BACTERIAL FLORA OF SPUTUM, ITS ANTIBIOGRAM AND ITS RELATIONSHIP WITH SEVERITY OF COPD IN PATIENTS WITH ACUTE EXACERBATION – A HOSPITAL BASED STUDY IN A TERTIARY CARE HOSPITAL

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CERTIFICATE FROM THE DEAN

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Dr. M.R.VAIRAMUTHU RAJU, MD.
THE DEAN,
Madurai Medical College,
Madurai.

CERTIFICATE FROM THE HOD

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DR.V.T. PREM KUMAR, M.D.,

Professor and HOD,
Department Of General Medicine,
Government Rajaji Hospital,
Madurai Medical College,
Madurai.

CERTIFICATE FROM THE GUIDE

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DR.R.PRABHAKARAN,M.D.,

Professor of Medicine ,
Department Of General Medicine,
Government Rajaji Hospital,
Madurai Medical College,
Madurai

DECLARATION

I, **Dr.S. RADHAKRISHNAN** declare that, I carried out this work on "**BACTERIAL FLORA OF SPUTUM, ITS ANTIBIOGRAM AND ITS RELATIONSHIP WITH SEVERITY OF COPD IN PATIENTS WITH ACUTE EXACERBATION – A HOSPITAL BASED STUDY IN A TERTIARY CARE HOSPITAL''** at the Department of Medicine, Govt. Rajaji Hospital during the period **NOVEMBER 2015 TO APRIL 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 or 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 **M.D Degree General Medicine Branch- I**; examination to be held in **April 2017.**

Place:Madurai

Dr.S. RADHAKRISHNAN

Date :

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CONTENTS

INTRODUCTION

In India, COPD is the second most common lung disorder after pulmonary tuberculosis. The disease frequently encountered in middle aged patients and also has increasing public health importance around the world. Estimate suggest that COPD will rise from the 6th to the 3rd most common cause of death worldwide by 2020**.**

Emphysema of any pathogenesis nearly always due to chronic obstructive pulmonary disease and rarely due to alpha 1 antitrypsin deficiency produce a state of abnormal lung hyperinflation .

Alteration produced in bronchial epithelium by the damaging action of smoking favour bacterial adhesion and colonization .In turn , airway colonization and chronic infections contribute to progressive pulmonary damage via the action of pro inflammatory substances in what is known as ‘’vicious circle theory’’.

Exacerbations mostly of infective etiology are a frequent cause of morbidity in COPD patients . Recent epidemiological study observed that ambulatory patients with moderate to severe COPD suffered an average of two episodes per year and require medical attention and engendered widespread prescription of antibiotics.

Bacterial isolates in acute exacerbation of COPD may vary depending on the geographical area, prevalence of bacteria in the community and hospital setting. So it is important to carry out community based as well as hospital based studies to determine the empirical antibiotic therapy as appropriate early antibiotic therapy in acute exacerbation of COPD will decrease the morbidity and mortality in these patients.

Over 90% of patients with acute exacerbation of COPD are treated with antibiotics, although the effectiveness of many is uncertain because of the emergence of resistant strains of most common respiratory pathogens in past 15 years .The acute exacerbations contribute to irreversible progression of disease. Hence, timely institution of correct management is imperative for the better prognosis.

This study is conducted to find out the bacteriological profile, its antibiotic sensitivity pattern and its correlation with severity of COPD in patients with acute exacerbation.

AIMS AND OBJECTIVES

TO FIND OUT THE BACTERIAL FLORA OF SPUTUM, ITS ANTIBIOGRAM AND ITS RELATIONSHIP WITH SEVERITY OF COPD IN PATIENTS WITH ACUTE EXACERBATION.

REVIEW OF LITERATURE

DEFINTION:

Chronic obstructive pulmonary disease is characterised by persistent airflow limitation that is not fully reversible ,usually progressive and associated with a chronic Inflammatory response in the airway and the lung to noxious particles or gases**.**

COPD encompasses two broad categories which includes chronic bronchitis and emphysema. By definition, chronic bronchitis is characterized by three months of chronic cough with expectoration for more than two years. Emphysema is denoted as abnormal distension of the air spaces, permanent which is distal to the terminal bronchioles with destruction of their walls without any obvious fibrosis.

EPIDEMIOLOGY

In India, common lung disorder next to the pulmonary tuberculosis is COPD. It is encountered mainly in the fourth decade. It has an equal incidence among peoples living in both rural and urban areas. COPD manifestation is rare below the age of 35 years.

RISK FACTORS

1) Tobacco smoking

2) Air pollution

3) Familial and Genetic factors

4) Recurrent respiratory tract infection in childhood

5) Occupational hazards due to inhalation of noxious fumes or organic or inorganic dust

Tobacco Smoking

It is the most predominant risk factor associated with a progression of COPD. It mainly contains vapourised chemicals and some noxious particulates which are suspended in the gaseous medium. Tobacco smoked is directly proportional to the cumulative amount, which are the culprit for the adverse effects. Pack years and smoking index are the most vital parameters which are used for categorizing the smoking exposure and possibility of the disease outcome.

Sustained and chronic cigarette smokers are more susceptible due to impaired ciliary movement, increased goblet cell secretion with hypertrophy of the respiratory secretory epithelium. Reid index is a well known pathological index used to assess the severity of the chronic bronchitis. It is

a ratio between the thickness of the mucus gland layer and the wall thickness which is between the cartilage and the epithelium.

Passive smoking and inhalation of environmental noxious fumes resulted in the deterioration of the pulmonary function. But their role in the manifestation of COPD remains uncertain.

Pack years	Number of packs of cigarettes smoked	X	Number of years of smoking
Smoking index	Number of cigarettes smoked per day	X	Number of years of smoking

AIR POLLUTION

It is a known fact, industrialized urban areas are prevalent in COPD patients. The heavy air pollutants includes mainly sulphur dioxide and wooden logs used for cooking, indoor pollution made by burning of cow dung cakes. Ambient air pollution in metropolitan cities has been frequently implicated as a causative agent for various respiratory diseases including COPD, especially in Asian countries.

PULMONARY TUBERCULOSIS:

The association of pulmonary tuberculosis with COPD has occasionally been described. The prevalence of airflow obstruction varies from 28 to 68% of patients with treated pulmonary tuberculosis.

ASTHMA:

Patients with active asthma were found to have 10-fold increased risk of chronic bronchitis and 17-fold increased risk of emphysema as compared to those without asthma even after adjustment for confounding factors. A subsequent review also suggests that a subset of patients with asthma may have COPD phenotype.

MISCELLANEOUS FACTORS

An increased association of COPD is reported with demographic and socioeconomic factors such as advancing age, low socioeconomic status, and urban residence with lower socioeconomic status. This association may perhaps be attributed to the greater prevalence of smoking and cumulative effects of smoking and other exposures with age. Low socioeconomic status and infections have been listed as additional risk factors.

OCCUPATIONAL HAZARDS

COPD is more prevalent among peoples who are working in an area where organic or inorganic or noxious fumes are rich in the atmosphere.

RECURRENT RESPIRATORY INFECTION IN CHILDHOOD

Precipitating infections are the main culprit for acute exacerbation in a chronic background of obstructive pulmonary disease. It is a factor which resulted in a significant increase in the morbidity and mortality. Release of enzymes from the first line defence mechanism known cells mainly the neutrophils contributes to the extensive lung damage. Viral respiratory infections in the infancy are the main culprits in causing airway obstruction in the later life

GENETIC MECHANISM

Studies have suggested monozygotic twins are prone to develop chronic bronchitis due to genetic predisposition and other mechanisms.

Alpha 1 antitrypsin is a serine protease inhibitor. It is an acute phase reactant. Its serum level rises in many inflammatory conditions. In homozygotes , during inflammatory conditions serum level will not rise. Alpha 1 antitrypsin deficiency in COPD patients is one to two percent. The level rises to 50 percent in very severe disease, usually affects younger age group. Alpha 1 antitrypsin inhibits elastase, collagenase and several other enzymes which help in protection of lung in clearing the secretions and prevention of infections. Alpha 1 antitrypsin deficiency is the strongest genetic factor in development of chronic obstructive pulmonary disease especially emphysema. Emphysema predominantly involve lower lobes of

the lungs, which is usually panlobular or pan acinar ; but in smokers it affects the upper lobe and it is of centrilobular or centriacinar type Protease inhibitors variants that encode alpha 1 antitrypsin have been recognized .Two alleles such as S allele and Z allele are associated with reduced and markedly reduced alpha 1 antitrypsin levels respectively.

Treatment with alpha 1 antitrypsin augmentation therapy is available in recent times. Linkage analysis of earlier onset disease among family members have evidenced various spirometric variations linked to appropriate regions of the chromosomes. Determinants of specific genetic coding regions yet to be identified.

PATHOLOGY OF COPD

In the spectrum of chronic bronchitis, there is hypertrophy of the glands which secrete mucus in the respiratory epithelium.. In COPD the major site for obstruction is airways which are smaller. Inflammatory cells predominantly neutrophils accumulated in the sub mucosa and the mucosal regions of the epithelium.Fibrosis involving the peribronchus and the accumulation of mucus plug in the intralumen of the bronchus also contributes to the pathology.

Emphysema is classified according to the involvement of regions distal to the Terminal bronchiole. Panacinar, as the name signifies the involvement of whole acinus involving central and peripheral portions. In centriacinar , region involving the respiratory bronchioles without involving the periphery. Another entity known As paraseptal involving the airspaces at the lobule periphery nearer to the pleura. Irregular pattern almost associated with scarring. It is frequently associated with pulmonary tuberculosis.

PATHOPHYSIOLOGY OF COPD

Two determinants of COPD, which encompasses chronic bronchitis and emphysema, they frequently coexist each other. There may be domination of one determinant over the other. Narrowing of the airway is a common pathology associated with both entity. Besides basic pathology in the

airways in chronic bronchitis , elastic recoiling capacity of lung alveoli in emphysema is lost. Increased work of breathing experienced by COPD patients are due to alteration in the pressure and airflow pattern.

Spirometry helps to determine the major lung function parameters such as **FVC** and **FEV1**. In COPD patients, alteration in the **FEV1/FVC ratio** and reduction in the FEV1 contributes towards the major morbidity. Responsiveness to the inhaled bronchodilators is maximum with COPD compared to asthma.

Imbalance between the elastic recoil of the alveolar sac and resistance offered by the airway towards the airflow determines the reduction in FEV1 and FEV1/FVC.

Residual volume and increase in the ratio of residual volume to total lung capacity, is mainly due to trapping of air. Total lung capacity is increased resulting in hyperinflation of lung which is a late manifestation of COPD.

Hyperinflation preserves airflow during peak expiration. It is due to increase in the lung volume which increases the elastic recoiling pressure. It results in the enlargement of airway which decreases the resistance of the airway. Hyperinflation is the compensatory mechanism to relieve the airway obstruction. However flattened position of the diaphragm resulted in the various adverse effects. The opposition zone between the abdominal wall and diaphragm is decreased, ineffective abdominal pressure during

inspiration to the chest wall is not applied. Abnormal movement due to hindering ribcage and it impairs the inspiration.

Muscle fibers of the flattened diaphragm are abnormally shorter than the normal diaphragm, resulting in the less capability of inspiratory pressures.

According to Laplace's law , p=2t/r.

p=trans pulmonary pressure producing the tidal breathing.

t=tension gradient of the flattened diaphragm

r=radius of the curvature

The flattened diaphragm has to generate tension to overcome the transpulmonary pressure to generate normal tidal breathing.

In COPD, partial pressure of oxygen is not altered until FEV1 is reduced to 50%. Cardiac abnormality such as pulmonary hypertension resulting in right ventricular failure and cor pulmonale features occurs mainly in individuals with FEV1 less than 25% of predicted value with reduction in the partial pressure of oxygen(less than 55mm of hg).

Mismatch between perfusion-ventilation and disproportionate ventilation are the penultimate features of COPD. It reflects the diverse pathological process within the parenchyma and the smaller bronchi. Mismatch between ventilation and perfusion resulted in reduction of partial pressure of oxygen.

PATHOGENESIS:

Alteration in the airflow due to obstruction in the smaller airway and emphysema is the major pathological sequence in COPD. Smaller airways surrounded by fibrosis contributes to the significant morbidity and mortality.

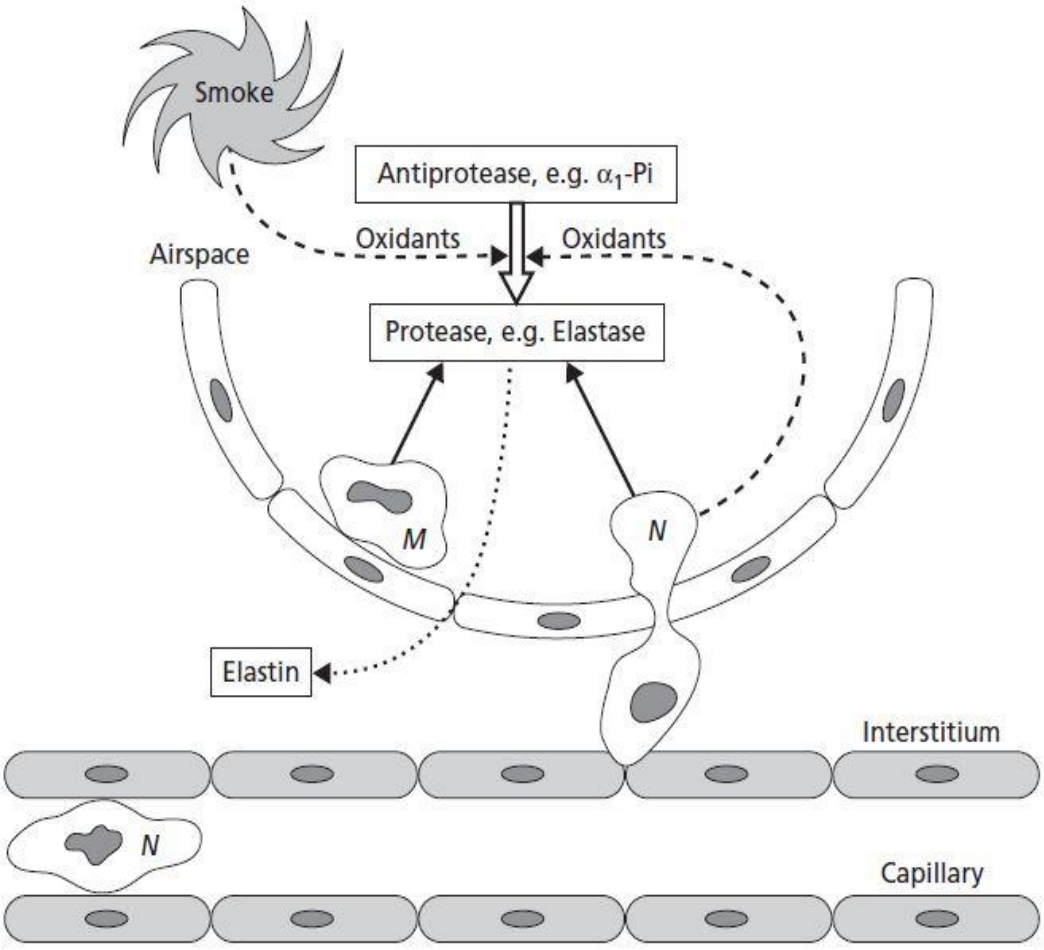
Collagenase activity increases during the pathogenesis in COPD. It is the major culprit resulting in accumulation of collagen surrounding the airway. Potential mechanism through which fibrosis is induced, by activation of fibrogenic cytokines predominantly growth factors such as TGF-BETA and IGF.

In emphysema pathogenesis is mainly due to recruitment of inflammatory cells in the distal air spaces due to chronic exposure to cigarette smoke. These cells damage the matrix of the lung parenchyma by releasing more potent proteinases which are elastolytic. The interaction between cell and the matrix is lost resulting in the apoptosis of the structural cells in the lung.

Extracellular matrix forms a integrity to the smaller airways and the lung parenchyma. It is offered mainly by elastin a predominant component of elastic fibers. The imbalance between degrading enzymes and inhibitors involved in elastin biology determines the abnormal permanent distension of air spaces.

Alpha 1 antitrypsin deficiency patients are more prone for emphysema due to lack in the inhibitor of neutrophil elastase.

Inactivation of Histone deacetylase2 resulted in the acetylated and more heterochromatin which exposes the transcription sites involving many proinflammatory cytokines resulting in recruitment of neutrophil. Cigarette smoke recruits the suppressor Tcells leading to production of macrophage elastase. Cleavage component of elastin acts as a signaling chemokine which traverse the destructive hypothesis.



Ciliary dysfunction caused by cigarette smoke traverse the fertile background for bacterial infection along with increase in neutrophill count. In final stage, there is an enormous inflammatory response suggesting that mechanisms of smoking induced disease differs from inflammation resulting after cessation of smoking.

The destructive collagenase are also induced by both structural and inflammatory cells. Finally the collagen content enormously increased resulting in the accumulation in the airways.

By degrading the matrix of lung parenchyma with defect in the cell anchoring leads to apoptosis. Reparative capacity of the damaged alveoli remains questionable.

Potential stimulus for constriction for pulmonary vasculature is hypoxia. Cross sectional area of pulmonary vasculature is reduced in COPD patients due to alteration in the vascular smooth musculature of artery and arteriole of pulmonary vessels. Acidosis and the polycythemia due to chronic hypoxia are the most notable events resulted in failure of right ventricle.

CLINICAL FEATURES

Useful physical signs in the diagnosis of COPD

Inspection:

Pursed-lip breathing

Use of accessory muscles of respiration

Jugular venous distension during expiration

Retraction of suprasternal, supraclavicular and intercostal spaces during inspiration

Short trachea

Pulsus paradoxus

Increased anteroposterior diameter of the chest (barrel-shaped chest)

Reduced chest movements

Peripheral edema

Dyspnea-relieving posture

Muscle wasting

Palpation:

Restricted chest expansion

Subxiphoid shift of maximum impulse of the heart

Percussion:

Chest hyperresonance

Obliteration of cardiac dullness

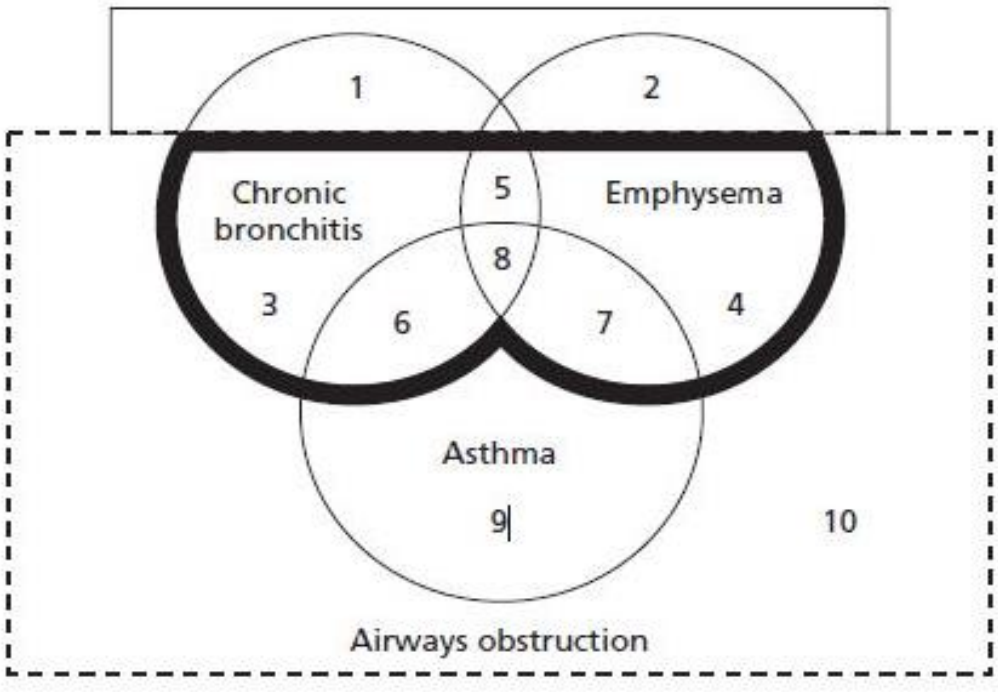
Lower level of liver dullness

Lower diaphragmatic levels

Auscultation:

Diminished breath sounds

Early inspiratory crackles



CHRONIC BRONCHITIS FEATURES:

Cough along with sputum production forms the mainstay of chronic bronchitis. History of chronic smoking is always present. Predominant cough during winter months is the earlier manifestation. Increase in the frequency of bronchial infection favours chronic bronchitis. Insufficient respiration occurs during acute exacerbation. Prominent bronchovascular

markings are pathognomonic feature in chronic bronchitis predominant COPD. Over weight and cyanosis picture favours the terminology '**BLUE BLOATERS'**. Crepitation and polyphonic wheeze with resonant lung is always associated. Incidence blood gas derangements such as hypoxia resulting in polycythaemia is common. Pulmonary vascular pathology and right sided heart failure are more prevalent in chronic bronchitis.

EMPHYSEMA FEATURES:

History of dyspnoea with minimal cough and scanty production of sputum is the main clinical feature of emphysema. The asthenic body build with evidence of loss of weight noted in the physical examination. The predominant usage of accessory muscles involved in respiration resulted in sternal lift in anterosuperior direction in each phase of inspiration. Tachypnea with prolonged expiratory phase through pursed lip is characteristic of emphysema. Leaning forward with extension of his arms to brace himself in sitting posture is known as tripod position. The intercostals spaces retract each other during each inspiration in the lower region of hemithorax which can be felt by palpation is known as hoover's sign. Apical impulse is usually visualized in the region between xiphoid and subxiphoid areas. Hyperresonant percussion note with absent or reduced cardiac dullness is a classical feature seen in COPD. The upper margin of liver is usually shifted to a lower level than the normal. Added sounds and abnormal air entry makes the clue to differentiate from normal variant –

compensatory emphysema. Since partial pressure of oxygen is maintained in emphysema, they are called as **PINK PUFFERS**. Gallop rhythm during presystole of the cardiac cycle is accentuated in the inspiratory phase of the respiration.

Since inflammatory cytokines such as tumor necrosis factor alpha is elevated resulting in malnutrition which is manifested as muscle wasting and it is an independent poor prognostic variable in COPD. Incidence of right sided heart failure and pulmonary hypertension is rare among emphysematous patients due to maintenance in the partial pressure of oxygen in normal range. Diffusing capacity with carbon monoxide used to differentiate chronic bronchitis and emphysema Decreased in emphysema and normal or slight variation in chronic bronchitis.

Advanced disease is manifested in form of universal wasting more predominantly in bitemporal areas. Digital Clubbing is usually not a significant finding in COPD.

Its presence should warrant an alternate pathology in lung parenchyma.

COPD ASSESSMENT:

It requires a confined stratification taking into account of all the factors. Four groups have been stratified by **GOLD GUIDELINES**

1) GROUP A- Low risk, less symptoms

2) GROUP B- low risk, more symptoms

3) GROUP C- high risk, less symptoms

4) GROUP D- high risk, more symptoms

Stage 3 or 4 with airflow limitation assessed by spirometry is given a label of high risk. Acute exacerbations more than 2 in no in the previous year are hospitalisation requiring exacerbations are also taken into account.

Symptoms are mainly assessed by

1) COPD Assessment Test

2) COPD Control questionare

3) Chronic respiratory questionare.

4) St George respiratory questionare.

Parameters which predicts the prognosis involves **BODE INDEX**

B- BODY MASS INDEX

O-OBSTRUCTION(Assessed by spirometry)

D-DYSPNOEA E-EXERCISE TOLERANCE

SPIROMETRY PARAMETERS

After post bronchodilator therapy , global initiative of lung disease have classified COPD using FEV1 as a major spirometry parameter.

>80% of the predicted- mild COPD.

50-80% of the predicted- moderate COPD

30%- 50% of the predicted- severe COPD

<30%- very severe COPD

Staging of COPD have been classified in similar manner from 1 to 4.

FEV1/FEC ratio of < 0.7 is also applicable.

COMORBIDITIES

1) Cardio Vascular Disorders

2) Skeletal muscle dysfunction

3) Nutritional deficiencies

4) Depression

5) Metabolic syndrome

6) Osteoporosis

7) Loss of body weight

8) Lung cancer

9) Hypercarbia related complications

AECOPD:

An acute exacerbation of COPD is an acute event characterized by sustained worsening of any of the patients respiratory symptoms (cough, sputum quantity and /or character,dyspnea) that is beyond normal day to day variation and leads to a change in medication , and where there other causes of acute breathlessness have been clinically excluded.

PRECIPITATING FACTORS:

Both infectious and non infectious precipitating factors have been implicated in AECOPD .

Infections are the most frequent cause of exacerbations .Both viral and bacterial infections have been detected during exacerbations.

H.influenza, Streptococcus pneumonia, Moraxella catarrhalis and Pseudomonas aeruginosa are strongly associated with the exacerbation.

Non infectious causes of exacerbation include non adherence to medication , inhalation of irritants like tobacco smoke or particles .Air pollution also the cause for AECOPD.

Conditions like heart failure, pulmonary embolism, cardiac arrhythmias, pneumothorax, pleural effusion, and pneumonia can cause acute worsening of symptoms in patients with COPD and are considered COPD exacerbation Mimics.

COPD is a progressive disease with a gradual decline in lung function. The course of COPD is however punctuated by exacerbations, some of which may be severe enough to cause hospitalizations; this may not only lead to increase in mortality, but is also associated with increased cost of treatment. Exacerbations are associated with a greater and irreversible decline in lung function.

The occurrence of a severe exacerbation requiring hospitalization increases the risk of further exacerbation. Patients have 25 times higher risk of readmission to hospital after the tenth hospitalization, as compared to the first hospitalization. In fact, there is five-fold increase in risk of death after tenth hospitalization.

Exacerbations are associated with progression of emphysema measured on serial CT scans. Moreover, exacerbations are associated with significant decline in Quality of life and add to the cumulative economic burden. The mortality is 40% at 1year in those requiring mechanical ventilation, and all-cause mortality may be as high as 49% at 3 years after hospitalization.

DIFFERENTIAL DIAGNOSIS OF AECOPD:

1) Pneumonia
2) Pulmonary embolism
3) Pneumothorax
4) Pleural effusion
5) Pulmonary edema
6) Paroxysmal atrial tachycardia (arrhythmias)

These need to be excluded in patients with acute worsening of breathlessness.

INVESTIGATIONS USED IN DIAGNOSING COPD

1) Spirometry

Spirometer consists of 11 parts.

1. Bell of the Spirometer

2. Paper speed selector

3. Paper

4. Pilot lamp

5. On/off power switch

6. Writing pen holder

7. Expiratory valve

8. Inspiratory valve

9. Bidirectional valve tap

10. Bell supporter

11. Pulley

PROCEDURE:

1. Fill three forth of the bell of the Spirometer with air or 100% oxygen.

2. Ask the subject to sit comfortably and relax.

3. Adjust the speed of the Spirometer at 60 mm/min.

4. Place a sterilized mouth piece in the subjects mouth in such a way that the mouth piece remain fitted between the teeth and lips.

5. Connect the mouth piece to the Spirometer.

6. Close the nostrils with the help of the nose clip.

7. Ask the subject to breathe in and out normally through the mouth; this is the Tidal volume.

8. Ask the subject to breathe in as much as possible after a normal expiration; this is the IRV; then also records a few normal breaths.

9. Ask the subject to exhale as much as he can after a normal inspiration to record ERV; and record a few normal breaths after that.

10. Ask the subject to breathe out forcefully with maximum effort possible after taking a deep inspiration; this records VC.

11. Calculate TV, IRV, ERV, VC and IC from these recordings (Height 1mm=30ml).

NORMAL VALUES OF PFT :

1. TV : 500ml

2. IRV : 3000ml

3. ERV : 1100ml

4. FVC : 4600ml

5. FEV1 : >80% of FVC

6. PEFR : 400-600L/min

7. RMV : 6000ml

8. MVV : 125-170L/min

9. Breathing reserve: 115-160L/min

10. Dyspneic index : >90%

Dyspneic index is also known as breathing reserve ratio (**BRR)**.

All lung volumes and capacities are about 15-25 % less in females. The values may be more in athlete's and tall persons and may be less in non-athlete and Asthenic persons.

FORCED VITAL CAPACITY (FVC):

FVC decreases in condition in which there is obstruction to the airways resulting in air trapping, for ex; bronchial asthma.

TIMED VITAL CAPACITY (FEV1):

FEV1 is the single most useful test to detect generalized airway obstruction. But this must be done properly to get the proper results, as it is effort dependent. This is also relatively non-specific in the sense that it gives the idea generalized obstruction (not specific for small airway obstruction).

FEV1 decreases in obstructive diseases of the lungs. Eg; bronchial asthma.

FEV1/FVC:

The ratio of FEV1 / FVC is approximately 0.75-0.80. This is more sensitive indicator of airway obstruction than FVC or FEV1 alone.

REVERSIBILITY TESTING IN COPD:

It has been traditionally believed that COPD patients do not show reversibility in airflow obstruction after administration of bronchodilators, and this concept was considered useful to differentiate COPD from asthma. Numerous studies have shown that patients with COPD may also show significant spirometric reversibility to bronchodilators. Besides, broncho-

dilator reversibility is not a variable that essentially signifies the presence of disease; it has also been demonstrated in healthy subjects.

Thus, reversibility testing does not help diagnosis of COPD. Also, lack of reversibility in COPD does not preclude a subsequent benefit from long-term maintenance bronchodilator therapy. Moreover, the response to ICS is not predicted by bronchodilator reversibility in COPD patients. Finally, bronchodilator reversibility varies temporally and does not correlate with clinically relevant outcomes such as mortality, hospitalization or exacerbation experience, making it an unreliable phenotype.

SCREENING SPIROMETRY:

Screening spirometry may help in detecting subjects with airflow obstruction before they develop clinical symptoms. This can be potentially beneficial in two ways: (a) diagnosis of COPD might improve smoking cessation rates, and (b) early treatment might alter disease prognosis. However, there is no conclusive evidence for either. Evidence for the notion that a diagnosis of COPD promotes smoking cessation is equivocal. Rather there is a conceivable risk that tobacco smokers informed to be having a normal lung function might be encouraged to continue smoking.

A post bronchodilator FEV1/ FVC < 0.7 confirms airway obstruction that is not completely reversible. Increased lung volumes may point to emphysema. PEFR is reduced, DLCO is normal or slightly reduced in patients with chronic bronchitis and severe reduction indicates associated

severe emphysema.

According to GOLD guidelines, patients have been categorised into mild (stage 1), moderate (stage 2), severe (stage 3) and very severe (stage 4) based on percentage predicted FEV1 of more than or equal to 80, 50 to 80, 30 to 50, <30 , respectively.

COPD- GOLD criteria

(BASED ON POST-BRONCHODILATOR FEV1)

GOLD Stage	SEVERITY	SPIROMETRY
I	Mild	FEV1/FVC<0.7 and FEV1 >80% predicted
II	Moderate	FEV1/FVC<0.7 and FEV1 >50% but <80% predicted
III	Severe	FEV1/FVC<0.7 and FEV1 >30% but <50% predicted
IV	Very Severe	FEV1/FVC<0.7 and FEV1 <30% predicted

Imaging –XRAY

Chest X-ray may be normal or show emphysematous changes. It is very useful in ruling out other differential diagnoses and in detecting complications of COPD, including life threatening ones like pneumothorax. Patients with chronic bronchitis may have thick bronchial walls which appear as tubular or tram track shadows with increased vascular markings.

Chest X-ray in symptomatic emphysematous patients reveals dark hyperlucent lung fields with decreased vascular markings,

characteristic bullae, flattened and pushed-down diaphragm and tube-like heart.

HRCT can readily detect emphysema but is not used routinely for the purpose of diagnosis. Contrast-enhanced computed tomography (CECT) chest may show a dilated pulmonary artery, indicating pulmonary hypertension.

- ✓ Bronchial wall thickening manifested by tramline shadows with dominant broncho vascular markings suggest chronic bronchitis.
- ✓ Hyperlucent lung fields with no peripheral vascular markings, emphysematous bullae, low level diaphragm, tubular heart suggest emphysema
- ✓ Dilated main pulmonary artery and its branches is more prominent when COPD progresses towards cor pulmonale.

3) DLCO-diffusion with carbon monoxide

4) 12 leads electrocardiogram

5) 2D echocardiography

6) Sputum examination

7) alpha1 antitrypsin level

DIFFERENTIAL DIAGNOSIS OF COPD:

Asthma

1) Early age of onset
2) Episodic symptoms with asymptomatic periods in between
3) Wide variation of symptoms day to day
4) Symptoms worse at night/early morning
5) Chronic productive cough is uncommon
6) History of atopy may be present
7) Family history of asthma may be present
8) Reversibility of airway obstruction
9) Increased diffusing capacity for carbon monoxide (DLCO)

Congestive heart failure

1) Cardiomegaly/pulmonary edema in chest X-ray
2) PFT suggestive of restrictive abnormality

Bronchiectasis

1) Copious purulent sputum
2) Clubbing, coarse crackles
3) HRCT shows bronchial dilatation and bronchial wall thickening

Tuberculosis

1) Fever, anorexia, weight loss
2) Chest X-ray opacity, fibrocavitary disease
3) Microbiological diagnosis

Constrictive bronchiolitis

1) Non-smoker, young age
2) History of rheumatoid arthritis, fume exposure, lung/bone marrow transplantation
3) HRCT shows mosaic attenuation

Diffuse panbronchiolitis

1) Non-smoker
2) Association with chronic sinusitis
3) HRCT shows centrilobular nodules, hyperinflation and air-trapping

INVESTIGATIONS IN AECOPD:

a)Pulse oximetry/Arterial blood gas analysis (wherever available) is helpful to confirm the diagnosis of acute, or acute on chronic, respiratory failure; and also assists in deciding supplemental oxygen therapy. As a general rule, a decline in PaO value by 10-15 mmHg suggests an acute deterioration in a patient with chronic respiratory failure.

b). Chest radiographs are worthwhile in excluding an alternative diagnosis like pneumonia, pneumothorax, pleural effusion, and others.

c). An electrocardiogram facilitates identification of coexisting cardiac abnormalities.

d)A complete blood count is useful in identifying anemia, polycythemia (hematocrit > 55%), and/or leukocytosis.

e). Blood biochemical tests aid in identifying coexisting electrolyte abnormalities or hepatic or renal dysfunction. The use of spirometry during an exacerbation is not recommended, as it can be difficult to perform and the results are inaccurate.

f.) Sputum cultures: Hemophilus influenzae, Streptococcus pneumoniae, and Moraxella catarrhalis are the most common bacterial pathogens involved in an exacerbation. In severe exacerbations requiring invasive ventilation, Pseudomonas aeruginosa is an important consideration, and sputum cultures may help in identifying the correct pathogen.

COMPLICATIONS OF COPD

1) Pneumothorax
2) Pulmonary artery hypertension
3) Polycythemia
4) Chronic cor pulmonale
5) Acute and chronic on chronic respiratory failure
6) Right sided heart failure
7) Recurrent episodes of acute exacerbations

POTENTIAL MARKERS USED IN PROGNOSIS AND EARLY DISEASE

1) ALPHA 1 ANTITRYPSIN deficiency
2) CFTR GENE mutation
3) MBL2 GENES
4) Fibrinogen, c reactive protein and other acute phase reactants during exacerbation.

POTENTIAL MEASURES TO REDUCE THE MORTALITY

Mortality in COPD can be reduced by following measures by

1. Cessation of smoking
2. Long term domiciliary oxygen therapy

SMOKING CESSATION

- ❖ PHARMACOLOGICAL MEASURES
- ❖ NICOTINE REPLACEMENT THERAPY

  Transdermal patch,Chewing gums, lozenges,Inhalers,Nasal spray

- ❖ NON NICOTINE PHARMACOTHERAPY

Bupropion 150 mg per day * 3 days followed by bd * 7 – 12 weeks.Drug should be started 1 week before quit date. Adverse effects of this drug are dizziness, headache, insomnia, nausea, xerostomia, hypertension, seizures. Avoid monoamine oxidase inhibitors to prevent serotonin syndrome.

Varenicline 0.5 mg per day * 3 days followed by bd * 4 days ,then 1 mg bd * 12-24 weeks.Start 1 week before quit date.

DOMICILIARY OXYGEN THERAPY

There are three forms of domiciliary supplementary oxygen therapy,

1.long term control oxygen therapy for atleast 15 hours daily in patients with chronic respiratory failure.

2.In exercise related hypoxemia portable oxygen therapy is supplemented.

3.Short term and short burst oxygen therapy as a palliative treatment for temporary relief of symptoms.

CRITERIA FOR LONG TERM OXYGEN THERAPY

1. Absolute indications – COPD , hypoxemia , edema , FEV1 < 1.5 L , FEC<2L , PaO2 < 55 mm hg , PaCO2 > 45 mm hg , P pulmonale > 3 mm in lead II ,III , aVF,pulmonary hypertension , corpulmonale , right ventricular hypertrophy, polycythemia with erythrocytosis with hematocrit > 56% , desaturation < 96% on exercise , refractory dyspnea associated with cardiac failure.
2. Relative indications – As mentioned above but without edema or PaCO2 >45mm hg.
3. Palliative

FEV1 is the strongest predictor of survival in long term oxygen therapy. It has been shown to affect the polycythemia which occurs during chronic hypoxemia. It reduces both hematocrit and red cell mass. However

with persistent smoking exposure which results in chronic elevation of carboxy hemoglobin decreases the effectiveness of long term oxygen therapy in correcting polycythemia. It showed a marked decrease in pulmonary artery pressure with breathing controlled oxygen therapy. It provides an evidence of improvement in cognitive function with little change in mood or quality of life. It showed a sustained improvement in exercise endurance in patients with COPD breathing supplemental oxygen. It is also associated with improvement in the sub maximal workrate ,with improvement in walking distance and ability to perform daily activities. With 6 months of long term oxygen therapy, there is a remarkable reduction in the mortality associated with COPD.

LONG TERM MANAGEMENT IN COPD

Bronchodilator therapy is the treatment to reduce the symptoms and increase exercise tolerance in COPD. The principle symptomatic bronchodilators can be divided into three groups based on their pharmacological properties.

1.Inhaled beta 2 agonists are preferred over oral preparations. It showed significant improvement in bronchodilation. In chronic bronchitis the decline in FEV1 was more rapid in those patients who used continuous beta 2 agonists.

2.Anticholinergics have time to peak effect of 30 to 60 minutes in most COPD patients , which is slower than beta 2 agonists but have a somewhat

longer time of effectiveness of 6 to 10 hours compared with beta 2 agonists. There is a conflicting evidence regarding the effects of ipratropium bromide on exercise in patients with COPD. It showed an increase in maximum exercise, ventilation and reduction in oxygen consumption at any given workload.

3.Theophyllines

The bronchodilator property of theophyllines is relatively limited in patients with COPD. Non bronchodilator effects of theophyllines such as improving right ventricular performance and their anti inflammatory actions are of questionable clinical significance. It has a narrow therapeutic index with experienced side effects. Theophylline metabolism is increased by cigarette smoking , anti convulsant drugs, rifampicin. Decreased by congestive cardiac failure , respiratory acidosis , liver cirrhosis , viral infection , old age, arterial hypoxemia , on drugs such as erythromycin , ciprofloxacin , cimetidine.

INHALED CORTICOSTEROID IN STABLE COPD:

ICS use decreased the risk of exacerbation and led to better quality of life and better FEV1 values in patients with severe COPD .However none of the study demonstrated any mortality benefit with ICS use. But it is mainly useful in COPD patients with more severe disease (FEV1<50%).

SIDE EFFECTS OF ICS:

1) Oropharangeal candidiasis
2) Hoarseness
3) Risk of pneumonia.

TRIPLE THERAPY:

The addition of Tiotropium to ICSs and LABA therapy may confer benefits in reducing all cause mortality, hospital admissions and oral corticosteroid bursts in COPD patients. Thus, triple therapy may be useful in patients with severe COPD FEV1(<50%) who are symptomatic despite single or dual bronchodilator therapy.

Oral methylxanthines can be used as an alternative in patients not taking inhalers for any reason or as an add-on therapy in patients continuing to have symptoms despite optimum inhaled therapy. Oral theophyilline given in low doses may augment the anti inflammatory effect of inhaled steroids.

ROLE OF PDE4 INHIBITORS IN STABLE COPD:

Roflumilast is an oral selective PDE4 inhibitor approved for the use in COPD patients. It is predominantly an anti-inflammatory agent rather than a bronchodilator. It is used to reduce exacerbations for patients with chronic bronchitis, severe and very severe COPD and frequent exacerbations that are not adequately controlled by long acting bronchodilators.

Dose : 500 micro gram once daily

Adverse effect : Gastrointestinal and weight loss.

CORTICOSTEROIDS

Chronic inflammation in large and small airways is a characteristic feature of COPD. The use of corticosteroids in COPD remains contentious particularly the prediction of which patients will respond to this treatment.

MANAGEMENT OF AECOPD:

SABA, with or without anticholinergic, are essential for symptomatic relief of airway obstruction, and constitute the first line of treatment.

There were no significant differences in FEV1 change in patients treated with beta-agonists or ipratropium bromide, and no additive benefit of adding ipratropium to beta-agonist. Also, the optimal dosing and frequency of bronchodilators in AECOPD is not established. There was no difference in clinical outcomes in patients treated every 4 hours with either 2.5 or 5 mg of nebulized salbutamol. There was also no significant difference in improvement in FEV 1between hourly and 20-min dosing of salbutamol.

The drugs can be delivered by the inhaled route either using pMDI with spacer or nebulizer. There is no significant difference in outcomes based on either method of administration.

In severe exacerbations, altered mental status favors the use of nebulized bronchodilators, while in others pMDI with spacer is preferred due to lower costs and lesser chances of infection. In any case, the patient should be switched over to pMDIs with spacer at the earliest. Importantly,

the drugs should not be nebulized using oxygen. Rather patients should receive supplemental oxygen separately through nasal prongs while nebulizing drugs using compressed air, with monitoring of oxygen saturation.

ROLE OF STEROIDS IN AECOPD:

The pathophysiology of AECOPD is due to severe inflammation triggered by infective and/or noninfective causes, and thus systemic corticosteroids have a role in managing this condition.

Systemic steroids shorten recovery time, improve lung function, oxygenation reduce length of hospital stay, and are associated with fewer treatment failures. A short course of oral prednisolone (or equivalent) at a dose of 30-40 mg/day is recommended for managing acute exacerbations. The duration of systemic steroid therapy should be 5-10 days. Intravenous steroids should be given in patients who are being mechanically ventilated or cannot tolerate oral medication. ICS are not routinely recommended in management of AECOPD.

ROLE OF ANTIBIOTICS IN AECOPD:

Infection is the common precipitating event in AECOPD. Antibiotics are used when there is increased dyspnoea, increase in sputum volume , increase in sputum purulence . Antibiotics should be prescribed for all exacerbations of COPD.

The choice of antibiotics should be guided by local flora and sensitivity pattern.

Fluoroquinolones should not be used routinely in treating AECOPD. Patients with AECOPD being managed in the outpatient setting may be treated with first line antibiotics.

Hospitalized patients or those requiring mechanical ventilation (noninvasive/invasive) should be treated with second line drugs. The duration of therapy should be 5-7 days.

The antibiotics that are used in managing AECOPD can be broadly classified as first-line (amoxicillin 500-1000 mg thrice a day for 5-7 days, doxycycline 100 mg twice a day for 5-7 days, azithromycin 500 mg once a day for 3 days) or second-line (amoxicillin/clavulanic acid 625 mg thrice a day for 5-7 days; second-generation or third-generation cephalosporins, e.g., cefixime 200 mg twice a day for 5-7 days).

Intravenous methylxanthines (theophylline or aminophylline) are considered second-line therapy, to be used only in select cases when there is insufficient response to short-acting bronchodilators. Current evidence does not favor routine use of methylxanthines in AECOPD.

NON INVASIVE POSITIVE PRESSURE VENTILATION:

Currently it is preferred for patient with COPD requiring mechanical ventilator support for reason like

1) Discomfort to the patient is very less
2) Less risk of infections
3) It counter balances the disadvantage of PSV and CPAP when used alone .

INDICATIONS FOR NIPPV INCLUDES:

1) Severe dyspnoea
2) Respiratory acidosis

INDICATION FOR INVASIVE MECHANICAL VENTILATION:

1) Non invasive positive pressure ventilation failure
2) Severe bradycardia
3) Cardiac and or respiratory arrest
4) Severe tachypnea
5) Uncontrolled respiratory secretions
6) Hemodynamic instability
7) Aspiration
8) Altered consciousness

PULMONARY REHABILITATION

The restoration of the individual to the medical , mental , emotional , social and vocational potential of which he/she is capable. The main aim of rehabilitation is to prevent the deconditioning that occurs with lack of exercise and immobility due to dyspnea and allow the patient to cope with the disease. Exercise training programmes have taken two approaches. The first is to attempt to improve cardiorespiratory fitness by aerobic exercises of 20 to 30 minutes duration atleast three times per week. It has been suggested that due to training effect, it is usually restricted to those patients with mild to moderate exercise limitation. Second approach is to improve their anaerobic fitness. In patients with very severe COPD, there are no established guidelines for pulmonary rehabilitation programmes, but carefully supervised exercise condition in the hospital setting , with oxygen supplementation should be considered in those who develop hypoxemia during exercise. Respiratory muscle training and ventilatory assist devices have been used to reduce the ventilator limitation during exercise.

The presence of resting hypercapnea is not a contraindication to pulmonary rehabilitation. Education of patients to understand the various components of the disease is intuitively valid. Mood disturbance particularly depression are very common in patients with advanced disease.

EXERCISE TRAINING

Expiratory flow rates during tidal breathing in patients with severe COPD are close to the maximum expiratory flow volume relationship. An increase in expiratory flow rate can occur during exercise in patients with COPD through dynamic hyper inflation. At the expense of increase in respiratory work , since tidal volume operates in a less compliant range of the pressure volume relationship and hence initiation of inspiration requires additional inspiratory pressure to overcome elastic recoil of the respiratory system. Continuous positive airway pressure overcomes the increased recoil pressure at the end of expiration , thus reducing and work of breathing.

CONTROLLED BREATHING TECHNIQUES

It attempts to diminish the breathlessness by training patients to breath efficiently. The treatment aims to

1. Restoration of diaphragm to a more normal position and function.

2. Decrease the respiratory rate by using a breathing pattern that diminishes air trapping and improves the respiratory duty cycle.

3. To diminish the work of breathing

4. To reduce dyspnea and allay patient anxiety.

The effects of different postures on respiratory muscle function have also been assessed. Diaphragmatic breathing exercises have been used to improve diaphragm function and are thought to be most helpful in patients with hyperventilation.

NUTRITION

Weight loss is common in patients with COPD particularly those with severe airway obstruction. Those patients with less than 90% of their ideal body weight are generally considered to be malnourished. Weight loss has been associated with a higher mortality in these patients. It would therefore seem logical to give nutritional support to patients with COPD. The weight gain is lost soon after cessation of nutritional support and any improvement in peripheral muscle performance and exercise capacity are also small and of short duration. However if sustained weight gain can be achieved this may improve survival. The theoretical complication of carbohydrate based diet increasing carbon dioxide production and hence hypercapnia in patients with COPD does not appear to be a problem. Obesity should be discouraged in patients with COPD in order to avoid additional strain on the cardio respiratory system , and appropriate dietary advice should be given.

VACCINATION

Influenza and pneumococcal vaccination is recommended for patients with COPD, although the specific evidence for this in COPD patients is lacking. They appear to be more effective in older patients and those with more severe disease or cardiac comorbidity.

LUNG TRANSPLANTATION

Lung transplantation developed from heart-lung transplantation , which was initially indicated for pulmonary vascular disease but was subsequently extended to other pulmonary conditions.

Indications :

1.Age<50 years for heart-lung transplantation or double lung transplantation

2.Age<60 years for single lung transplantation

3.Patients with an estimated life expectancy of less than 18 months

Contraindications :

1.Malnutrition is a relative contraindication; ideally , recipients should be within 15 kg of their ideal body weight

2. Recurrent or persistent pulmonary infections are a contraindication to single lung transplantation.

Other considerations :

1. Previous thoracic surgery increases the risk of hemorrhage
2. Cor pulmonale is not a contraindication to single lung transplantation
3. Psychological stability is necessary
4. Absence of other major organ dysfunction should be demonstrated.

LUNG VOLUME REDUCTION SURGERY :

The rationale for this technique is to reduce the volume of over inflated emphysematous lung by 20 to 30% , with the aim of improving the elastic recoil of the lungs, diaphragm configurations , chest wall mechanics and gas exchange. The technique is usually performed via a median sternotomy , without the need for cardiopulmonary bypass. Careful selection is necessary on the basis of a distended thorax, predominantly upper lobe disease and severe functional disability despite a programme of pulmonary rehabilitation. The improvements that have occurred upto 6 months after surgery are better than conventional medical treatment with bronchodilators and corticosteroids. Thoracoscopic laser pneumoplaty has been developed as an alternative to the more conventional excisional surgery. The Nd:YAg laser appears to be a safer technique than carbon di oxide laser. It relies on the fact that at operation the lung that remains represents the most affected areas and would absorb most energy; thus scarring and contraction would be concentrated at these sites.

COPD and its complication are related to the chronic history. Management of exacerbations requires ventilator support with controlled oxygen therapy with or without assisted ventilation. Non invasive ventilation is the preferred form.

Presence of PHT and cor pulmonale are contraindications .

BULLECTOMY:

It includes removal of a large bulla that does not contribute to gas exchange , decompressing the adjacent lung parenchyma.

ORGANISMS CAUSING AECOPD AND ITS FEATURES AND ANTIBIOTIC SENSITIVITY

Streptococcus pneumonia

Morphology:

- It is a Gram positive, lanceolate diplococcus, capsulated, nonmotile and nonsporing.
- They are readily stained with aniline dyes. The capsule is demonstrated as a clear halo in India ink preparations.

Cultural characteristics:

- It grows only in enriched media. They are aerobes and facultative anaerobes.
- The required pH is 7.8 and optimum temperature is 37^{o}C with 5-10% CO_2.
- On blood agar after incubation for 18 hours the colonies are small, dome shaped and glistening with area of green

discoloration around. On further incubation colonies become flat with raised edges and central umbonation like a carom coin appearance.

- In an anaerobic condition colonies in blood agar is surrounded by a zone of beta hemolysis due to oxygen labile hemolysin o

Biochemical Reactions:

- Pneumococci ferments several sugar forming acid. It is tested in HISS serum water.
- Pneumococci are bile soluble if 10% deoycholate solution is placed in pneucoccal colony in a blood agar the colony lysis within few minutes.
- Its is catalase negative and optochin sensitive.

Antigenic property:

- It has a type specific capsular polysachharide.Based on the capsular polyssacharide it is classified as type I,II,III,IV.Type four has more than 90 serotypes.
- **QUELLENG REACTION**-when a suspense of pneumoccocci is mixed with drop of type specific antiserum and methylene

blue the capsule become apparently swollen and sharply delineated and refractile.

- An abnormal protein that precipitates with somatic c ag of pneumococci appears in acute phase sera of cases of pneumonia know as c reactive protein.
- It produce oxygen labile hemolysin and leucocidin the virulence of pneumococci depends on capsule and production of toxin called pneumolysin.

Pathogenicity:

- Pneumococci colonise human nasopharynx causes infection of middle ear ,phara nasal sinuses and respiratory tract infections.
- Infections of meninges, heart, peritoneum and joints also occur.
- Most common bacteria causing lobar and bronchopneumonia and also causes tracheobronchitis and empyema.
- It is associated with acute exacerbation of chronic bronchitis.

Lab diagnosis:

- In acute phase of lobar pneumonia rusty sputum contains pneumococci in large numbers and demonstrated by gram stain.

- Sputum is inoculated in blood agar plates and incubated overnight. In infants serum coated laryngeal swabs may be used for cultures.
- In scanty specimens isolation is done by intraperitoneal inoculation in mice.
- In acute stage of pneumonia organism is obtained by blood culture in glucose broth.
- In case of meningitis gram staining of CSF is used for isolation.
- Capsular polysaccharide can be demonstrated in blood, urine and CSF by counter immune electrophoresis.

HAEMOPHILUS INFLUENZAE

Morphology:

- Gram negative, non motile, non sporing bacillus exhibiting pleomorphism.
- In sputum-coccobacillary form.
- In CSF-bacillary filamentous form.
- The bacilli stains with Loeffler's methylene blue.

Cultural characteristics:

- Factor X and Factor V are required for its growth. It is both aerobic and anaerobic organism. Optimum temperature required is 37^{o}C.
- It grows well in blood agar but requires factor V along with it. Hence when grown along with streaked plate of blood agar with Staph aureus, large well developed colonies are formed along the streak exhibiting **SATELLITISM**.
- **Levinthals's medium** and **Fildes agar** is best for primary isolation of H.influenzae.

Biochemical reactions:

- Glucose and xylose are fermented with acid production.
- Catalase and oxidase reactions are positive.
- It is destroyed by heating to 55^{o}C for 30 minutes, refrigeration, drying and disinfectants.

Antigenicity:

- Three major surface antigens: **Capsular polysachharide, outer membrane protein, lipooligosachharide.**
- Six capsular subtypes are available-type a to f.
- Isolates from invasive infections belong to type b.
- OMP antigens of Hib are classified into 13 subtypes.

Pathogenecity:

- Diseases caused by Haemophilus influenza can be grouped into invasive and non invasive.
- Invasive infections include meningitis, laryngoepiglottitis, conjunctivitis, bacteremia,pneumonia,arthritis,endocarditis and pericarditis.

- Non invasive infections include otitis media,sinusitis and exacerbations of chronic bronchitis and bronchiectasis.

Lab diagnosis:

- CSF culture in case of meningitis shows pleomorphic gram negative bacilli.
- Capsular polysaccharide antigen can be demonstrated in CSF by latex agglutination test.
- Blood cultures are positive in cases of laryngoepiglottitis and pneumonia.

Pseudomonas

Morphology:

- It is a slender Gram negative bacilli, motile by a polar flagellum. pili are present.
- It is nonencapsulated with a mucoid slime layer. The mucoid strains have abundance of extracellular polysachharides composed of alginate polymers. This forms a loose capsule in which microcolonies of the bacillus are enmeshed and protected from host defences.

Cultural characteristics:

- It Is an obligate aerobe but can grow anaerobically if nitrate is available. Optimum temperature required is 37^{o}C.
- It produces large opaque irregular colonies with a distinctive musty, mawkish earthy smell.
- It grows well on **MacConkey agar and Dextrose Chocolate agar media forming non lactose fermenting colonies.**
- Pseudomonas aeruginosa produces pigments which include pyocyanin and fluorescin. Pyocyanin inhibits growth of many bacteria.

Biochemical reactions:

It is oxidative and non fermentative.

Peptone water sugars are useful for detecting acid production.

Indole,Methyl red test,Voges-Proskauer test and H_2S test are negative.Catalase ,oxidase and arginine dihydrolase test are positive.

Pathogenecity:

- Pesudomonas aeruginosa is the most troublesome agent causing nosocomial infections.

- It causes suppurative otitis media in the community outside hospitals.
- Localized lesions of wounds,bedsores,eye infections,urinary tract infections are common.
- It is the most common cause of infection in burns.It causes iatrogenic meningitis following lumbar puncture.It causes posttracheostomy pulmonary infection.
- Septicemia and endocarditis occurs in debilitated due to concomitant infection, malignancy or immunosuppressive therapy.
- It is responsible for infantile diarrhea and sepsis.Self limited febrile illness(Shaghai fever) is seen in some tropical areas

Lab diagnosis:

It grows readily in most media. For pigmented strains, selected media such as **cetrimide agar can be used.**

<u>Moraxella</u>

- Moraxella catarrhalis is a Gram negative cocci arranged in pairs.
- It grows readily on nutrient agar.

- Optimum temperature is 18-42^{o}C.
- It produces nonpigmentes colonies and non fermenting sugars.
- It is a part of normal pharyngeal flora but causes respiratory infections like otitis media, sinusitis, tracheobronchitis and pneumonia.
- Moraxella lacunata are short,plumpy Gram negative bacilli arranged in pairs.
- They are non flagellated but have sluggish motility.
- Strictly aerobic,grows in ordinary media.They are oxidase,catalse positive;indole and H_2S negative and non fermentative.

KLEBSIELLA

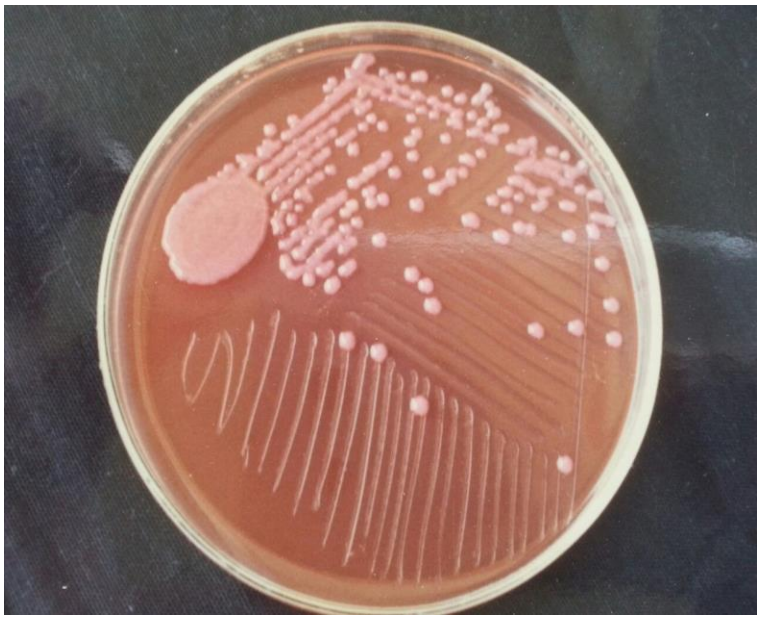
- It is a nonmotile capsulated rods that grow well on ordinary media forming **large dome shaped mucoid colonies** of varying degree of stickiness.
    - It ferments sugar and produce acid and gas.
    - It is indole and methyl red test negative and VP and citrate test positive. It produces urease.

Pathogenicity:

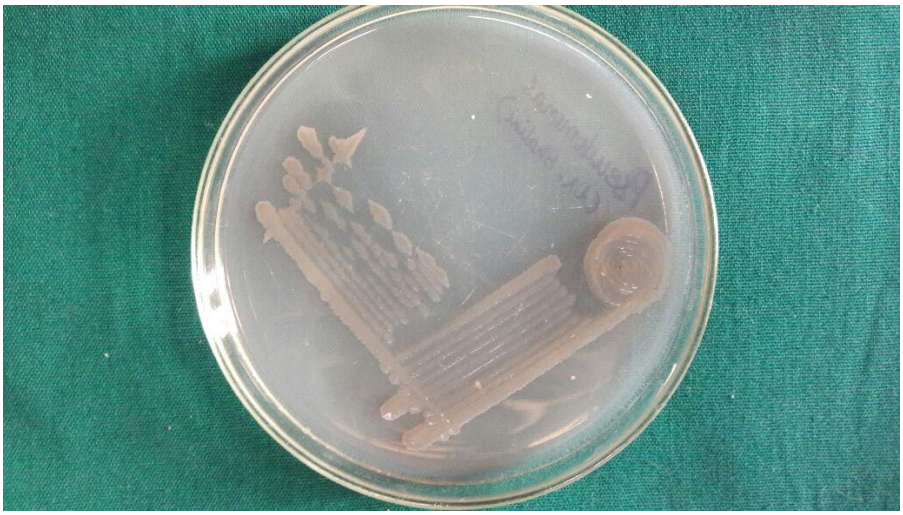
- It is an important cause of noscocomial infection causes pneumonia , UTI, pyogenic infection and septicemia.
- Klebsiella pneumonia occurs in alcoholics chronic bronchopulmonary diseases and diabetes.
- Serotypes 1,2 &3 are responsible for pneumonia.
- Diagnosis is made by culturing and biochemical reactions.

Among these Streptococcus , H.influenza , Moraxella are sensitive to Ceftriaxone and Cefotaxime. Pseudomonas and klebsiella respond well to aminoglycosides and quinolones.

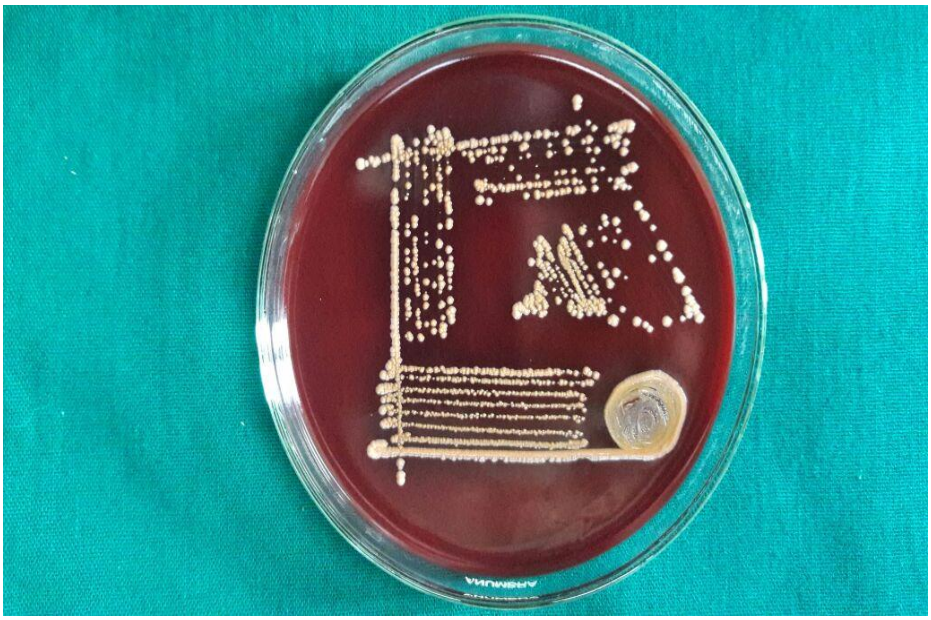
CULTURE PLATE SHOWING KLEBSIELLA GROWTH:



CULTURE PLATE SHOWING PSEUDOMONAS GROWTH:



CULTURE PLATE SHOWING STAPHYLOCOCCUS GROWTH:



MATERIALS AND METHODS

STUDY POPULATION:

100 patients who has been presented with Acute exacerbation of COPD in General medicine ward at Government Rajaji Hospital were included in the study.

INCLUSION CRITERIA:

1. Patients with Age 40-70 years
2. All patients admitted with a primary admitting diagnosis of acute exacerbation of COPD.
3. All patients must have a Prior confirmed diagnosis of COPD on the basis of FEV1/FVC<0.70.
4. Exacerbation of COPD will be diagnosed on basis of worsening of atleast one of these symptoms- dyspnea, cough, sputum production

EXCLUSION CRITERIA:

1) Previously diagnosed bronchial asthma ,cystic fibrosis, bronchiectasis
2) Clinical or radiological evidence of pneumonia and Tuberculosis.
3) Patients who received any type of antibiotic treatment over the past 5 days prior to the sampling of sputum.

LAB INVESTIGATIONS:

1) Sputum culture and sensitivity
2) Chest X ray
3) Spirometry

DATA COLLECTION:

Patients who present with acute exacerbation of COPD will be admitted in hospital. History of smoking will be noted down for all patients. Sputum samples will be collected for all patients after rinsing the mouth twice with plain water. Routine hematological investigations and chest radiography (PA view) will be done on the day of presentation.

All the patients will be treated with nasal oxygen, Intravenous empirical Antibiotics, steroids and salbutamol nebulisation. After stabilization spirometry will be done for all patients and the severity of COPD will be assessed using FEV1.

The sputum samples will be subjected to direct gram staining and culture on two sheep blood agar (SBA), McConkey agar (MA) and chocolate agar (CA) plates. Antibiotic sensitivity for the pathogenic organisms isolated in culture was done by Kirby-Bauer method .

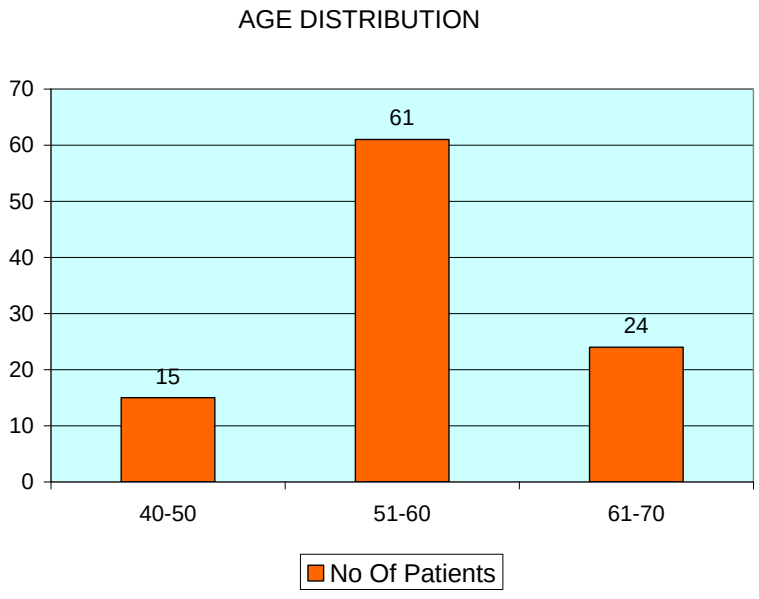
Statistical Analysis :

The information collected regarding all the selected cases were recorded in a master chart. Data analysis was done with the help of computer by using SPSS 16 software and Sigma Stat 3.5 version (2012). Using this software mean, standard deviation and ‘p’ value were calculated through One way ANOVA, Chi square test and P value of < 0.05 was taken as significant.

OBSERVATION AND RESULTS

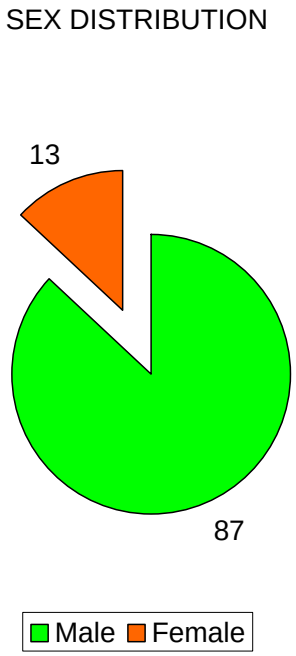
Age	No Of Patients
40-50	15
51-60	61
61-70	24
Total	100
Mean	55.76
SD	5.857

In our study patients of 40 to 70 years were included. Among this 15 patients were between 40-50 years of age, 61 patients were between 51-60 , 24 patients were between 61-70 years of age. There is no significant association between age and organism causing AECOPD.



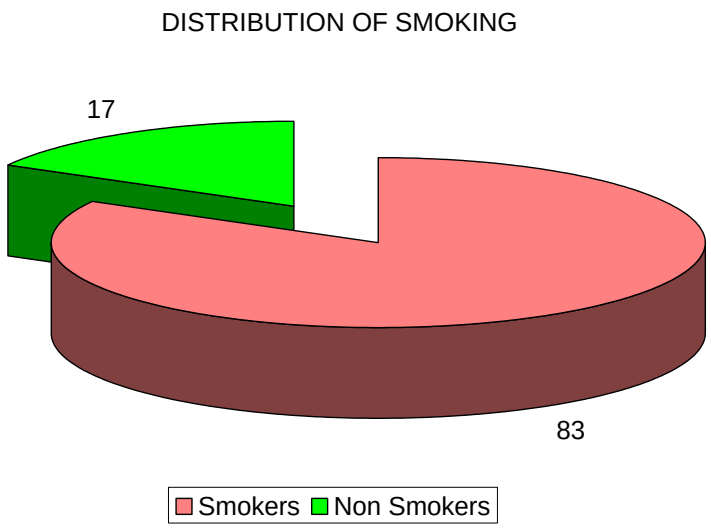
Sex	No Of Patients
Male	87
Female	13
Total	100

Of the total 100 patients, 87 were males and 13 were females .This is because smoking , the important risk factor for COPD is common in males.



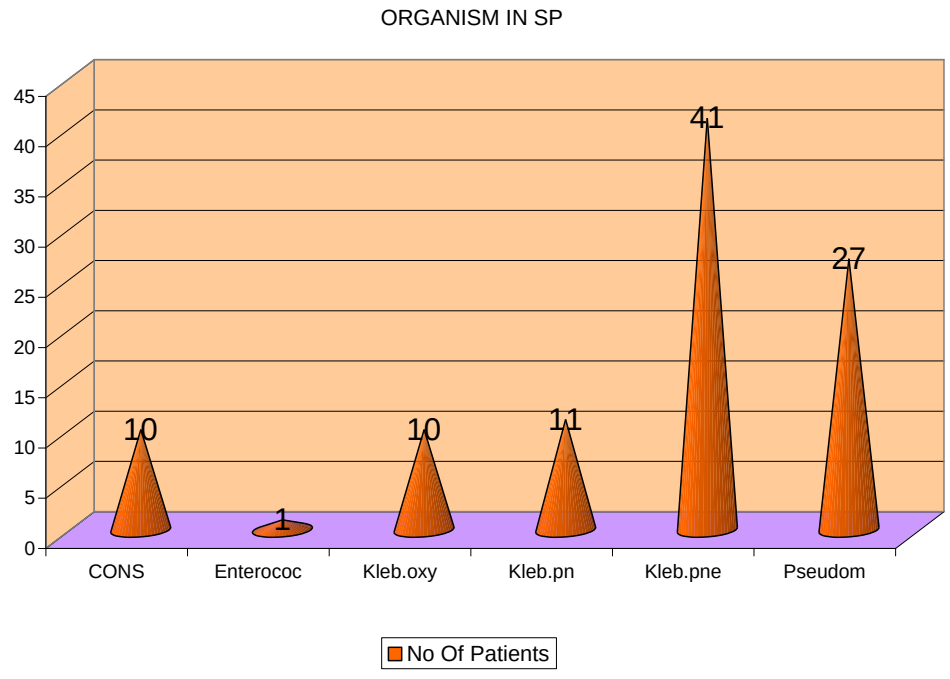
Smoking	**No of Patients**	FEV1		P'Value
		Mean	SD	
Smokers	83	57.771	15.318	0.685
Non Smokers	17	59.412	14.301	NS
Total	100			

In total of 100 patients 83 were smokers, 17 were non smokers. But there is no significant correlation between smoking and organism causing AECOPD. On reviewing several studies on Indian male patients 83.2% were associated with smoking. There is no significant relation between smoking and organism isolated. P value is not statistically significant.



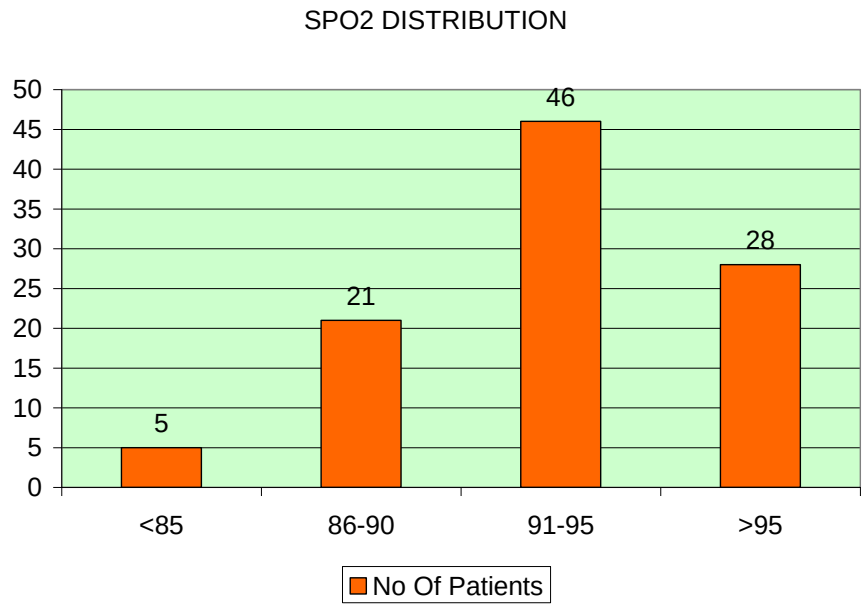
Organism in sputum	No Of Patients
CONS	10
Enterococ	1
Kleb.oxy	10
Kleb.pne	52
Pseudomo	27
Total	100

Among the 100 patients, in sputum culture Klebsiella pneumonia was grown in 52 % patients , pseudomonas was grown in 27% patients, CONS (coagulase negative staphylococcus) was grown in 10% patients and klebsiella oxytoca was grown in 10% patients.. Enterococcus was isolated in 1% patient.



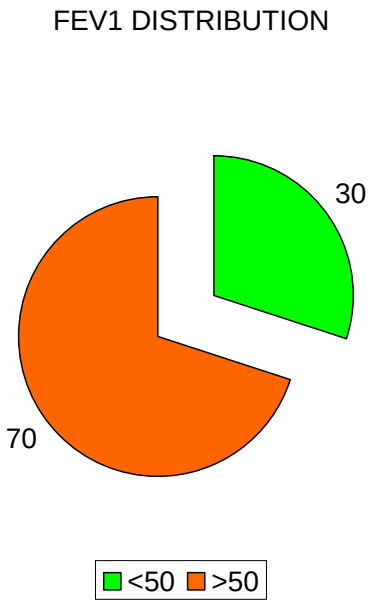
Spo2%	No of Patients
<85	5
86-90	21
91-95	46
>95	28
Total	100
Mean	92.73
SD	3.902

Saturation of the patient is recorded using finger pulse oximetry at the time of admission for all patients of AECOPD. .Saturation is <85 in 5 patients. Its 86-90% in 21 patients. 91 -95 in 46 patients. >95% in 28 patients



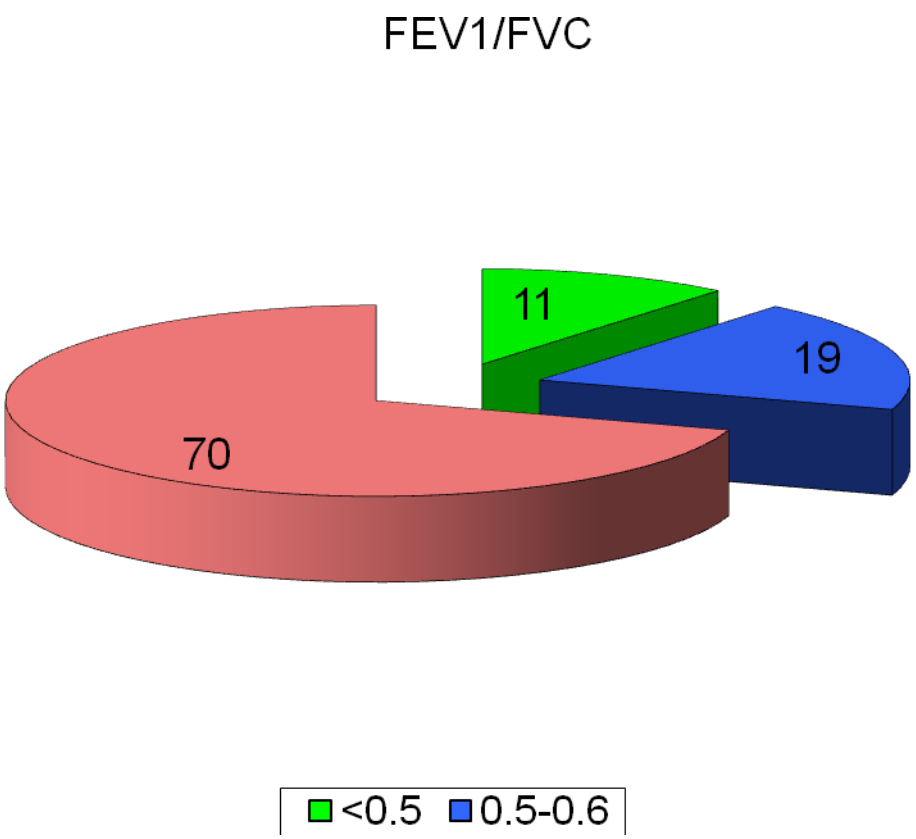
FEV1	No Of Patients
<50	30
>50	70
Total	100
Mean	58.05
SD	15.093

Among the 100 patients included in the study 30% patients have FEV1 < 50, 70% patients have FEV1 > 50.



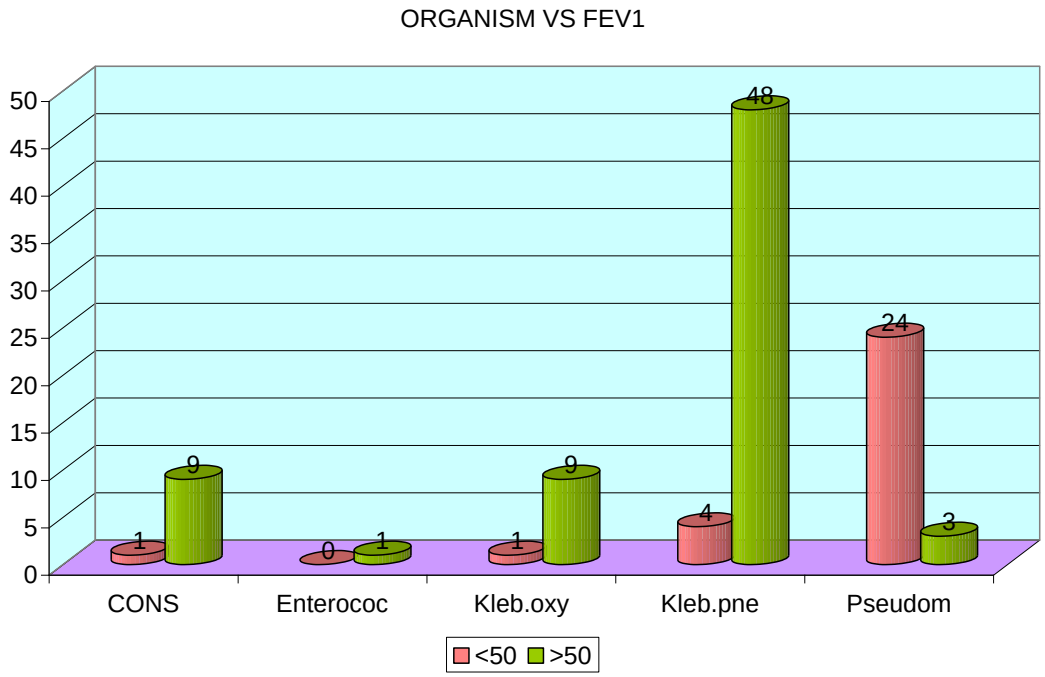
FEV1/FVC	No of Patients
<0.5	11
0.5-0.6	19
>0.6	70
Total	100
Mean	0.609
SD	0.0714

FEV1/FVC was also calculated. Ratio is < 0.5 in 11% patients, **0.5-0.6 in 19 patients ,> 0.6 in 70% patients.**



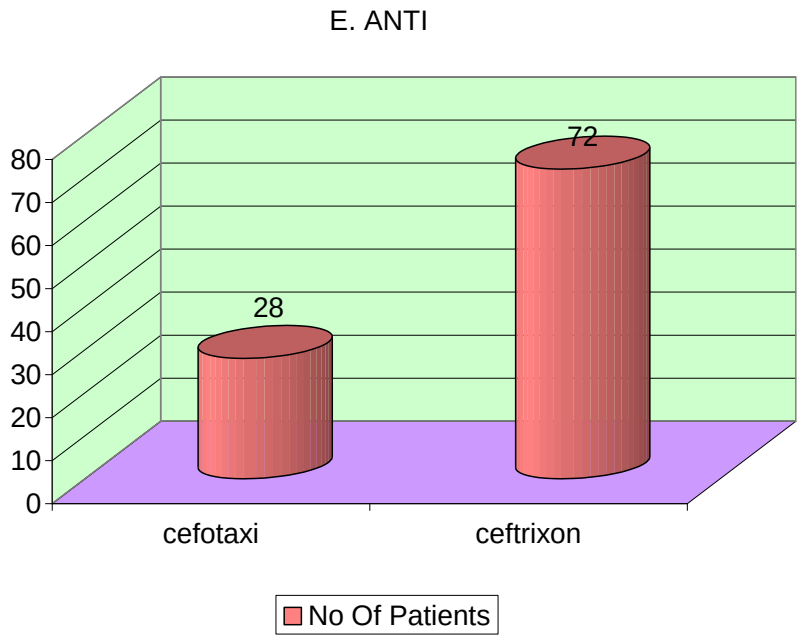
Relationship with FEv1 & Organism	No Of Patients	<50	>50
CONS	10	1	9
Enterococ	1	0	1
Kleb.oxy	10	1	9
Kleb.pne	52	4	48
Pseudom	27	24	3
Total	100	30	70

Among the 100 patients, Pseudomonas was isolated predominantly in patients with FEV1 < 50 (24 cases).



Empirical Antibiotic	**No Of Patients**
cefotaxime	28
ceftriaxone	72
Total	100

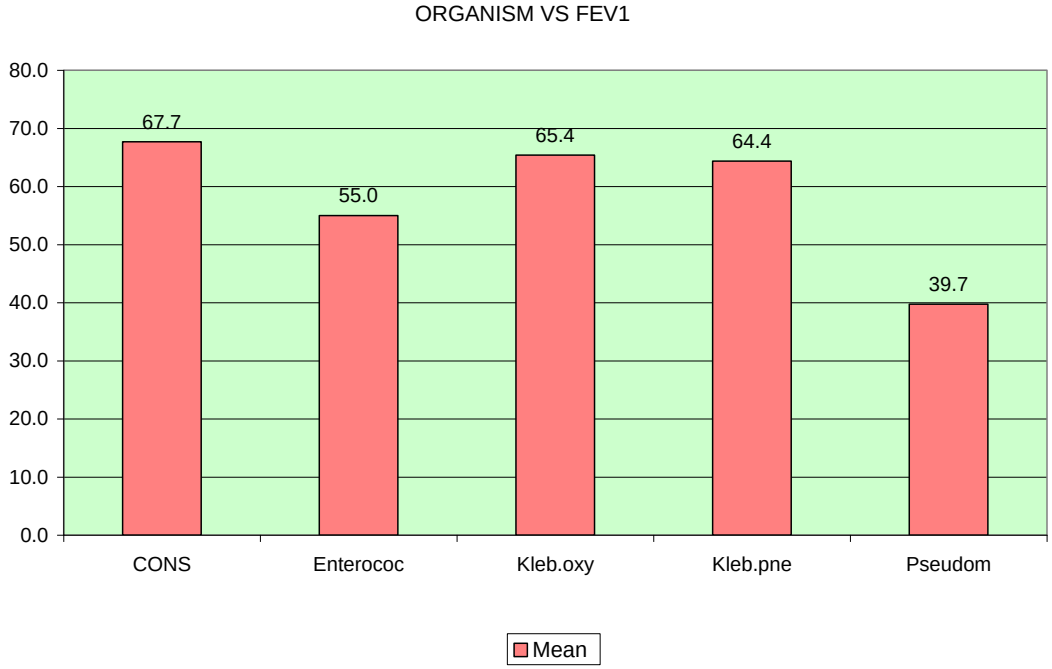
Among the 100 patients, 72 patients were started on Ceftriaxone as empirical antibiotic.28 patients were started on cefotaxime



	No Of Patients	**Relationship with FEv1 & Organism**	SD	P'Value
CONS	10	67.7	9.956	
Enterococ	1	55	0	
Kleb.oxy	10	65.4	10.211	<0.001
Kleb.pne	52	64.35	10.39	
Pseudom	27	39.741	10.041	
Total	100			

Among the 100 patients in the study population, 52% patients positive for klebsiella pneumonia, 27% patients have Pseudomonas, 10% patients have klebsiella oxytoca, 10% patients have CONS, 1%have Enterococcus.

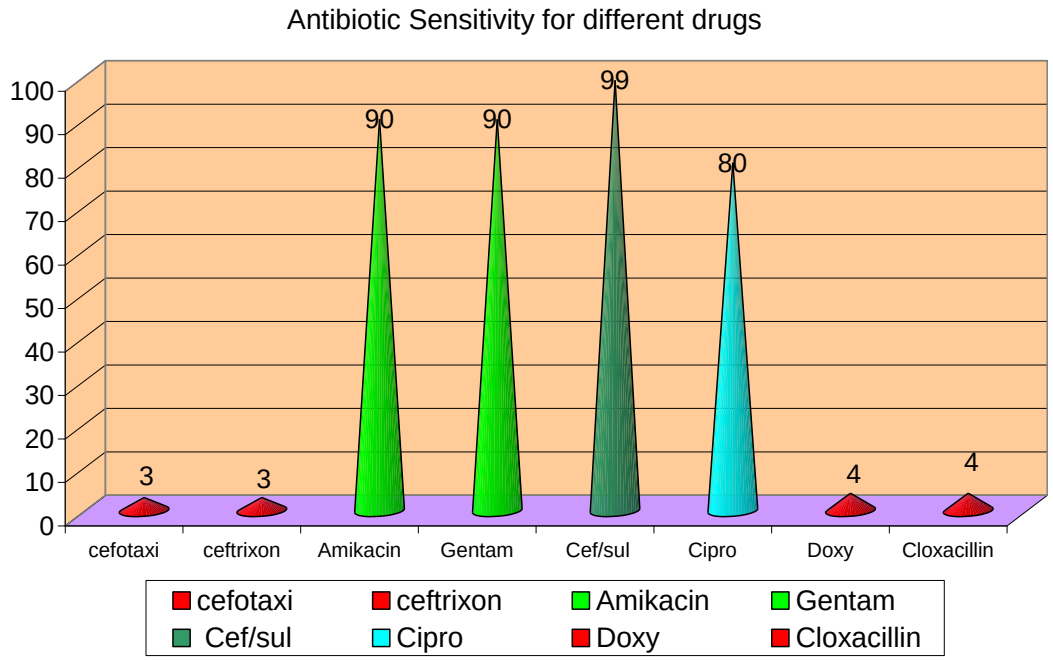
Patients with FEV1 <50% have Pseudomonas predominantly in culture.So there is significant correlation between FEV1 and organism isolated .It is statistically significant as P value <0.001.



Antibiotic sensitivity	R	S
cefotaxi	97	3
ceftrixon	97	3
Amikacin	10	90
Gentam	10	90
Cef/sul	1	99
Cipro	20	80
Doxy	96	4
Cloxacillin	96	4

Among the 100 patients 97% patients were. resistant to cefotaxime and ceftriaxone.

About 90% patients are sensitive to Aminoglycosides. 99% sensitivity to all organisms for Cefeperazone sulbactum. Doxycycline and Cloxaciliin were resistant in 96% of patients



ANTIBIOTIC SENSITIVITY OF VARIOUS ORGANISMS

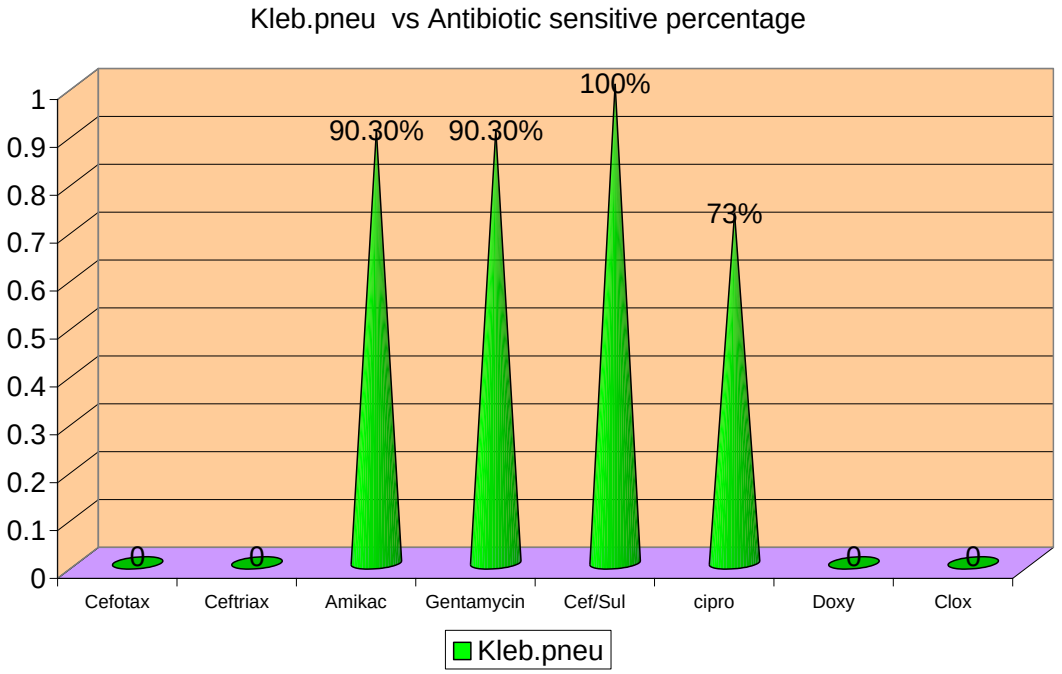
IN THE STUDY

Antibiotic / Organism	CEFO TAX		CEF TRIAX		AMK		GTM		CFS		CIPRO		DOXY		CLOX	
	R	S	R	S	R	S	R	S	R	S	R	S	R	S	R	S
KLEBS. PNE	52	nil	52	nil	5	47	5	47	nil	52	14	38	52	Nil	52	nil
PSEUDO	27	NIL	27	nil	2	25	2	25	Nil	27	3	24	27	NIL	27	Nil
CONS	NIL	10	Nil	10	Nil	10	Nil	10	Nil	10	6	4	10	Nil	10	Nil
KLEB OXYTO CA	10	Nil	10	Nil	1	9	1	9	Nil	10	3	7	7	3	7	3
ENTERO	1	Nil	1	Nil	Nil	1	Nil	1	1	Nil	1	Nil	Nil	1	1	Nil

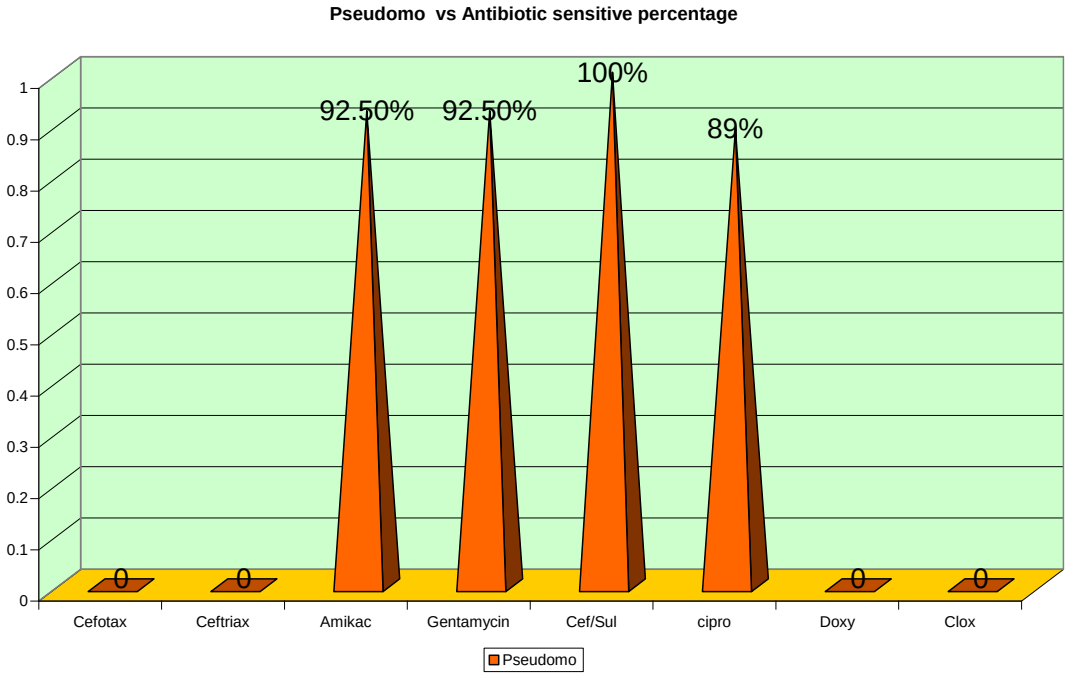
ORGANISMS AND ANTIBIOTIC SENSITIVITY IN PERCENTAGE:

	Cefotax	Ceftriax	Amikac	Gentamycin	Cef/Sul	cipro	Doxy	Clox
Kleb.pneu	Nil	nil	90.3%	90.3%	100%	73%	Nil	Nil
Pseudomo	Nil	Nil	92.5%	92.5%	100%	89%	Nil	Nil
Kleb.oxytoca	Nil	nil	90%	90%	100%	70%	30%	30%
CONS	100%	100%	100%	100%	100%	30%	Nil	Nil
Enterococcus	Nil	Nil	100%	100%	Nil	Nil	100%	Nil

ANTIBIOTIC SENSITIVITY PATTERN OF KLEBSIELLA PNEUMONIA



ANTIBIOTIC SENSITIVITY PATTERN OF PSEUDOMONAS



DISCUSSION

In our study total of 100 patients were studied after applying the inclusion criteria and exclusion criteria. Sputum culture and its antibiogram is detected and severity of COPD was assessed by pulmonary function test using FEVI value.

AGE:

In our study patients of 40 to 70 years were included. Among this 15 patients were between 40-50 years of age, 61 patients were between 51-60 , 24 patients were between 61-70 years of age. There is no significant association between age and organism causing AECOPD.

SEX:

Of the total 100 patients, 87 were males and 13 were females .This is because smoking , the important risk factor for COPD is common in males.

SMOKING:

In total of 100 patients 83 were smokers, 17 were non smokers. But there is no significant correlation between smoking and organism causing AECOPD. On reviewing several studies on Indian male patients 83.2% were associated with smoking.

ORGANISM IN SPUTUM:

Among the gram positive organisms isolated streptococcus pneumonia H.influenza was the most commonest with 45%in a study by Gompertz S, et al

Similar study by Anja Ede et al shows that Streptococcus pneumonia, non typable H.influenza and to some extent Moraxella are responsible for AECOPD

In contrast to western literature Indian Literature review shows no isolates of H. influenza in AECOPD patients. Staphylococcus aureus, Streptococcus pneumoniae, and Streptococcus pyogenes were most common gram positive organisms causing AECOPD according to Madhavi et al.

In our study of 100 patients, in sputum culture Klebsiella pneumonia was grown in 52 % patients , pseudomonas was grown in 27% patients, CONS (coagulase negative staphylococcus) was grown in 10% patients and klebsiella oxytoca was grown in 10% patients.. Enterococcus was isolated in 1% patient.

There were no isolates of H.influenza, Streptococcus pyogenes amd moraxella in our study.

So predominantly Klebsiella pneumonia was grown in sputum culture in AECOPD patients admitted in Govt Rajaji Hospital Madurai.

Next to klebsiella pneumonia, Pseudomonas was the second most common organism grown in culture. Klebsiella oxytoca and CONS were also grown in sputum culture in 10 patients among the 100.

On the contrary to the routine school of thought Gram positive organisms like Streptococcus pneumonia, H.influenza and Moraxella cattarhalis are responsible for Acute excacerbation of COPD . But in our study the organism responsible for AECOPD are predominantly Gram negative group .

SPo2 :

Saturation of the patient is recorded using finger pulse oximetry at the time of admission for all patients of AECOPD. .Saturation is <85 in 5 patients. Its 86-90% in 21 patients. 91.5% in 46 patients. >95% in 28 patients.

FEV1 & FEV1/FVC:

Spirometry was done for all patients with AECOPD after stabilization . Using this FEV1 was measured. Based on that, patients were classified in to four classes according to GOLD guidelines.

Among the 100 patients included in the study ,30% patients have FEV1 < 50,70% patients have FEV1 > 50. FEV1/FVC was also calculated. Ratio is < 0.5 in 11% patients,0.5-0.6 in 19 patients ,> 0.6 in 70% patients.

As per GOLD guidelines (2010) for defining COPD, FEV1 should be ≤ 80%.

In our study most of the cases having FEV1 values ranging from 30% - 79%. Hence there is an high correlation between severity of COPD and FEV1. Our study has statistically documented this fact.

The FEV1/ FVC ratio also one of the criteria for defining COPD. Swanney et al (2008) documented the importance of this ratio in their study. In our study the FEV1/ FVC ratio ranges from 0.5 – 0.69. Thus statistically proving that there is a relation between FEV1/ FVC ratio and severity of COPD.

EMPIRICAL ANTIBIOTIC:

As per the literature and various studies like Anand patel et al shows Gram positive organism like Streptococcus pneumonia, H.influenza and Moraxella cattarhalis are responsible for Acute excacerbation of COPD and these were sensitive to Ceftriaxone, Piperacillin tazobactum and ciprofloxacin.

Previously ampicillin and amoxicillin were the standard treatment in AECOPD. Due to emergence of resistance among respiratory pathogens their utility had been limited. Aminopenicillins with beta lactamase inhibitor is a better choice. Cephalosporins were also effective in AECOPD patients according to various previous studies.

In most of studies 100% of Streptococcus were sensitive to 3 generation cephalosporins either cefotaxine or ceftriaxone

Klebsiella pneumonia was the most common organism isolated from madhavi et al study . We observed that third generation cephalosporin ceftriaxone was the most effective antibiotic against the *Streptococcus pneumoniae,* but these results is contrary to various other studies which found that piperacillin-tazobactum was most effective against *Streptococcus pneumonia*.

So based on various previous studies third generation cephalosporins particularly Ceftriaxone and Cefotaxime were started as empirical antibiotic for all patients included in our study.

Among the 100 patients, 72 patients were started on Ceftriaxone as empirical antibiotic.28 patients were started on cefotaxime.

ORGANISMS AND PERCENTAGE OF ANTIBIOTIC SENSITIVITY:

Among the 100 patients in the study population, 52% patients positive for klebsiella pneumonia, 27% patients have Pseudomonas, 10% patients have klebsiella oxytoca, 10% patients have CONS, 1%have Enterococcus.

Based on the antibiotic sensitivity pattern percentage of sensitivity to antibiotics is depicted in the following table.

	Cefotax	Ceftriax	Amikac	Gentamycin	Cef/Sul	cipro	Doxy	Clox
Kleb.pneu	Nil	nil	90.3%	90.3%	100%	73%	Nil	Nil
Pseudomo	Nil	Nil	92.5%	92.5%	100%	89%	Nil	Nil
Kleb.oxytoca	Nil	nil	90%	90%	100%	70%	30%	30%
CONS	100%	100%	100%	100%	100%	30%	Nil	Nil
Enterococcus	Nil	Nil	100%	100%	Nil	Nil	100%	Nil

SUMMARY

- In our study 100 patients were recruited, their sputum culture and antibiotic sensitivity pattern assessed. The relationship between the organism causing Acute exacerbation and severity of COPD was assessed using FEV1.

- In our study patients of 40 to 70 years were included. Among this 15% patients were between 40-50 years of age, 61% patients were between 51-60, 24 %patients were between 61-70 years of age. There is no significant association between age and organism causing AECOPD.

- In our study out of the total 100 patients, 87% were males and 13%were females .This is because smoking, the important risk factor for COPD is common in males. There is no significant correlation between the organism causing AECOPD and sex of the patient.

- In total of 100 patients 83% were smokers, 17% were non smokers. But there is no significant correlation between smoking and organism causing AECOPD.

- Among the 100 patients included in the study, 30% patients have FEV1 < 50%. patients have FEV1 > 50%.

- Among the 100 patients, in sputum culture Klebsiella pneumonia was grown in 52% patients, pseudomonas was grown in 27% patients, CONS (coagulase negative staphylococcus) was grown in 10% patients and klebsiella oxytoca was grown in 10%patients.. Enterococcus was isolated in 1% .

- Among the 100 patients, 72% patients were started on Ceftriaxone as empirical antibiotic.28% patients were started on cefotaxime.

- Klebsiella pneumonia organisms were grown in 52% patients and among those 100% were sensitive to Cefeperazone sulbactum, 90.3% of patients were sensitive to Amikacin and Gentamycin, 73% of patients were sensitive to Ciprofloxacin.

- Pseudomonas was grown in 27% patients. Among those patients 100% sensitive to Cefeperazone sulbactum, 92.5% were sensitive to Amikacin and Gentamycin, 89% of patients were sensitive to ciprofloxacin.

- Among 30% patients with FEV1 <50% Pseudomonas grew in 24 patients , klebsiella pneumonia grew in 4 patients, Klebsiella oxytoca & CONS grew in 1 patient.

- Hence Pseudomonas has significant association in causing severe exacerbation of COPD.

- There is no significant association between organism in the sputum and age, sex, smoking in causing AECOPD.

CONCLUSION

Acute exacerbation of COPD is one of the major causes of morbidity and mortality worldwide. Apart from steroids, Nasal oxygen and salbutamol nebulisation antibiotics have very significant role in reducing the mortality and duration of hospital stay.

Previously Gram positive organisms like Streptococcus pneumonia , H.influenza and Moraxella cattarhalis were considered to be the major cause for Acute exacerbation of COPD. Hence antibiotics with predominant Gram positive coverage was chosen as the empirical antibiotic of choice in treating patients with acute exacerbation.

But in this study conducted in our institution, Gram negative organisms like Klebsiella pneumonia and Pseudomonas were responsible for majority of the acute exacerbation. These organisms were predominantly sensitive to Cefeperazone sulbactum, Amikacin and Gentamycin. Ciprofloxacin also equally sensitive to most of the organisms, but it can't be used as an empiric antibiotic of choice where Tuberculosis is endemic.

Hence revision of the choice of empirical antibiotic is essential and would go a long way in treating patients with acute exacerbation. In the same time proper antibiotic policy to be developed and implemented in a hospital to prevent the emergence of resistance.

LIMITATION OF THE STUDY

This study has its own limitation. The number of patients in this study is small. Hence generalizations of results of the study have to be made with caution.

The study population involved patients seeking medical care in our hospital which is a tertiary care center and hence they may not represent the general population.

This study is a observational study .Longitudinal studies with serial assessment of the variables would be more informative. So, longitudinal studies with large study population and population based studies are needed to circumvent this limitation.

ABBREVIATIONS

COPD	-	Chronic Obstructive pulmonary disease
AECOPD	-	Acute exacerbation of Chronic Obstructive pulmonary disease
PFT	-	Pulmonary Function Test
GOLD	-	Global Initiative of Obstructive Lung Disease
TV	-	Tidal Volume
FEV_1	-	Forced Expiratory Volume at first second
FVC	-	Forced Vital Capacity
ERV	-	Expiratory Reserve Volume
IRV	-	Inspiratory Reserve Volume
PEFR	-	Peak Expiratory Flow Rate
MMV	-	Maximum Voluntary Ventilation
BRR	-	Breathing Reserve Ratio
ICS	-	Inhalational corticosteroids
KLEB.PNE	-	klebsiella pneumonia
PSEUDOM	-	pseudomonas
KLEB OXY	-	klebsiella oxytoca
CONS	-	coagulase negative staphylococcus aureus.

KEY TO MASTER CHART

CEFOTAX	-	CEFOTAXIME
CEFTRIAX	-	CEFTRIAXONE
AMIKA	-	AMIKACIN
GENTA	-	GENTAMYCIN
CIPRO	-	CIPROFLOXACIN
CFS	-	CEFEPERAZONE SULBACTUM
DOXY	-	DOXYCYCLINE
CLOX	-	CLOXACILLIN
KLEB.PNEU	-	KLEBSIELLA PNEUMONIAE
PSEUDO	-	PSEUDOMONAS
CONS	-	COAGULASE NEGATIVE STAPH AUREUS
KLEB.OXY	-	KLEBSIELLA OXYTOCA
R	-	RESISTANT
S	-	SENSITIVE
S	-	SMOKER
NS	-	NON SMOKER

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PROFORMA

Name:

Age / Sex:

IP no:

Occupation:

Presenting complaints:

Past History:

h/o previous Bronchial asthma, Drug intake, Tuberculosis

Personal history

smoker/ nonsmoker

alcoholic/ non alcoholic

Clinical Examination:

General Examination:

Consciousness, Pallor, jaundice, Clubbing, Lymphadenopathy, cyanosis

Vitals:

PR

BP

RR

SpO2

Systemic examination:

CVS:

RS:

ABDOMEN:

CNS:

Laboratory investigations:

Hb, Tc Dc ESR

Chest x ray

Sputum culture and sensitivity

Spirometry

Diagnosis

Duration of hospital stay

Condition at discharge

serial no	Name	Age	Sex	Smoker	Spo2%	FEV1	FEV1/ FEC	E.Anti	Org in sp	cefotaxi	ceftrixon	Amikacin	Gentar
1	Mr.Ramar	47	M	S	96	73	0.68	ceftrixon	Kleb.pn	R	R	S	S
2	Mrs.Mallika	62	F	NS	96	75	0.67	cefotaxi	CONS	R	R	R	R
3	Mr.Anandh	52	M	S	97	77	0.63	ceftrixon	Kleb.pn	R	R	S	S
4	Mr.Thiraviam	54	M	S	91	44	0.54	ceftrixon	Pseudom	R	R	S	S
5	Mr.Raja	55	M	S	93	55	0.65	ceftrixon	Kleb.pn	R	R	S	S
6	Mrs.Selvi	57	F	NS	89	47	0.57	ceftrixon	Kleb.oxy	R	R	S	S
7	Mr.Chinnan	63	M	S	83	26	0.48	ceftrixon	Pseudom	R	R	S	S
8	Mr.Selvam	56	M	S	96	62	0.67	cefotaxi	Kleb.pn	R	R	S	S
9	Mr.Mani	55	M	S	94	72	0.65	ceftrixon	Kleb.pn	R	R	R	R
10	Mr.Narayanan	53	M	S	86	45	0.56	ceftrixon	Pseudom	R	R	S	S
11	Mr.Ramakrish	52	M	S	92	44	0.54	ceftrixon	Kleb.pn	R	R	S	S
12	Mr.Chinnathevar	46	M	S	95	74	0.67	ceftrixon	Kleb oxy	R	R	S	S
13	Mr.Pandi	65	M	NS	96	51	0.62	ceftrixon	Pseudom	R	R	R	R
14	Mr.Mariappan	51	M	S	97	61	0.62	cefotaxi	Kleb.pn	R	R	S	S
15	Mrs.Thillai	55	F	NS	94	56	0.66	cefotaxi	Kleb.pn	R	R	S	S
16	Mr.Sholan	66	M	S	88	25	0.43	ceftrixon	Pseudom	R	R	R	R
17	Mr.Ravi	57	M	S	96	58	0.63	cefotaxi	Kleb.pn	R	R	R	R
18	Mr.Nambi	58	M	S	94	67	0.65	ceftrixon	CONS	S	S	S	S
19	Mr.Arumugam	56	M	S	97	75	0.61	ceftrixon	Kleb.pn	R	R	S	S
20	Mr.Balu	68	M	S	98	64	0.62	cefotaxi	Kleb.pn	R	R	S	S
21	Mr.Pandeswaran	44	M	S	93	55	0.65	ceftrixon	Enterococ	R	R	S	S
22	Mr.Anandhkumar	42	M	S	94	51	0.67	cefotaxi	Kleb.pne	R	R	S	S
23	Mr.Aravind	61	M	S	93	64	0.65	ceftrixon	Kleb.pne	R	R	S	S
24	Mr.Veluyutam	55	M	S	95	56	0.64	ceftrixon	Kleb.oxy	R	R	S	S
25	Mr.Solai	54	M	S	87	33	0.53	ceftrixon	Pseudom	R	R	S	S
26	Mr.Mari	56	M	S	94	62	0.66	cefotaxi	Kleb.pne	R	R	S	S
27	Mr.Natarajan	63	M	S	96	67	0.68	cefotaxi	Kleb.pne	R	R	S	S
28	Mrs.Rajeshwari	44	F	NS	84	41	0.55	ceftrixon	Pseudom	R	R	S	S
29	Mr.Pallavan	58	M	S	97	44	0.54	ceftrixon	CONS	S	S	S	S
30	MR.Velu	57	M	S	89	44	0.54	ceftrixon	Pseudom	R	R	S	S

31	Mr.Balakrish	52	M	S	92	58	0.62	cefotaxi	Kleb.pne	R	R	R	R
32	Mr.Durai	64	M	S	94	55	0.65	ceftrixon	Kleb.pne	R	R	S	S
33	Mr.Gowtham	46	M	S	95	74	0.64	cefotaxi	kleb.oxy	R	R	S	S
34	Mr.Harshith	51	M	S	91	62	0.68	ceftrixon	Kleb.pne	R	R	S	S
35	Mr.James	58	M	S	94	77	0.67	cefotaxi	Kleb.pne	R	R	R	R
36	Mr.Kalaiselvan	56	M	S	95	56	0.64	cefotaxi	Kleb.pne	R	R	S	S
37	Mrs.Sundari	57	F	NS	98	77	0.65	cefotaxi	CONS	S	S	S	S
38	Mr.Mahesh	58	M	S	88	42	0.56	ceftrixon	Pseudom	R	R	S	S
39	Mr.Logeswaran	62	M	S	94	72	0.65	cefotaxi	Kleb.pne	R	R	S	S
40	Mr.Prathap	59	M	S	87	47	0.51	ceftrixon	Pseudom	R	R	S	S
41	Mr.Praveen	52	M	NS	94	63	0.65	ceftrixon	Kleb.pne	R	R	S	S
42	Mr.Ruban	55	M	S	95	69	0.63	ceftrixon	Kleb.pne	R	R	S	S
43	Mr.Mathew	54	M	S	96	76	0.67	ceftrixon	Kleb.pne	R	R	S	S
44	Mr.Natesan	52	M	S	94	71	0.66	ceftrixon	Kleb.pne	R	R	R	R
45	Mr.Parthiban	53	M	S	86	27	0.43	ceftrixon	Pseudom	R	R	S	S
46	Mr.Ponraj	46	M	S	88	24	0.47	cefotaxi	Pseudom	R	R	S	S
47	Mr.Sunder	61	M	S	93	78	0.62	ceftrixon	Kleb.pne	R	R	R	R
48	Mrs.Bavani	52	F	NS	96	72	0.64	ceftrixon	Kleb.pne	R	R	S	S
49	Mr.Balu	54	M	S	84	47	0.57	ceftrixon	Pseudom	R	R	S	S
50	Mr.Duraipandi	48	M	S	96	58	0.65	cefotaxi	Kleb.pne	R	R	S	S
51	Mr.Chinnaiah	66	M	S	93	62	0.68	ceftrixon	Kleb.oxy	R	R	S	S
52	Mr.Harshan	58	M	S	96	61	0.64	ceftrixon	Kleb.pne	R	R	S	S
53	Mrs.Saraswathi	62	F	NS	86	49	0.59	Cefotaxi	Pseudom	R	R	S	S
54	Mr.Kuppan	59	M	S	92	58	0.67	ceftrixon	Kleb.pne	R	R	S	S
55	Mr.Logan	56	M	S	95	77	0.65	ceftrixon	CONS	R	R	S	S
56	Mr.Rajan	64	M	S	89	33	0.43	ceftrixon	Pseudom	R	R	S	S
57	Mrs.Devi	47	F	NS	94	67	0.68	ceftrixon	Kleb.pne	R	R	S	S
58	Mr.Manickam	52	M	S	96	64	0.62	ceftrixon	Kleb.oxy	R	R	R	R
59	Mr.Veeranan	55	M	S	90	38	0.46	ceftrixon	Pseudom	R	R	S	S
60	Mr.Bala	54	M	S	91	55	0.65	ceftrixon	Kleb.pne	R	R	S	S
61	Mr.Velpandi	53	M	S	97	78	0.62	cefotaxim	Kleb.pne	R	R	S	S
62	Mr.Pandi	55	M	S	95	67	0.68	ceftrixon	Kleb.pne	R	R	S	S

63	Mr.Ramesh	57	M	S	97	62	0.66	ceftrixon	Kleb.pne	R	R	S	S
64	Mr.Muthu	51	M	S	98	64	0.71	ceftrixon	Kleb.pne	R	R	S	S
65	Mrs.Usha	43	F	NS	93	78	0.62	ceftrixon	Kleb.oxy	R	R	S	S
66	Mr.Rajarajan	61	M	S	88	33	0.43	ceftrixon	Kleb.pne	R	R	S	S
67	Mr.Nikilan	63	M	S	95	72	0.64	ceftrixon	CONS	R	R	S	S
68	Mr.Rajendran	56	M	S	92	49	0.59	Cefotaxi	Kleb.pne	R	R	S	S
69	Mr.Jose	53	M	S	96	78	0.62	ceftrixon	Kleb.pne	R	R	S	S
70	Mr.Bose	58	M	NS	95	64	0.62	ceftrixon	Kleb.oxy	R	R	S	S
71	Mrs.Banumathy	48	F	NS	89	38	0.46	Cefotaxi	Pseudom	R	R	S	S
72	Mr.Prakash	64	M	S	94	74	0.67	ceftrixon	Kleb.pne	R	R	S	S
73	Mr.Selvan	66	M	S	96	72	0.65	ceftrixon	CONS	R	R	S	S
74	Mr.Aadavan	59	M	S	84	26	0.48	Cefotaxi	Pseudom	R	R	S	S
75	Mr.Paraman	49	M	S	94	78	0.62	ceftrixon	Kleb.pne	R	R	S	S
76	Mr.Ilango	56	M	S	95	56	0.66	ceftrixon	Kleb.pne	R	R	S	S
77	Mr.Elavarasan	57	M	S	90	25	0.43	ceftrixon	Pseudom	R	R	S	S
78	Mr.Karuppu	51	M	S	95	77	0.65	Cefotaxi	Kleb.pne	R	R	S	S
79	Mr.Ramesh	62	M	S	93	61	0.62	ceftrixon	Kleb.pne	R	R	S	S
80	Mr.Nallan	59	M	S	86	45	0.56	ceftrixon	Pseudom	R	R	S	S
81	Mr.Ramesh	44	M	S	96	52	0.67	ceftrixon	Kleb.pne	R	R	S	S
82	Mr.Arumugam	54	M	S	87	34	0.54	ceftrixon	Pseudom	R	R	S	S
83	Mr.Selvakumar	62	M	S	95	56	0.64	Cefotaxi	Pseudom	R	R	S	S
84	Mr.Kalaipandi	55	M	S	94	62	0.66	ceftrixon	CONS	R	R	S	S
85	Mrs.Revathi	58	F	NS	96	67	0.68	ceftrixon	Kleb.pne	R	R	S	S
86	Mr.Baskar	64	M	S	89	45	0.54	ceftrixon	Pseudom	R	R	S	S
87	Mr.Chinnamuthu	58	M	S	92	58	0.62	ceftrixon	Kleb.pne	R	R	S	S
88	Mr.Kalaivanan	61	M	S	94	77	0.67	ceftrixon	Kleb.oxy	R	R	S	S
89	Mrs.Maheswari	62	F	NS	89	44	0.56	Cefotaxi	Kleb.pne	R	R	S	S
90	Mr.Thanush	52	M	S	96	76	0.68	Cefotaxi	Kleb.pne	R	R	S	S
91	Mr.Veeranan	62	M	S	96	69	0.64	ceftrixon	CONS	R	R	S	S
92	Mr.Arumugam	46	M	S	94	62	0.66	ceftrixon	Pseudom	R	R	S	S
93	Mrs.Pandiselvi	60	F	NS	96	79	0.66	ceftrixon	Kleb.pne	R	R	S	S
94	Mr.Gunaselan	51	M	S	98	75	0.67	ceftrixon	Kleb.pne	R	R	S	S

95	Mr.Natarajan	59	M	NS	82	42	0.56	ceftrixon	Pseudom	R	R	S	S
96	Mr.Muthiah	66	M	S	92	58	0.62	ceftrixon	Kleb.oxy	R	R	S	S
97	Mr.Avudaiyan	48	M	S	95	62	0.66	ceftrixon	CONS	R	R	S	S
98	Mr.Durai	57	M	S	87	47	0.57	Cefotaxi	Pseudom	R	R	S	S
99	Mr.Pandi	55	M	S	95	69	0.63	Cefotaxi	Kleb.pne	R	R	S	S
100	Mr.Ramanan	56	M	S	86	37	0.43	ceftrixon	Pseudom	R	R	S	S

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Name of the Candidate	:	Dr.S.Radhakrishnan
Course	:	PG in MD General Medicine
Period of Study	:	2014-2017
College	:	MADURAI MEDICAL COLLEGE
Research Topic	:	Bacterial flora of sputum, its antibiogram and its relationship with severity of COPD in patients with acute exacerbation – A hospital based study in a tertiary care hospital
Ethical Committee as on	:	16.03.2016

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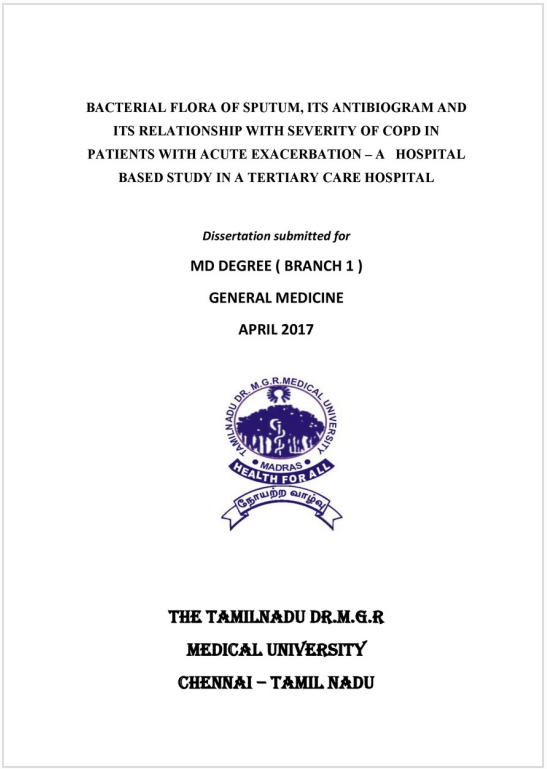

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Dissertation submitted for

MD DEGREE (BRANCH 1)

GENERAL MEDICINE

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