

Serum Creatinine:

Serum creatinine in blood is an important indicator of renal health because, it is an easily measurable by product of muscle metabolism. It is excreted unchanged by the kidneys.

Most clinical laboratories now align their creatinine measurements against a new standardized Isotope Dilution Mass Spectrometry (IDMS) method to measure serum creatinine

Serum creatinine value of 1.2 mg/dl is the cut off value, above which is defined as the patient has renal dysfunction.

Smoking status :

Smoking status of the patient was recorded using CDC guidelines definition: [51]

Current smoker - who has smoked greater than 100 cigarettes in his lifetime and now smokes every day or some days

Former smoker - who has smoked greater than 100 cigarettes in their lifetime and does not currently smoke.

Never smoker - who has not smoked greater than 100 cigarettes in their lifetime.

BIOMASS EXPOSURE :

This is particularly in house hold females who are exposed to bio mass fuel while cooking during olden days .

STATISTICAL ANALYSIS :

Statistical analysis was done using the Microsoft Excel and SPSS software with the help of a statistician. P value is used to assess the significance of correlation between variables. A statistically significant correlation is one in which Pearson correlation is used to assess the strength of correlation between variables Pearson correlation:

- > 0.5 – strong correlation
- 0.3-0.5 – moderate correlation
- < 0.3 - weak correlation

Chi-square Test:

Chi-square test is performed between two groups and its statistical significance is calculated.

The chi-square (χ^2) test of independence is used to test for a statistically significant relationship between two categorical variables.

The term "degrees of freedom" is used to refer to the size of the contingency table on which the value of the Chi Square statistic has been computed

$$\chi^2 = \sum \frac{(\text{observed} - \text{expected})^2}{\text{expected}}$$

P value is calculated using Excel CHITEST function:

If P value $\leq 0.05 \rightarrow$ statistically significant

If P value $> 0.05 \rightarrow$ statistically insignificant

RESULTS AND ANALYSIS

Table 1: Age Distribution

Age (In years)	Case	
	No's	%
41-50 years	25	17.0
51-60 years	54	36.2
61-70 years	46	31.9
71-80	14	9.9
>80 years	7	5.0
Total	146	
Range	40-87 years	
Mean	61.14 years	
S.D	10.43 years	

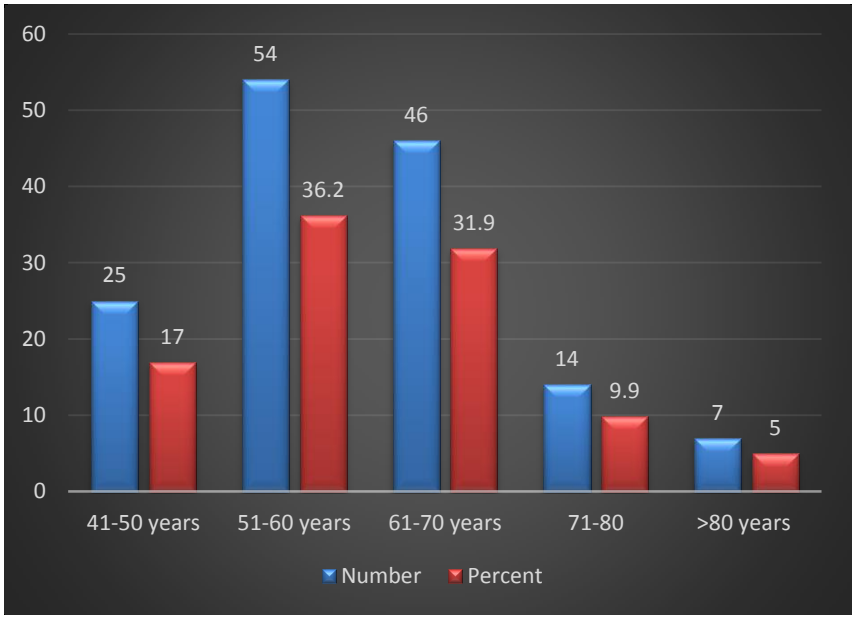


Fig 1: Distribution of age in my study population

Table 2: Gender distribution

	Cases	
	No	**%**
Male	110	75
Female	36	25
Total	146	100.0

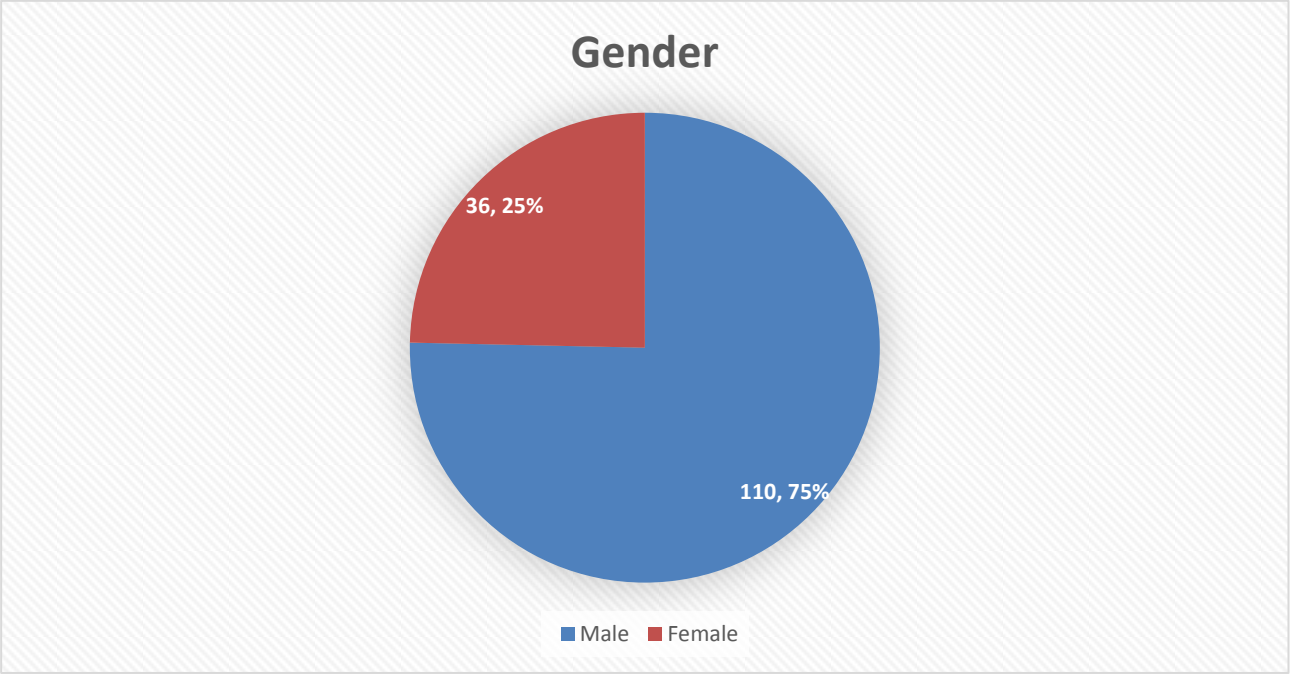


Fig 2: Pie Chart showing Distribution of age in my study population

Table 3: Duration of illness :

Duration of illness	Cases	
	No	%
< 10 years	68	47
>10 years	78	53
Total	146	100.0

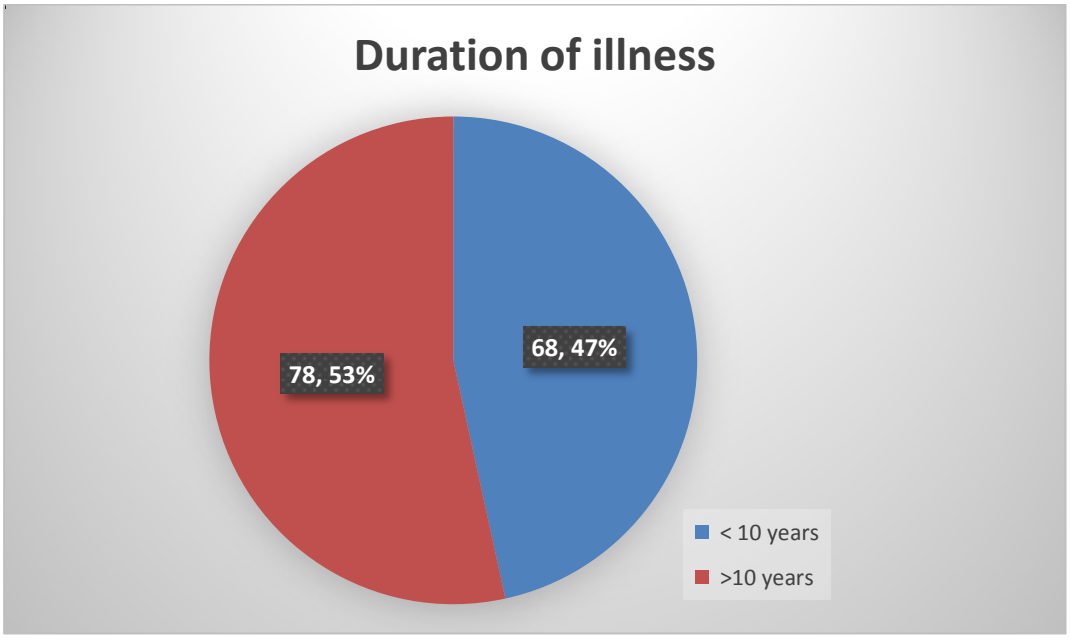


Fig 3: Distribution of duration of illness in my study population

Table 4: Creatinine level

Creatinine level	Cases	
	No	%
0.6-1.2 mg/dl	136	93
>1.2	10	7
Total	146	100.0

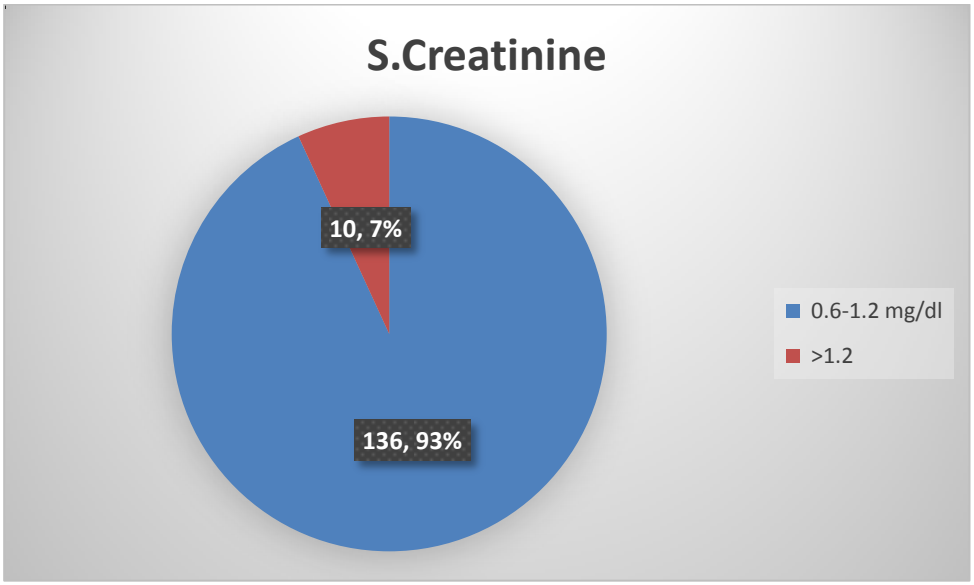


Fig 4: Distribution of S.Creatinine levels in my study population

Table 5: Diabetes Mellitus status

Diabetes Mellitus	Cases	
	No	**%**
Yes	13	9
No	133	91
Total	146	100.0

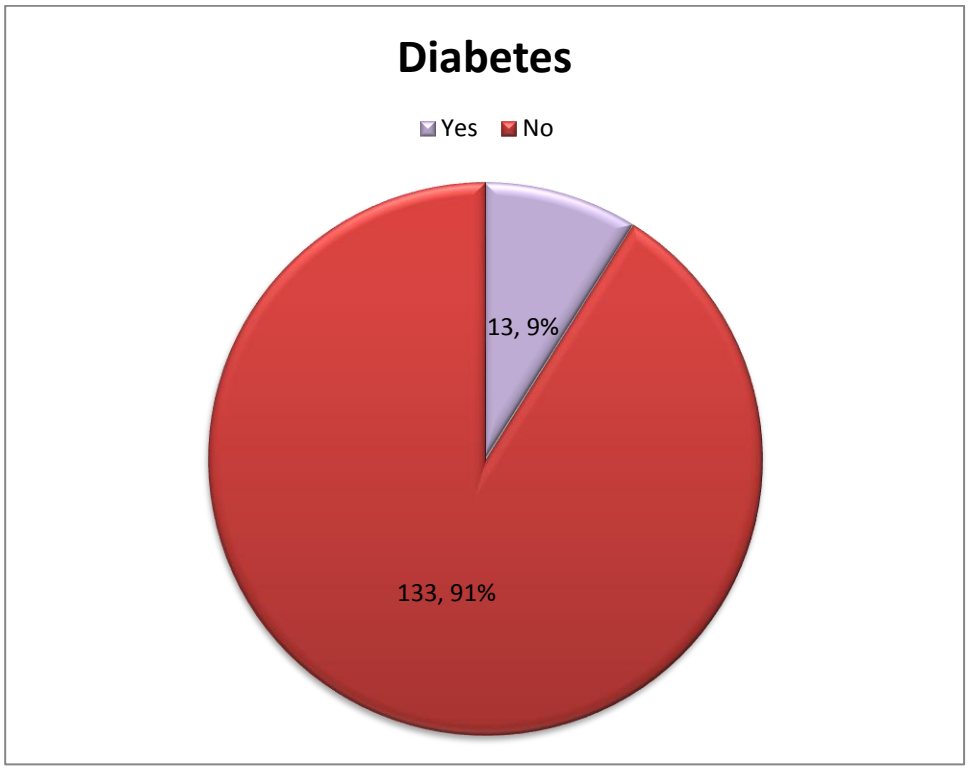


Fig 5: Distribution of diabetes mellitus status in my study population

Table 6: Hypertension status

HTN	Cases	
	No	%
Yes	11	8
No	135	92
Total	146	100.0

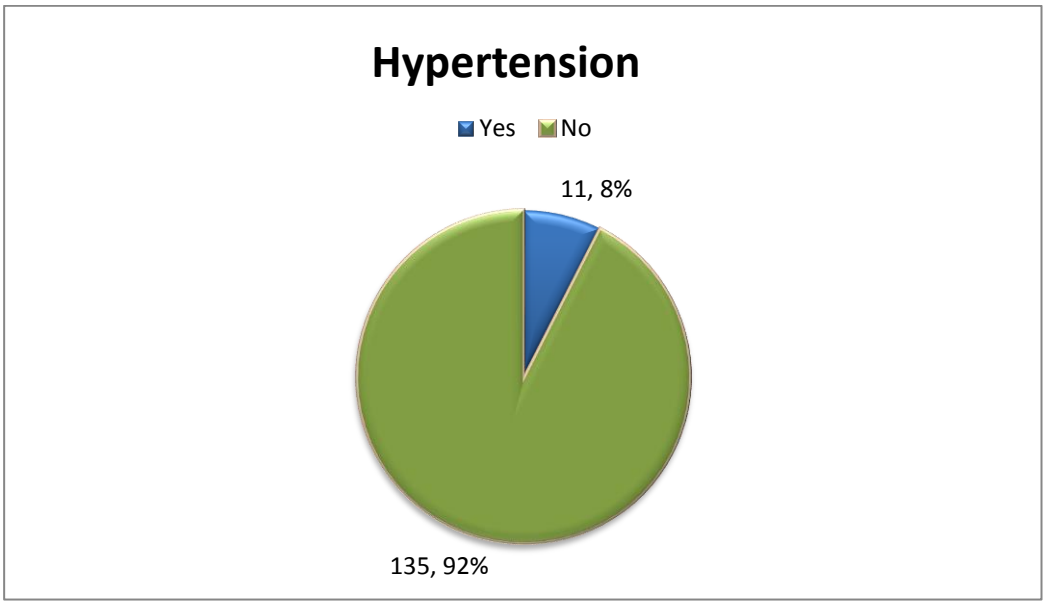


Fig 6: Distribution of hypertension status in my study population

Table 7: Severity of obstruction in PFT

PFT Degree of obstruction	Cases	
	No	%
Mild	77	54.6
Moderate	32	21.3
Severe	37	24.1
Total	146	100.0

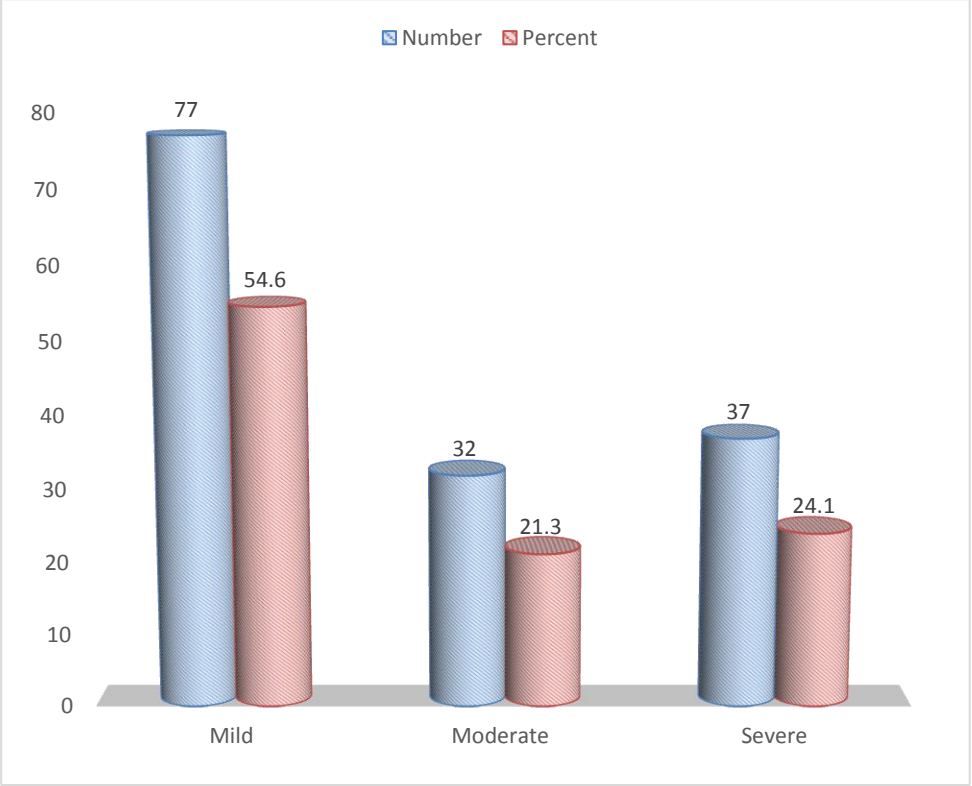


Fig 7: Distribution of severity of obstruction in PFT in my study population

Table 8.1 : eGFR

eGFR	Cases	
	No	%
≥ 90	24	17.0
60- 89	51	34.8
30-59	63	42.6
15-30	8	5.7
Total	146	100.0
Mean	64.89	
SD	26.5	
Range	21.8—149.8	

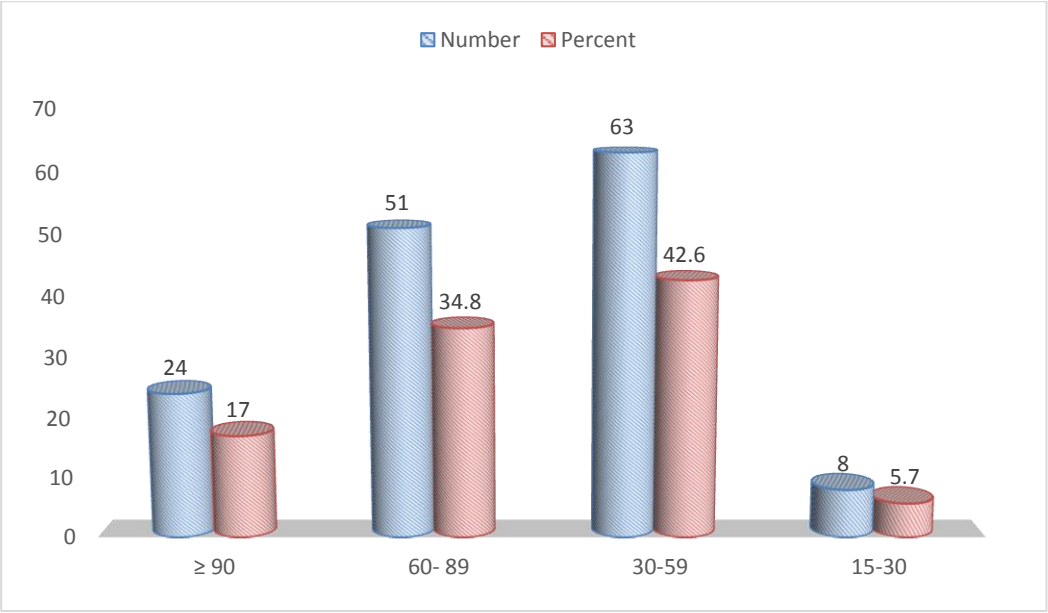


Fig 8.1 : Distribution of eGFR status in my study population

Table 8.2 : Distribution of Renal function defects

eGFR ml/min	Cases	
	No	%
≥ 90	24	17.0
<90	122	81.0
Total	146	100.0

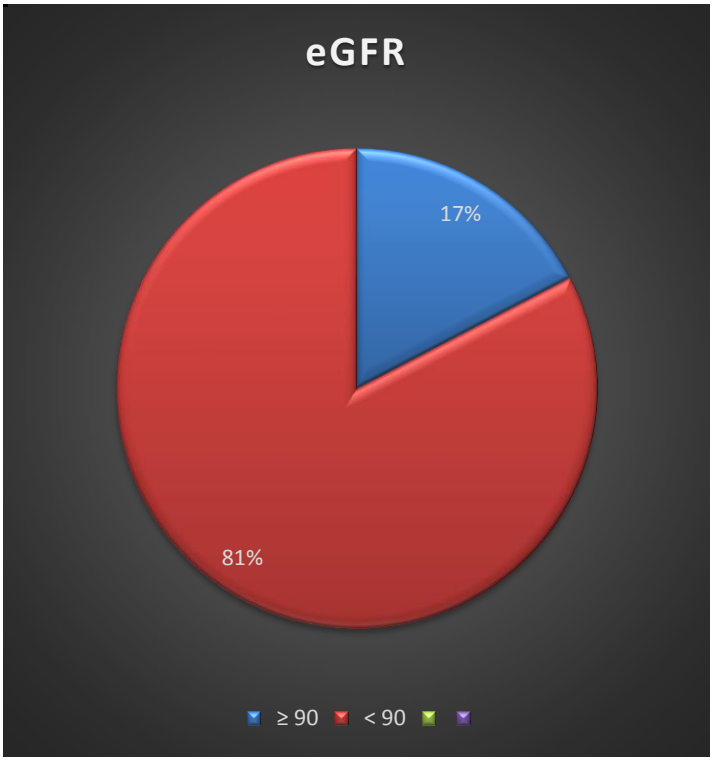


Fig 8.2 : Distribution of Renal function defects

Table 9: Comparison of Duration of illness with their eGFR values

	Cases with eGFR values					P value
Duration of illness	>90	60-89	30-59	15-30	**Total**	
< 10 years	21	31	16	0	68	< 0.005*
>10 years	3	20	47	8	78	<0.005*
Total	24	51	63	8	146	

*significant P <0.05

Data are expressed as N (%). Chi Square test was applied to find statistically significant association between groups based on duration of illness and efgr.

P <0.05 was considered to be statistically significant.

	Cases eGFR			P value
Duration of illness	>90ml/min	<90ml/min	**Total**	
< 10 years	21	47(38.5%)	68	< 0.005*
>10 years	3	75(61.5%)	78	< 0.005*
Total	24	122(100%)	146	

Table 10: Comparison of severity of obstruction with their eGFR values

Severity of Obstruction	eGFR				Total	P value
	90	61-89	31-59	15-30		
Mild	24 (32)	33 (42)	20 (26)	0	77	<0.05*
Moderate	0	14(43.3)	17 (53.4)	1(33.3)	32	
Severe	0	4(10.8)	26(70.2)	7(18.9)	37	
Total	24	51	63	8	146	

*significant P <0.05

Data are expressed as N (%).

Chi Square test was applied to find statistically significant association between groups based on severity of obstruction and efgr.

P <0.05 was considered to be statistically significant .

Table 11: Comparison of S. Creatinine levels with gender

S. Creatinine	SEX		Total	P value Df=1
	Male	Female		
Normal	101	35	136	>0.05
Abnormal	9	1	10	
Total	110	36	146	

*significant P <0.05

Data are expressed as N (%). Chi Square test was applied to find statistically significant association between groups based on S.creatinine and Gender.

P <0.05 was considered to be statistically significant

Table 12: Comparison of severity of obstruction with their eGFR values

Severity of Obstruction	**eGFR CCml/min**		Total	P value
	<90	**>90**		
Mild	54 (70)	23 (30)	77	<0.05*
Moderate	32 (100)	0	32	
severe	37 (100)	0	37	
Total	123	23	146	

***significant**

Data are expressed as N (%).

Chi Square test was applied to find statistically significant association between groups based on severity of obstruction and efgr. It was found to be statistically significant among groups

P <0.05 was considered to be statistically significant

Table 13: Comparison of hypertension status with their eGFR values

Hypertension	**eGFR CCml/min**	**eGFR CCml/min**	Total	P value
	<90	**>90**		
Present	10 (91)	1 (9)	11	>0.05 (NS)
Absent	113 (83)	22 (17)	135	
Total	123	23	146	

Data are expressed as N (%).

Chi Square test was applied to find statistically significant association between groups based on hypertension status and efgr. It was found to be not statistically significant among groups

P <0.05 was considered to be statistically significant .

Table 14: Comparison of diabetes mellitus with their eGFR values

Diabetes mellitus	**eGFR (CC) ml/min**	**eGFR (CC) ml/min**	Total	P value
	<90	**>90**		
Present	12 (92.3)	1 (7.7)	13	>0.05 NS
Absent	111 (82.9)	22(17.1)	133	
Total	123	23	146	

Data are expressed as N (%).

Chi Square test was applied to find statistically significant association between groups based on diabetes mellitus status and efgr. It was found to be not statistically significant among groups

P <0.05 was considered to be statistically significant .

RESULTS

Our study includes 146 patients . Among them all are above 40 years of age . It includes 110 males and 36 females . The increased male population is due to prevalence of smoking habits more among males . Range of age is from 48-87 years . Mean Age is 61 years .

Prior history of pulmonary tb were present in 48 (33%) of the study population and without such history is 98(67%).

Smoking / Biomass exposure is present in almost all patients , contributing to the nature of illness. 11 were hypertensive and 13 were diabetics .

Taking 10 years of duration of illness as a borderline , patients were divided into those who have illness greater than or equal to 10 years and less than 10 years . The former includes 78 (53%) and the latter includes 68 (47%) .

Based on degree of obstruction , 54.0% were mild obstructive , 21.3% shown moderately obstructive , 24.7 % were severely obstructive .When creatinine clearance estimated using Cockgroft gault equation in our study , only 17% have got values above 90ml/min and 81% were below 90 ml/min . Based on KDIGO guidelines 2012 , CKD stages based on creatinine clearance

were made among the study population which showed 17% in stage 1 (normal), 34.8% in stage 2 , 42.6% in stage 3 and 5.7% in stage 4 . There is a significant correlation between severity of obstruction and severity of renal function defects .

Urine proteins using dipstick method to detect proteinuria / macro albuminuria were negative in all patients .

DISCUSSION

This cross sectional study was conducted on 146 Chronic Obstructive Pulmonary Disease patients in Government Thiruvoeeswarar Hospital of thoracic medicine . This research was done in order to estimate the prevalence of renal function defects in Chronic Obstructive Pulmonary Disease patients.

In the present study, the prevalence of renal dysfunction is 81%, among them the prevalence of overt renal failure was 7% and prevalence of concealed renal failure was 34.9%. Various studies has been done in India to estimate the prevalence of renal dysfunction among general population. Ajay K Singh et al had done a study called SEEK(Screening and Early Evaluation of Kidney Disease) and found that prevalence of CKD with eGFR< 60 was approximately 6%.

Singh et al had done a study among urban and semi urban delhi population and had found that prevalence of renal failure (eGFR<60) was 6% among urban population and 4.2% among semi urban population. In a study done by Tiwari et al the prevalence was 4%. Hence by comparing with other indian studies the prevalence of renal dysfunction is 4 times higher among COPD when compared with the general population.

Ibrahim l.Elmahallawy et al [52] reported an increased incidence of 46% of renal dysfunction among them prevalence of overt renal failure was 20% and prevalence of concealed renal failure was 26%.

Raffaele Antonelli Incalzi et all [53] reported an incidence of 43% of renal dysfunction among them prevalence of overt renal failure was 22.2% and prevalence of concealed renal failure was 20.8%.

Takayuki Yoshizawa et all [54] found that 31% of the study population developed renal dysfunction.

Sharanya et al [55] reported an incidence of 37% of renal dysfunction among COPD patients.

Bjarte Gjerde et all [56] had a prevalence of 9.6% in Female COPD patients and 5.1% in male COPD patients.

In our study, the prevalence of renal dysfunction in high among the COPD patients where the mean age under study is > 60.

When duration of COPD has taken as a criteria , as the duration increases , the percentage of patients falling into overt renal failure (egfr < 60ml/min) increases , it is 61.5 % in group with duration >10 years compared to 38.5 % in group with duration < 10 years .

In our study population Diabetes and Hypertension were significantly associated with the development of renal dysfunction. In our study Prevalence of Renal dysfunction among diabetes and hypertension were 92% and 91% taken eGFR>90 being normal . The prevalence is higher when compared with the general population. But the population in our study group is very low for the results to be significant and comparable . In a study done by Rajesh et al in Haryana the prevalence of renal dysfunction (eGFR < 60) in diabetes mellitus was 16.9%.In a study done by Deidra et al in United States the prevalence of renal dysfunction (eGFR < 60) in Hypertension was 19.6%.

Ibrahim l.Elmahallawy et al [52] had done a backward stepwise logistic regression model and found that the presence of comorbidities like Diabetes and Hypertension were significantly associated with the development of Concealed renal dysfunction.

In our study , Urine proteins using dipstick method to detect proteinuria /macro albuminuria were negative in all patients which indicates there is no significant association between copd and proteinuria in our study population .

In a study done by Festo K. Shayo and Janet Lutale , the studied population, 25/104 (24%) patients had albuminuria and 16/104 (15.4%) patients had CVD. Albumin-creatinine ratio (ACR) was then calculated to determine the level of albuminuria and expressed as mg/mmol. ACR < 2

mg/mmol for male and < 2.8 mg/mmol for female defined normo albuminuria, ACR ≥ 2.5–29.9 mg/mmol for male and ≥ 3.5–29.9 mg/mmol for female defined albuminuria and ACR ≥ 30 mg/mmol for both male and female defined macroalbuminuria/proteinuria . Abnormal urine albumin (Albuminuria and Proteinuria) was present in all patients with CVD. In the subset of 46 COPD patients assessed for severity, 60.9% (95%CIs 46.1–73.9) had moderate COPD and 30.4% (95% CIs, 17.9–49.0) severe COPD. Albuminuria was moderately significantly associated with COPD severity .

In a study done by Solfrid Romundstad , Thor Naustdal1, Pal Richard Romundstad, Hanne Sorger1 and Arnulf Langhammer , a 12-year follow-up study of 3129 participants in the second survey of the Nord-Trøndelag Health Study (HUNT), Norway , for all GOLD stages of COPD, microalbuminuria was negatively associated with survival, although the associations were not significant (fig. 2). In modified GOLD stage I multivariable adjusted hazard ratio for all-cause mortality was 1.39 (95% CI 0.69–2.83), in GOLD stage II the hazard ratio was 1.30 (95% CI 0.90–1.90) and in GOLD stage III/IV the hazard ratio was 1.14 (95% CI 0.59–2.19).

CONCLUSION

1. In our study, the prevalence of renal dysfunction is 81%, among them the prevalence of overt renal failure was 7% (eGFR <60 ,Creatinine >1.2) and prevalence of concealed renal failure was 34.9%.Among the Female COPD patients who had renal dysfunction all the 20% had concealed renal failure (eGFR<60, Creatinine<1.2).

2. Significant risk factors associated with the development of renal dysfunction in COPD patients are:
    - Age > 60
    - Duartion of illness
    - Severity of obstruction
    - Associated with Diabetes And Hypertension

3. Even though Diabetes and Hypertension are associated with the development of Renal dysfunction, their prevalence in our study population in very low to make significant association .

4. Urine proteins / macroalbuminuria doesn't make any correlation with COPD , severity or duration of COPD in our study .

LIMITATIONS

1. This is a hospital based study, extrapolating the results of the study to the general population may not be accurate enough, hence further studies has to be done in the general population.

2. This is a cross sectional study done in a single centre and controls were not included in the study.

3. Glomerular Filtration Rate (GFR) was not measured directly. However Cockgroft gault equation is a reliable surrogate for measured GFR in both the healthy elderly and the diseased population.

4. Specific inflammatory markers like C-Reactive Protein, IL-6 and fibrinogen were not seen in the study. The correlation between renal dysfunction and these bio markers would have given a better outcome.

5. Urine micro albuminuria , USG KUB may have been done to add to the early diagnosis of renal failure with more precicion .

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ABBREVIATIONS

COPD	-	Chronic obstructive pulmonary diseases
CKD	-	Chronic Kidney Disease
SNP	-	Single Nucleotide Polymorphism
TNF-α	-	Tumour Necrosis Factor -alpha
BMI	-	Body Mass Index
PHT	-	Pulmonary hypertension
ESR	-	Erythrocyte sedimentation rate
FEV1	-	Forced expiratory volume in one second
FVC	-	Forced vital capacity
DM	-	Diabetes Mellitus
SHT	-	Systemic Hypertension
HIF	-	Hypoxia inducible factor
RBF	-	Renal Blood Flow
e GFR	-	Estimated Glomerular Filtration Rate

PROFOMA

- Place:
- PATIENT'S DEMOGRAPHY :
- Id No:
- Date:
- Name:
- Age:
- Gender:
- Address:
- Phone:
- Occupation: _____
- Weight - kgs
- SYMPTOMATOLOGY**:**

Yes/No

Cough with expectoration

Shortness of breath Yes/No

Fever Yes/No

- PAST HISTORY:

- Prior TB treatment: Yes/No

- H/O any nephrotoxic drug intake : Yes/No
- Past medical history Yes/No

- Any comorbid illness Yes/No

(DM/SHT/BA/COPD/epilepsy/HIV/CAD/CKD)

PERSONAL HISTORY**:**

- Addictions: Smoking/ alcohol/ tobacco/substance abuse
- Marital status: married/ unmarried
- Children: Yes/No

- PFT:
- X RAY CHEST:
- RBS:
- BLOOD PRESSURE:
- S.CREATININE :
- B. UREA :
- URINE PROTEIN :
- CREATININE CLEARANCE :

ETHICAL COMMITTEE APPROVAL CERTIFICATE

INSTITUTIONAL ETHICS COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID. No. 120/2018 Meeting held on 26.04.2018

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "TO STUDY THE PREVALANCE OF RENAL FUNCTION DEFECTS IN COPD PATIENTS USING CREATININE CLEARANCE AND URINE PROTEIN ANALYSIS" submitted by Dr. R. Vignesshkanth P.G. in TB and Respiratory Medicine, Govt. Kilpauk Medical College, Chennai-10.

The Proposal is **APPROVED.**

The Institutional Ethical Committee expects to be informed about the progress of the study any Adverse Drug Reaction Occurring in the Course of the study any change in the protocol and patient information /informed consent and asks to be provided a copy of the final report.

3.5.2018
DEAN
Govt. Kilpauk Medical College,
Chennai-10.

26-4-18

ME 1 Sec> Ethical Committee

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URKUND

Urkund Analysis Result

Analysed Document:	INTRODUCTION - PLAGIARISM 4.docx (D57545015)
Submitted:	10/23/2019 9:22:00 PM
Submitted By:	vignesshkanth@gmail.com
Significance:	16 %

Sources included in the report:

https://www.news-medical.net/health/Chronic-Obstructive-Pulmonary-Disease-Process.aspx
https://slideplayer.com/slide/7392404/
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Instances where selected sources appear:

32

CERTIFICATE - II

This is to certify that this dissertation titled “TO STUDY THE PREVALENCE OF RENAL FUNCTION DEFECTS IN COPD PATIENTS USING CREATININE CLEARANCE AND URINE PROTEIN ANALYSIS ” of the candidate Dr.R.Vignesshkanth with registration Number 201727253 for the award of M.D in the branch of Tuberculosis and Respiratory diseases. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows 16% percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

Prof. Dr. P.M.RAMESH , M.D (TB&RD),
HOD, Department of TB and Respiratory Diseases,
Government Kilpauk Medical College,
Chennai.

PATIENT CONSENT FORM

STUDY DETAIL	**:**
STUDY CENTRE	**:**
PATIENT'S NAME	**:**
PATIENT'S AGE	**:**
IDENTIFICATION NUMBER	**:**

I confirm that I have understood the purpose and procedure of the above study. I have the opportunity to ask questions and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that the sponsor of the clinical study, others working on the sponsor's behalf, the ethical committee and the regulatory authorities will not need my permission to look at my health records, both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However I understand that my identity would not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including haematological, biochemical, radiological tests.

Patient's name and address: Signature/thumb impression:

Place: Date:

Name of the investigator: Signature of the investigator:

Place: Date:

சுய ஒப்புதல் படிவம்

ஆய்வு செய்யப்படும் தலைப்பு: **"TO STUDY THE PREVALENCE OF RENAL FUNCTION DEFECTS IN COPD PATIENTS USING CREATININE CLEARANCE AND URINE PROTEIN ANALYSIS "**

ஆராய்ச்சி நிலையம்: நெஞ்சகத் துறைப் பிரிவு, கீழ்ப்பாக்கம் மருத்துவக்கல்லூரி அரசு மருத்துவமனை, சென்னை.

பங்கு பெறுபவரின் பெயர்:

உறவு முறை:

பங்கு பெறுபவரின் எண்:

பங்கு பெறுபவர் இதனை ( ) குறிக்கவும்

மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களைக் கேட்கவும், அதற்கான தகுந்த விளக்கங்களைப் பெறவும் வாய்ப்பளிக்கப்பட்டது. ( )

நான் இவ்வாய்வில் தன்னிச்சையாகத்தான் பங்கேற்கிறேன். எந்தக் காரணத்தினாலோ எந்தக் கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகிக் கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ( )

இந்த ஆய்வு சம்மந்தமாகவும், மேலும் இது சார்ந்த ஆய்வு மேற்கொள்ளும்போதும், இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளைப் பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்துகொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ( )

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும்

மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும், அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ( )

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன். எனக்குக் கொடுக்கப்பட்ட அறிவுரைகளின் படி நடந்துகொள்வதுடன், இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறாக நோய்க்குறி தென்பட்டாலோ உடனே அதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ( )

இந்த ஆய்வில் எனக்கு மருத்துவப் பரிசோதனை செய்து கொள்ள மற்றும் ஆய்வில் பங்கேற்க நான் முழு மனதுடன் சம்மதிக்கிறேன்.( )

பங்கேற்பவரின் கையொப்பம் / கட்டைவிரல் ரேகை:_____

இடம்: _____

தேதி: _____

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்::

ஆய்வாளரின் கையொப்பம் _____

இடம் _____

தேதி _____

ஆய்வாளரின் பெயர் _____

PARTICIPANTS' INFORMATION SHEET

Investigator : **DR.R.VIGNESSHKANTH**

Name of the participant :

Study title: "TO STUDY THE PREVALENCE OF RENAL FUNCTION DEFECTS IN COPD PATIENTS USING CREATININE CLEARANCE AND URINE PROTEIN ANALYSIS".

What is the purpose of this research?

We aim at studying the the clinical data with symptom analysis, functional assessment using PFT, the radiological picture with chest X ray to rule out other pulmonary co morbidities . RBS and BP measurements to detect DM, SHTN. Biochemical assessment using S.creatinine , B.urea , Urine protein and calculating Creatinine clearance using COCKCROFT GAULT equation . By analysing the population we aim at finding out the prevalence of renal function defects in COPD patients .

Discomforts and risks: NIL

Confidentiality:

Patients who participate in the study and their details will be maintained confidentially and at any cost, those details will not be let out.

Right to withdraw:

Patients will not be forced to complete the study. At any cost, in such circumstances the treatment will not be compromised.

Signature/Thumb impression of the participant:

Signature of the investigator:

Date :

Place :

NAME	AGE	SEX	SMOKING / BIOMASS EXPOSURE	WT IN KGS	DURATION OF ILLNESS	CREATININE	PT SEQUALE	DM	HYPER TENSION	PFT - DEGREE OF OBSTRUCTION	URINE PROTEINS	eGFR / CC (ml/min)
GUNASEKAR	48	M	PRESENT	44	3	0.6	NO			MILD OBSTRUCTION	NIL	93.7
RAJ	45	M	PRESENT	35	8	0.6	NO			SEVERE OBSTRUCTION	NIL	76.97
MURALI	45	M	PRESENT	33	5	0.6	NO			SEVERE OBSTRUCTION	NIL	80.21
NARAYANAN	75	M	PRESENT	32	20	1	NO			SEVERE OBSTRUCTION	NIL	28.89
RAMMOORTHY	45	M	PRESENT	29	4	0.6	NO			MILD OBSTRUCTION	NIL	63.77
KAMARAJ	58	M	PRESENT	48	8	0.6	NO			MILD OBSTRUCTION	NIL	91.11
CHITRALEKHAN	71	M	PRESENT	55	15	2	NO			SEVERE OBSTRUCTION	NIL	26.35
SRINIVASAN	50	M	PRESENT	40	7	0.6	NO			MILD OBSTRUCTION	NIL	83.33
MOHAN	45	M	PRESENT	39	5	1	NO			MILD OBSTRUCTION	NIL	51.46
RAMESH	58	M	PRESENT	35	16	0.6	NO			MILD OBSTRUCTION	NIL	66.44
SHANMUGAM	70	M	PRESENT	45	20	0.8	NO			MILD OBSTRUCTION	NIL	55
PANNEER SELVAM	64	M	PRESENT	30	10	1	NO			SEVERE OBSTRUCTION	NIL	32
GURUSWAMY	67	M	PRESENT	35	12	1.3	YES			SEVERE OBSTRUCTION	NIL	27
PRAKASH	65	M	PRESENT	49	15	1	YES			MILD OBSTRUCTION	NIL	60
MOHAN	46	M	PRESENT	35	6	0.6	YES			MODERATE OBSTRUCTION	NIL	76
MURUGESH	53	M	PRESENT	50	5	0.6	YES		HYPER TENSION	MILD OBSTRUCTION	NIL	101
RAJA	43	M	PRESENT	40	5	0.6	YES			MILD OBSTRUCTION	NIL	90
GAJENDRAN	72	M	PRESENT	53	15	1	YES			MILD OBSTRUCTION	NIL	50
NATRAJAN	62	M	PRESENT	44	11	1.2	YES			MILD OBSTRUCTION	NIL	40
GLORY SELVAMANI	65	F	PRESENT	45	8	1	YES	DM	HYPER TENSION	MILD OBSTRUCTION	NIL	40
PREMA	60	F	PRESENT	30	10	0.8	YES			MILD OBSTRUCTION	NIL	35
MAHESWARI	55	F	PRESENT	45	5	1	YES			MILD OBSTRUCTION	NIL	45
AMUDHA	55	F	PRESENT	38	7	0.6	YES			MODERATE OBSTRUCTION	NIL	64
SUBRAMANI	75	M	PRESENT	40	10	0.8	NO			MODERATE OBSTRUCTION	NIL	45
VELU	44	M	PRESENT	35	5	0.6	YES		HYPER TENSION	MILD OBSTRUCTION	NIL	78

ARUMUGAM	60	M	PRESENT	45	18	1.3	YES			SEVERE OBSTRUCTION	NIL	38
VELU	42	M	PRESENT	40	3	0.6	NO			MILD OBSTRUCTION	NIL	90.74
SELVAM	72	M	PRESENT	42	16	1	NO			MODERATE OBSTRUCTION	NIL	39.67
SUBRAMANIAM	60	M	PRESENT	38	10	1	NO			MILD OBSTRUCTION	NIL	42.2
NAGAMUTHU	68	M	PRESENT	45	8	0.8	NO	DM		MILD OBSTRUCTION	NIL	56.25
MURALI .T	58	M	PRESENT	44	5	0.6	NO			MODERATE OBSTRUCTION	NIL	83.52
RAJENDRAN	56	M	PRESENT	39	6	0.6	YES			SEVERE OBSTRUCTION	NIL	75.83
THIRUNAVUKKARAS	83	M	PRESENT	45	15	1	NO			SEVERE OBSTRUCTION	NIL	35.63
KOTTESWARI	63	F	PRESENT	73	10	0.9	YES	DM	HYPER TENSION	MILD OBSTRUCTION	NIL	86.74
ARUMUGAM	60	M	PRESENT	34	12	0.8	NO			SEVERE OBSTRUCTION	NIL	47.22
GANESHAN	70	M	PRESENT	60	20	1.1	NO			SEVERE OBSTRUCTION	NIL	53.03
KABALI	55	M	PRESENT	30	5	0.7	YES			MILD OBSTRUCTION	NIL	50.6
KULLAMMAL	84	F	PRESENT	40	16	0.9	NO			SEVERE OBSTRUCTION	NIL	34.57
SABUL HAMEED	60	F	PRESENT	55	10	0.6	NO			MILD OBSTRUCTION	NIL	101.85
MANI	62	F	PRESENT	64	20	1.2	NO			MODERATE OBSTRUCTION	NIL	57.8
RABIYA	51	F	PRESENT	60	8	0.9	NO			MILD OBSTRUCTION	NIL	70
JAYA	62	F	PRESENT	54	10	0.6	NO			MILD OBSTRUCTION	NIL	101.9
THANIKACHALAM	65	M	PRESENT	65	15	0.9	NO			MILD OBSTRUCTION	NIL	69.4
SUBBAMMAL	70	F	PRESENT	35	15	0.8	NO			MODERATE OBSTRUCTION	NIL	49.6
MARIAMMAL	55	F	PRESENT	45	5	0.6	NO	DM		MILD OBSTRUCTION	NIL	75.3
KAVIN	66	M	PRESENT	55	16	1	YES			MILD OBSTRUCTION	NIL	56.5
AMRUDHIN	64	M	PRESENT	55	20	1.3	NO			MILD OBSTRUCTION	NIL	44.7
CHERAN	55	M	PRESENT	40	12	0.9	NO			MILD OBSTRUCTION	NIL	52.5
DHARANI	65	M	PRESENT	39	10	0.7	NO			MILD OBSTRUCTION	NIL	52.1
PARTIBAN	45	M	PRESENT	30	6	0.5	YES			MILD OBSTRUCTION	NIL	79.2
SIRANUJA	55	F	PRESENT	30	5	0.8	NO			SEVERE OBSTRUCTION	NIL	37.6
DHAVOOD	56	M	PRESENT	30	17	1.3	YES			SEVERE OBSTRUCTION	NIL	26.92
RAJENDRAN	59	M	PRESENT	35	13	1	YES			SEVERE OBSTRUCTION	NIL	39.38
DAMODHARAN	68	M	PRESENT	40	12	0.7	NO			MILD OBSTRUCTION	NIL	57.1
MUNIRATHNAM	64	M	PRESENT	69	10	0.6	YES			MILD OBSTRUCTION	NIL	121.4
SHANMUGAM	70	M	PRESENT	45	15	0.9	NO			MODERATE OBSTRUCTION	NIL	48.61
RAJAMANIKKAM	62	M	PRESENT	54	7	0.9	NO		HYPER TENSION	MILD OBSTRUCTION	NIL	65

ARTHUR	58	M	PRESENT	65	8	0.5	NO			MILD OBSTRUCTION	NIL	148.5
THAMBIDURAI	40	M	PRESENT	65	2	0.9	NO			MILD OBSTRUCTION	NIL	94.3
JOTHI	63	M	PRESENT	55	15	0.9	NO			MILD OBSTRUCTION	NIL	65.4
KESAVAN	71	M	PRESENT	60	12	1	NO			MODERATE OBSTRUCTION	NIL	57.5
THIRUMURUGAN	65	M	PRESENT	45	9	0.5	NO			MILD OBSTRUCTION	NIL	93.8
RUKMANI	79	F	PRESENT	40	18	1	NO			SEVERE OBSTRUCTION	NIL	23.8
LOGANATHAN	60	M	PRESENT	60	16	0.9	NO			MILD OBSTRUCTION	NIL	74.9
RAJENDRAN	65	M	PRESENT	55	10	0.8	YES			MILD OBSTRUCTION	NIL	71.6
THANGAVEL	58	M	PRESENT	55	11	0.6	YES			MILD OBSTRUCTION	NIL	104.4
SOLAI	55	M	PRESENT	55	8	0.8	NO			MILD OBSTRUCTION	NIL	81.2
PATTAMMAL	65	F	PRESENT	65	7	0.7	YES		HYPER TENSION	MILD OBSTRUCTION	NIL	82.2
RAJARAJAN	60	M	PRESENT	60	18	1.1	NO	DM		MILD OBSTRUCTION	NIL	60.6
KOSAMMAL	45	F	PRESENT	70	5	0.8	YES			MILD OBSTRUCTION	NIL	115.45
KANNAN	53	M	PRESENT	60	8	0.6	YES	DM		MILD OBSTRUCTION	NIL	120.8
JAYAKUMAR	72	M	PRESENT	40	15	1.2	NO	DM		MILD OBSTRUCTION	NIL	41.98
SRIMATHI	49	F	PRESENT	45	4	0.5	NO			MILD OBSTRUCTION	NIL	96.7
RANI	55	F	PRESENT	60	8	0.5	NO			MILD OBSTRUCTION	NIL	120.4
ABDHULLAH	55	M	PRESENT	50	10	0.9	NO			MODERATE OBSTRUCTION	NIL	65.6
NATRAJAN	76	M	PRESENT	60	18	1	NO			MILD OBSTRUCTION	NIL	53.33
RAJARAM	65	M	PRESENT	45	14	0.8	NO			MILD OBSTRUCTION	NIL	58.6
VASU	57	M	PRESENT	53	8	0.8	YES			MILD OBSTRUCTION	NIL	76.4
SAMPATH	60	M	PRESENT	64	15	0.9	NO			MILD OBSTRUCTION	NIL	79
SAKUNTHALA	79	F	PRESENT	43	20	1.1	NO			SEVERE OBSTRUCTION	NIL	33.12
KRISHNAN	53	M	PRESENT	45	7	0.7	NO			MODERATE OBSTRUCTION	NIL	77.7
MOHAN	68	M	PRESENT	45	12	1	YES		HYPER TENSION	MODERATE OBSTRUCTION	NIL	45
SARADHA	57	F	PRESENT	45	13	0.9	YES			MODERATE OBSTRUCTION	NIL	49
SAROJA	60	F	PRESENT	45	15	1.1	YES			SEVERE OBSTRUCTION	NIL	38.6
LYKATH ALI	60	M	PRESENT	65	14	1	YES			MODERATE OBSTRUCTION	NIL	72.2
KANAGAIAH	70	M	PRESENT	65	20	1.2	YES	DM		MODERATE OBSTRUCTION	NIL	52.7
RAJA	53	M	PRESENT	62	12	0.5	YES			MILD OBSTRUCTION	NIL	149.8
RAMUZA	47	F	PRESENT	30	5	0.6	YES			MODERATE OBSTRUCTION	NIL	54.9
MURUGESAN	60	M	PRESENT	55	6	0.5	YES			MILD OBSTRUCTION	NIL	122.2

PERUMAL	55	M	PRESENT	65	8	0.8	YES			MILD OBSTRUCTION	NIL	95.9
SYED AHMED	71	M	PRESENT	60	14	0.9	YES		HYPER TENSION	MILD OBSTRUCTION	NIL	63.9
DHANAPAL	62	M	PRESENT	65	12	0.6	YES			MILD OBSTRUCTION	NIL	117.4
AUSTAN	60	M	PRESENT	60	8	0.8	NO	DM		MODERATE OBSTRUCTION	NIL	83.3
MADHI HUSSAIN	86	M	PRESENT	54	25	1.2	NO			SEVERE OBSTRUCTION	NIL	33.75
MOHD.ALI	60	M	PRESENT	45	18	0.8	YES			MILD OBSTRUCTION	NIL	62.5
PALANIVEL	80	M	PRESENT	50	16	1.1	NO			SEVERE OBSTRUCTION	NIL	37.88
SUBRAMANI	70	M	PRESENT	45	20	1.6	NO			MODERATE OBSTRUCTION	NIL	27.34
DESAPPAN	43	M	PRESENT	40	5	0.7	NO			MODERATE OBSTRUCTION	NIL	76.98
ARUMUGAM	56	M	PRESENT	43	5	0.9	YES	DM		MODERATE OBSTRUCTION	NIL	55.7
KUPPU	65	F	PRESENT	37	8	0.9	NO			SEVERE OBSTRUCTION	NIL	36.4
NIJAMUDHIN	70	M	PRESENT	59	15	0.9	YES			MILD OBSTRUCTION	NIL	63.73
KULLAN	70	M	PRESENT	45	20	0.9	NO			SEVERE OBSTRUCTION	NIL	48.61
ANNAMALAI	65	M	PRESENT	52	12	0.86	NO			MILD OBSTRUCTION	NIL	67.7
DHANALAKSHMI	60	F	PRESENT	51	14	0.7	NO			MILD OBSTRUCTION	NIL	81
MUTHAMMAL	60	F	PRESENT	48	12	0.8	NO			MILD OBSTRUCTION	NIL	56.7
KANNAYIRAM	68	M	PRESENT	57	15	0.8	NO			MILD OBSTRUCTION	NIL	71.3
ALLIS	82	F	PRESENT	40	20	0.8	NO			SEVERE OBSTRUCTION	NIL	34.2
FAKRUDHIN	87	M	PRESENT	58	15	1.1	YES			SEVERE OBSTRUCTION	NIL	38.8
ANTHONY DAS	47	M	PRESENT	64	7	0.8	NO			MILD OBSTRUCTION	NIL	103.33
KANNIYAMMAL	60	F	PRESENT	52	11	0.8	NO			MODERATE OBSTRUCTION	NIL	61.4
MADHAVAN	67	M	PRESENT	47	12	0.7	NO	DM	HYPER TENSION	MODERATE OBSTRUCTION	NIL	68.1
RAMASAMY	53	M	PRESENT	43	3	0.6	NO			MODERATE OBSTRUCTION	NIL	86.6
RAMANADHAN	70	M	PRESENT	47	15	1.4	NO			MILD OBSTRUCTION	NIL	32.64
THANGAM	55	F	PRESENT	52	5	0.6	YES		HYPER TENSION	MODERATE OBSTRUCTION	NIL	87
MURUGESAN	60	M	PRESENT	38	6	0.6	NO			MILD OBSTRUCTION	NIL	70.4
SELVARAJ	45	M	PRESENT	47	2	0.5	NO			MILD OBSTRUCTION	NIL	124
VELUMANI	65	M	PRESENT	36	12	1	NO			SEVERE OBSTRUCTION	NIL	37.5
JAYARAMAN	48	M	PRESENT	68	6	0.8	NO			MILD OBSTRUCTION	NIL	108.6
SRINIVASAN	84	M	PRESENT	44	21	1.2	YES		HYPER TENSION	SEVERE OBSTRUCTION	NIL	28.52

PUGALENDHI	50	M	PRESENT	34	5	0.6	NO			MILD OBSTRUCTION	NIL	70.83
RANI	60	F	PRESENT	51	7	0.7	YES			MILD OBSTRUCTION	NIL	81
SRINIVASAN	53	M	PRESENT	36	11	0.8	NO			MODERATE OBSTRUCTION	NIL	54.4
SAKTHI	56	F	PRESENT	49	8	0.8	NO	DM		MODERATE OBSTRUCTION	NIL	60.7
PARTIBAN	70	M	PRESENT	47	28	0.8	YES			MODERATE OBSTRUCTION	NIL	57.12
INDHRADEVI	65	F	PRESENT	46	20	1.5	NO			SEVERE OBSTRUCTION	NIL	31.94
VIJAYA	54	F	PRESENT	45	12	1	NO			SEVERE OBSTRUCTION	NIL	45.7
PALANISAMY	68	M	PRESENT	59	18	1.1	NO			MODERATE OBSTRUCTION	NIL	53.6
GOVINDHARAJ	70	M	PRESENT	44	20	1.1	NO			SEVERE OBSTRUCTION	NIL	38.9
SINGARAVELAN	70	M	PRESENT	41	18	1.2	NO			SEVERE OBSTRUCTION	NIL	33.2
SUBEDHA	55	F	PRESENT	38	8	0.8	NO			SEVERE OBSTRUCTION	NIL	47.7
SELVAM	48	M	PRESENT	39	4	0.6	NO			MILD OBSTRUCTION	NIL	83.1
KOKILA	40	F	PRESENT	43	6	0.5	NO			MILD OBSTRUCTION	NIL	101.5
PALANI	60	M	PRESENT	52	15	0.7	NO			MILD OBSTRUCTION	NIL	82.5
SELLADURAI	65	M	PRESENT	64	12	0.8	YES			MILD OBSTRUCTION	NIL	83.3
MUNUSAMY	68	M	PRESENT	47	10	0.9	YES	DM		MODERATE OBSTRUCTION	NIL	52.2
JAYAKUMAR	62	M	PRESENT	38	12	1.1	NO			SEVERE OBSTRUCTION	NIL	37.4
PERUMAL	80	M	PRESENT	55	18	1	NO			MODERATE OBSTRUCTION	NIL	45.8
SAMSUDHIN	76	M	PRESENT	53	16	1.3	NO			SEVERE OBSTRUCTION	NIL	36.2
SUNDHAR	45	M	PRESENT	47	4	0.8	NO			MILD OBSTRUCTION	NIL	77.5
MUTHUSAMY	48	M	PRESENT	33	6	0.6	NO			MILD OBSTRUCTION	NIL	70.3
ELUMALAI	81	M	PRESENT	40	20	1.5	NO			SEVERE OBSTRUCTION	NIL	21.85
VISHWANATH	55	M	PRESENT	45	12	1	NO			MODERATE OBSTRUCTION	NIL	53.1
RAJENDRA PRASADH	45	M	PRESENT	50	10	0.8	NO			MODERATE OBSTRUCTION	NIL	82.5
RAJAMANI	52	F	PRESENT	48	15	0.7	NO			SEVERE OBSTRUCTION	NIL	71.2
VEDAVALLI	60	F	PRESENT	40	20	1.1	NO			SEVERE OBSTRUCTION	NIL	34.3
MANJUNATH	70	M	PRESENT	56	22	1	NO			SEVERE OBSTRUCTION	NIL	54.4

Title: TO STUDY THE PREVALENCE OF RENAL FUNCTION DEFECTS IN COPD PATIENTS USING CREATININE CLEARANCE AND URINE PROTEIN ANALYSIS

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INTRODUCTION: COPD a major concern of the developing world has been associated with a number of comorbidities . Hypoxia and Renin angiotensin activation induced renal injury is an unexplored area of concern .

AIM AND OBJECTIVE: To estimate the level of renal function defects in COPD patients using creatine clearance by cockcroft gault equation and urine protein analysis.

MATERIALS AND METHODS:Over a period of 1 year , a cross sectional study done among COPD patients by calculating creatinine clearance using cockcroft gault equation . RFT values were calculted among newly diagnosed and previously diagnosed COPD patients as per GOLD guidelines. From RFT , Creatinine Clearance is calculated using cockcroft gault equation.

RESULTS: Creatinine clearance was calculated among 146 patients and found to be significantly reduced with a prevalence of 81% , overt renal failure of 7% , concealed renal failure of 34.9% . Risk of renal failure using different range of creatinine clearance values has been tabulated .

LIMITATION : Normal group is not compared . Includes Diabetic and hypertensive sub population .

CONCLUSION: Renal function is impaired in COPD patients .

REFERENCES:

1. Prevalence of concealed and overt chronic renal failure in patients with COPD Author links open overlay panelAbdelsadek H.Al-AaragaGehan F.Al-MehyaOsama I.MohammadaRasha M.HendyaShymaa M.TawfikaMahmoud H.ImambaChest Department, Faculty of Medicine, Benha University, EgyptbGeneral Medicine Department, Faculty of Medicine, Benha University, Egypt.

Keywords: RFT,COPD,CREATININECLEARANCE.