BACTEROLOGICALPROFILE AND ANTIBIOTIC SENSITIVITY PATTERN IN SPUTUM CULTURE OF ELDERLY PATIENTS WITH ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

By

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LIST OF ABBREVIATIONS

COPD - Chronic Obstructive Pulmonary Disease

AECOPD - Acute Exacerbation of Chronic Obstructive Pulmonary Disease

GOLD - Global Initiative for Chronic Obstructive Lung Diseases

QoL - Quality of Life

NCMH - National commission on Macroeconomics & Health

PSB - Protected specimen brush

ATS - American thoracic society

FEV - Forced Expiratory Volume

FVC - Forced Vital Capacity

WHO - World Health Organisation

NHLBI - National Heart Lung 7 Brain Institute

ICMR - Indian Council of Medical Research

BAL - Broncho Alveolar Lavage

ACOS - Asthma COPD overlapSyndrome

MMSE - Mini-Mental State Examination

CT - Computed Tomography

EFL - Expiratory Flow Limitation

PCR - Polymerase Chain Reaction

EELV - End Expiratory Lung Volume

DH - Dynamic Hyperinflation

IC - Inspiratory Capacity

ERS - European Respiratory Society

PR - Pulmonary rehabilitation

ABSTRACT

BACKGRAOUND:

Chronic obstructive pulmonary disease is a chronic non-communicable disease and its prevalence dramatically increases with age and leads to decreased quality of life in elderly.Knowledge of local bacteria implicated the sensitivity patterns of AECOPD in patients at this geographical area that would facilitate an early introduction of a proper antibiotic, which would reduce the mortality, morbidity and improve the prognosis and Quality of Life among the elderly patients.

MATERIAL AND METHODS:

This study is a prospective study carried out in 66 cases of Acute Exacerbation of Chronic Obstructive Pulmonary Disease aged more than 60 years. A detailed history was taken, clinical examination was carried out, relevant blood investigations, chest x ray, Pulmonary function test, sputum examination consisting of Gram staining, Ziehl-Neelsen staining and Culture/Sensitivity pattern were studied. The results and observations of the study are as follows.

RESULTS:

The age group of patients varied from 60 to 91 years with a mean age of 70.63 years. Most of the patients presented with typical complaints of exacerbations, that is increased breathlessness and cough which was productive in nature. P Pulmonale was the most common finding noted in ECG in 62% of the patients. Pulmonary function test was conducted in 58 patients in the study. Among them 75.7% patients showed obstructive and 12.3% showed pseudo restrictive pattern. On gram staining of the sputum, Gram positive cocci were isolated from 39.4% of the patients, Gram negative bacilli in 22.7% of the patients, and mixed in 11% of the patients. Bacteriological isolation by sputum culture showed *Streptococcus pneumoniae* as the most common

organism isolated in 16(24.2%) patients. Among all the tested antibiotics for various gram negative and gram-positive organisms, maximum number of patients were sensitive to Cefoperazone that is in 53% of patients. *Streptococcus pneumoniae*, which was the most common isolate, was sensitive to Cefoperazone, Linezolid, Piperacillin and Clindamycin in decreasing frequency. All case mortality in this study was seen in 1(1.5%) patient.

CONCLUSION:

Exacerbations of COPD in elderly result in substantial worsening of the general condition of their quality of life. Bacterial infection is the most common triggering factor for exacerbations of COPD in elderly. Knowledge of the local bacteria with their sensitivity pattern resulting in exacerbations in the local geographical area would help in prompt management of them.

Adequate awareness regarding the immunization among the elderly COPD patients, their caregivers and the treating doctor would prevent many exacerbations and hence improved quality of life. Elderly patient with COPD requires special attention because of high susceptibility of older people to disease, medication is more and the number of drugs to be taken daily increases progressively with age.

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INTRODUCTION

"Chronic obstructive pulmonary disease (COPD) is characterised by the slowly progressive impairment of airflow in lung function and worsening of breathlessness, exercise capacity and impairment of quality of life with time[(1)(2)].The rate of decline varies from individual to individual. In a subset of patients, this steady decline is punctuated in the natural course by episodes of increased symptoms, labelled as "acute exacerbations".

Exacerbations are acute worsening of clinical condition in COPD patients. An acute exacerbation of COPD (AECOPD) was defined in the GOLD 2014 update as "an acute event characterized by worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication"[(1)].

The chronic airflow limitation is a characteristic of COPD; which is caused by a mixture of small airways disease (Obstructive bronchitis) and parenchymal destruction (Emphysema), the relative contributions of which vary from person to person.

The high prevalence of COPD has made the disease a leading cause of morbidity and mortality worldwide which induces an economic and social burden that is both substantial and increasing day by day[(3)].The global prevalence of COPD data is difficult to estimate due to wide differences in survey methods, diagnostic criteria, and analytical approaches. Based on BOLD (Burden of Obstructive Lung Diseases) and other large scale epidemiological data, it is estimated that the number of COPD cases was 384 million in 2010 with a prevalence of 11.7%[(4)].

In the survey conducted for the global standardised death rates for both sexes in 2015, COPD ranked third with about 3.2 million people dying of the disease

annually. The two leading causes of death have been Ischemic heart disease and cerebrovascular disease.

Like China, "India also plays a significant role in the percentage of COPD mortality which is estimated to be amongst the highest in the world; i.e. more than 64.7 estimated age standardized death rate per 100,000 amongst both sexes as mentioned in the WHO Global InfoBase Updated on 20th January 2011 (India 102.3 and China 131.5). This if translated would approximately amount to 556,000 in case of India (>20%) and 1,354,000 cases in China (about 50%) out of a world total of 2,748,000 annually"[(5)].

COPD is also associated with a significant economic and social burden to the society. AECOPDs account for the largest proportion of the COPD burden on the healthcare system. Murthy KJR et al estimated that COPD could cause an economic burden of up-to Rs 56 billion in 2016 based on the estimates made during 2001-2005 assuming that the practice of treating COPD would remain same[(4)].

Treating COPD and associated co morbidities require institutional resources and there is a need of regular hospitalizations which can be cumbersome for the individuals as well as the health system. The rate of hospitalization can be four times among elderly aged more than 65 years when compared to younger ones. The mean length of hospital stays for COPD ranges from 4.5 to 16 days in normal to intensive care. Moreover, the social structure of India does not provide adequate protection to the elderly resulting less adherence to the treatment.

Health status has been emphasized as one of the most important consequence measures in COPD. A vast majority of population suffer a sharp decline in the Quality of Life (QoL) after acute exacerbations. A prospective cohort which was followed for

six months showed that only 26% of the patients were both alive and able to report a good, very good, or excellent QoL.

The occurrence of COPD is a complex interplay between the genes and environment. Cigarette smoking is by far the most common environmental risk factor in the causation of COPD. Even though smoking is the leading cause less than 50% of the heavy smokers develop COPD during their lifetime[6]. Other risk factors include passive smoking, air pollution, protease inhibitor deficiency, occupation, chronic bronchopulmonary infection and airway hyperresponsiveness.

Among the episodes of AECOPD, more than 75% the of episodes are incited by infections[7]. Environmental pollution has also been implicated in a small proportion of patients up to 10%[8]. Decreased air temperature, increased exposure to sunshine, and decreased humidity were also found to be responsible for triggering exacerbations of COPD. "The National Commission on Macroeconomics and Health (NCMH) estimates of prevalence of COPD showed that burden of COPD were found to be more in rural India and would be increasing all the time"[4].

The proof that bacterial infections are the causation factors for AECOPD comes from the isolation of pathogens from the lower respiratory tract secretions obtained by different techniques during episodes of exacerbations. "Studies which employed bronchoscopic sampling with a protected specimen brush (PSB) to obtain uncontaminated lower airways secretions have found approximately 30% of sputum cultures and 50% of bronchial secretion cultures associated with the presence of potential pathogenic bacteria"[9][10].Various studies on isolation of pathogens associated with AECOPD suggested that the presence of pathogens was clinically and geographically unpredictable.

Old age and comorbidity go hand in hand in misdiagnosing and undertreating COPD in elderly. There is a disparity between practice guidelines and treatment among the elderly COPD patient. The management of elderly patients with COPD should encompass a multidisciplinary approach. Along with assessment of the lung ventilator performance and functional impairment, nutritional status and mental health should be evaluated.

Knowledge of local bacteria implicated in and the sensitivity patterns of AECOPD would facilitate an early introduction of a proper antibiotic would reduce the mortality, morbidity and improve the prognosis and Quality of Life among the patients. The data about the bacteria involved in AECOPD in our area is sparse and very less studied.

Hence the following study was undertaken to study the bacteriological profile and antibiotic sensitivity pattern in sputum culture of elderly patients with AECOPD.

AIMS AND OBJECTIVES

1) To identify and establish bacteriological profile and antibiotic sensitivity pattern in sputum culture of elderly patients with acute exacerbation of chronic obstructive pulmonary disease admitted in our hospital.
2) To study the mode of presentation in elderly with AECOPD.
3) To analyse morbidity pattern and mortality.

REVIEW OF LITERATURE

HISTORICAL LANDMARKS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

The evolution of knowledge regarding COPD and its components- emphysema, and chronic bronchitis covers 200 years of history.

Earliest references to the description of emphysema includes: "Bonet's description of voluminous lungs in 1679; Morgagni's description of 19 cases in which the lungs were "turgid", particularly from air; and Baille's illustrations of the emphysematous lung"[11].

Badham, in 1814, "used the word catarrh to refer to the chronic cough and mucus hypersecretion which are the cardinal symptoms of chronic bronchitis. He also described bronchiolitis and chronic bronchitis as disabling disorders"[11].

In 1821, Laennec beautifully described the component of emphysema in his 'A treatise on the disease of the chest and on mediate auscultation', "The disease which I designate by this title is very little known and has not hitherto been correctly described by any author. I for a long time thought it very uncommon, because I had observed only a few cases of it: but since I have made use of the stethoscope, I have verified its existence as well on the lining as the dead subject, and am led to consider it as by no means infrequent. I consider many cases of asthma, usually deemed nervous depending on this cause. The chief reason of this affection having been so completely overlooked is, that it is in some sort merely the exaggeration of the natural condition of the viscous". Laennec even had described a combination of emphysema and chronic bronchitis[11].

Spirometer was invented by John Hutchinson in 1846. The instrument could be used to measure only vital capacity(11). In 1947, Tiffeneau and Pinelli added the

concept of timed vital capacity as a measure of airflow, for spirometry to become complete as a diagnostic instrument[11].

In 1916, Osler's principles and practice of medicine believed emphysema was caused by excessive pressure in the alveoli[11].

"Gaensler in 1950 introduced the concept of the air velocity based index based on Tiffeneau's work and later the forced vital capacity, which is the foundation of FEV_1 and FEV_1/FVC percent"[11].

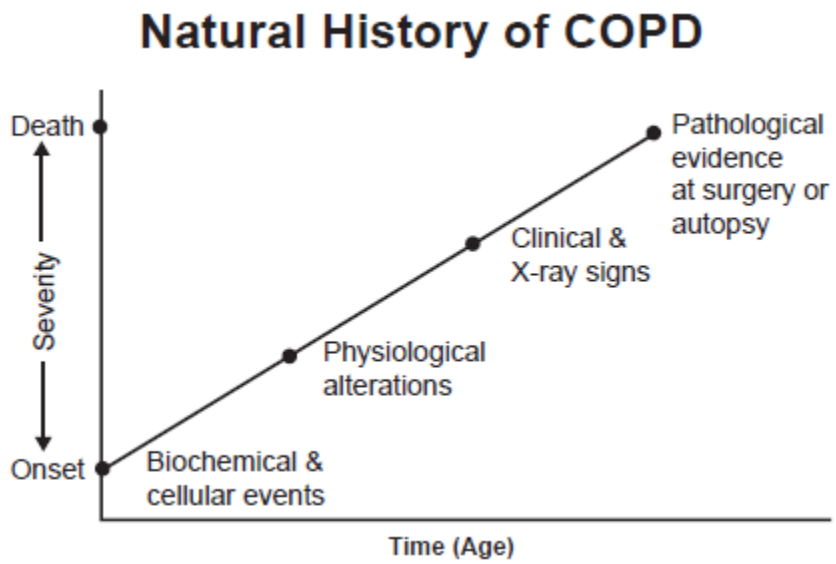
Ronald Christie in 1944 suggested that "The diagnosis should be considered certain when dyspnea on exertion, of insidious onset, not due to bronchospasm, or left ventricular failure, appears in a patient who had some physical signs of emphysema together with chronic bronchitis and asthma"[11].

Barach and Bickerman in 1956 edited the first comprehensive text book, "Pulmonary emphysema". In total, 17 eminent clinicians and scientists made a significant contribution to this book edited by Barach and Bickerman[11].

Hinshaw and Garland in 1956 composed the "first edition of the textbook of respiratory medicine", which shows,"A nice picture of a Collins 13.5 litres recording spirometer and shows capacity spirograms that demonstrate airflow limitation in emphysema"[11].

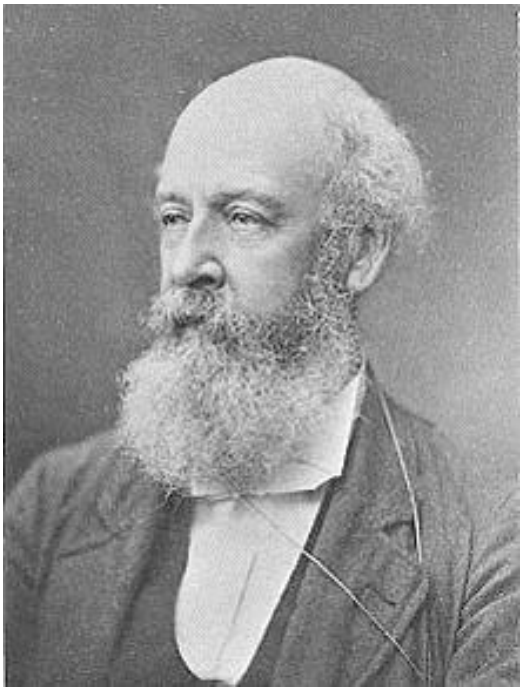
"The CIBA guest symposium in 1959 and the American Thoracic Society Committee on Diagnostic Standards in 1962, the two landmark meetings defined the components of COPD, which are foundations for our definition today"[11].

The American Thoracic Society (ATS) defined chronic bronchitis in clinical terms including chronic cough lasting at least three months in a year for at least two years. To the contrary, ATS defined emphysema in anatomic terms of enlarged alveolar spaces and loss of alveolar walls.



In a study conducted by Burrows and Earle done in Chicago, the course and prognosis of 200 patients diagnosed with COPD were studied. “In his further studies he recognized that patients with a low a low FEV_1/FVC percentage predicted the onset of rapid decline in FEV_1 over time.” He termed this phenomenon as “The Horse Racing Effect”[(11)].

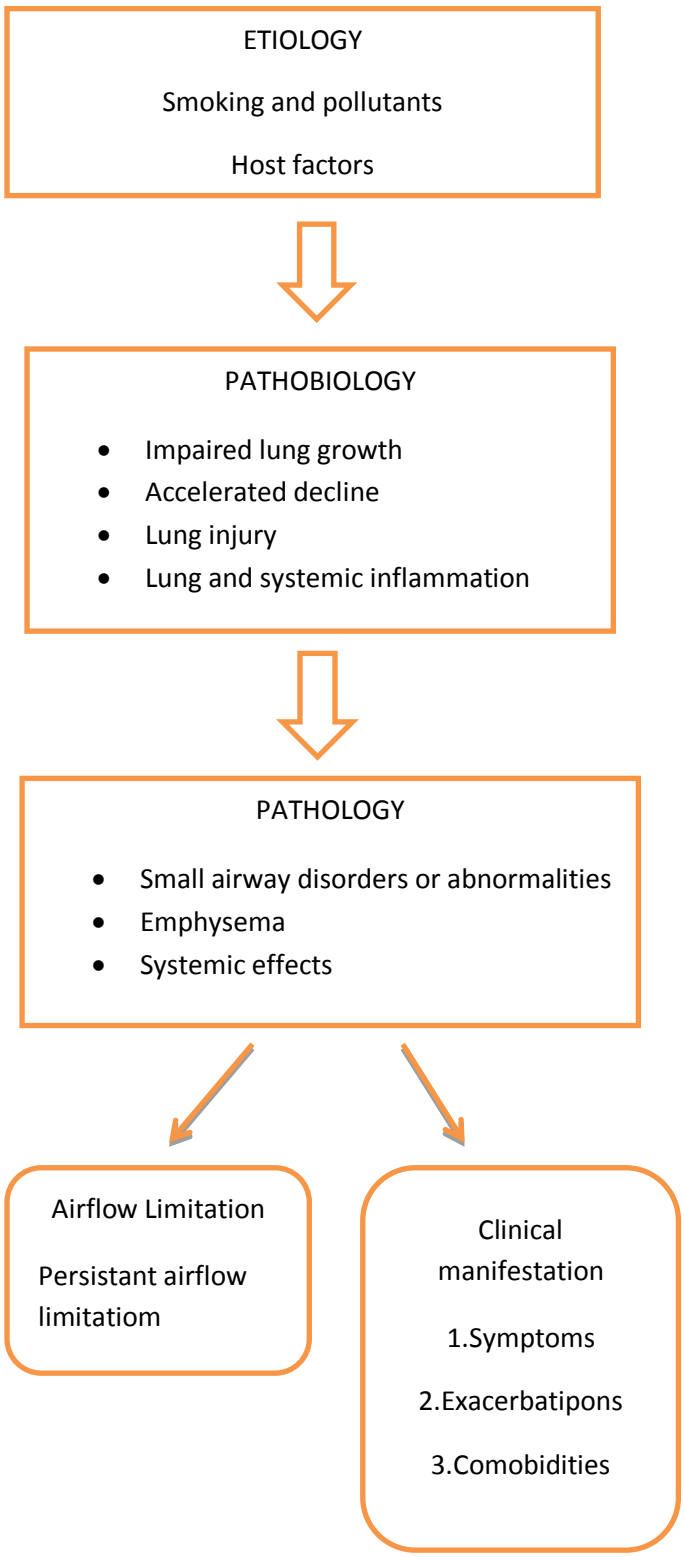
In 2001, the “Global Initiative of Obstructive Lung Disease (GOLD)” was launched by the “World Health organization (WHO)” and “National Heart, Lung and Blood Institute (NHLBI).”By studying and considering all the international standards, GOLD penned out a new classification of the severity of COPD, and it is now widely and graciously accepted by majority of the organizations and societies.



Charles Badham, (17 April 1780 – 10 November 1845)

René-Théophile-Hyacinthe Laennec, (17 February 1781 – 13 August 1826)

ETIOLOGY, PATHOBIOLOGY AND PATHOLOGY OF COPD



DEFINITIONS

Chronic Obstructive Pulmonary Disease (COPD)

GOLD 2018 report defines COPD as a common, preventable and treatable disease that is characterised 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[12].

Acute Exacerbation of COPD

GOLD 2018 report defines AECOPD as,"an acute worsening of respiratory symptoms that result in additional therapy"[12].

AGE RELATED CHANGES IN THE RESPIRATORY SYSTEM:

Physiological changes in the respiratory system with age contribute to impaired pulmonary function and to the increased prevalence of COPD.

In general, physiological changes includes a progressive reduction in compliance of the chest all, reduction in strength of the respiratory muscles, and anatomical changes to the lung parenchyma and peripheral airways. Osteoporosis and kyphosis induced changes in shape of chest wall mechanics[13][14]. The functional consequences of these changes on the respiratory system include decreased peak inspiratory and expiratory airflows, vital capacity and efficiency of gas exchanges. Based on observations made from multiple studies, at the age of 10 years, "FEV1 would be expected to decrease by about 30% and forced vital capacity by about 20% compared with values at the age of 20 years"."At the age of 70 years, the expected FEV1/FVC ratio would be about 74%, a value approaching the 70% criterion used for diagnosing significant obstruction"[15].Loss of elastin results in increased residual volume and significant increase in dead space[13]. All of these changes contribute to an increase likelihood of COPD in elderly, and critical to geriatric considerate, these age-related changes may be less amenable to treatment. These changes also pose a diagnostic difficulty.

AETIOLOGY AND RISK FACTORS OF COPD IN ELDERLY:

Age:

Age is one of the prominent risk factors for COPD. "COPD is common in older people, with an estimated prevalence of 10% in the US population aged more than 75 years"(16)."COPD accounts for most of the people on continuous and chronic oxygen therapy that is on average a population exposure to smoke and pollutants"[17].All these observations point towards the effect of cumulative exposure to smoke and pollutants. To add, telomere shortening, a distinctive sign of aging process, characterizes COPD patients, and age and COPD additively promote it[18].

Many other similarities between aging lung and COPD lung are worth mentioning: "Vital capacity declines by 10-20 mL yearly in normal aging, about 30 mL in COPD patients, whereas residual volume increases in both normally aging and COPD lung. To add to it, elastic recoil, mucociliary clearance, mucosal immunity, and vascular reserve decrease in the elderly, and more, in COPD"[19].

Chronic hypersecretion of mucus and persistent airflow obstruction:

Many studies have proved bar doubt that the prevalence of cough and sputum is more in smokers compared to non-smokers. These features arise from abnormalities in multiple lung sites. "Bronchial gland enlargement in the proximal conducting airways is the main mechanism behind persistent cough and sputum production. In case a smoker stops smoking permanently, then in 90 % of them the sputum production will cease"[20]. The persistent airflow obstruction arises from damage to the peripheral airways and airspaces and is persistent after the cessation of cigarette smoking.

Many studies have proved bar doubt that the prevalence of cough and sputum is more in smokers compared to non-smokers. To be more implicative, the presence

of chronic bronchitis has almost been confined to cigarette smokers. According to the Indian Council of Medical Research (ICMR) commissioned four city multicentres based INSEARCH-1 studies, "Smokers had 3 times more risk of developing COPD as compared to non-smokers and bidi workers were at higher risk of developing COPD than their cigarette counterparts."

Cigarette smoking:

Various data suggesting that tobacco smoking is the eminent etiological factor in COPD is overwhelming, and smoking is believed to be the cause of 85-90% of all COPD men in the industrialized world(21)(22).Not all cases of COPD will have tobacco smoking as a risk factor. The factors that identify the cigarette smoker who is susceptible for development of progressive airflow limitation are still a matter of debate and research.

On an average, cigarette smokers have a high annual rate of decline in FEV1 of about 50 mL, which is nearly double the average value of 30mL annually present in non-smokers. However, there is considerable variation in the decline in FEV1, with some smokers showing very rapid rates of decline.The quantity of cigarette smoke inhaled and the amount of tar, nicotine, and other constituents in the cigarettes are among the other factors which complicate the association between the number of cigarettes smoked and the rate of decline in FEV_1.

Passive smoking:

Several studies regarding the relationship between environmental tobacco smoking (passive smoking) and the development of chronic airflow obstruction shows a non-significant trend to an increased relative risk from passive smoking[(23)(24)].

Air Pollution:

There is still a debate whether a long-term exposure to outdoor air pollution is a predictor for development of COPD. Air pollution still appears to be one of the factors implicated in the development of mucus hypersecretion, although the association between airflow limitation and accelerated decline in FEV_1 is less clear[(25)].

There is strong evidence that indoor air pollution due to use of wood and biomass (cow dung cakes) as fuel leads to development of COPD. This in fact might be even more important risk factor than smoking in rural India. In some areas it has been estimated that exposure to smoking as a result of indoor cooking can explain up to 50% of cases of COPD[(26)].

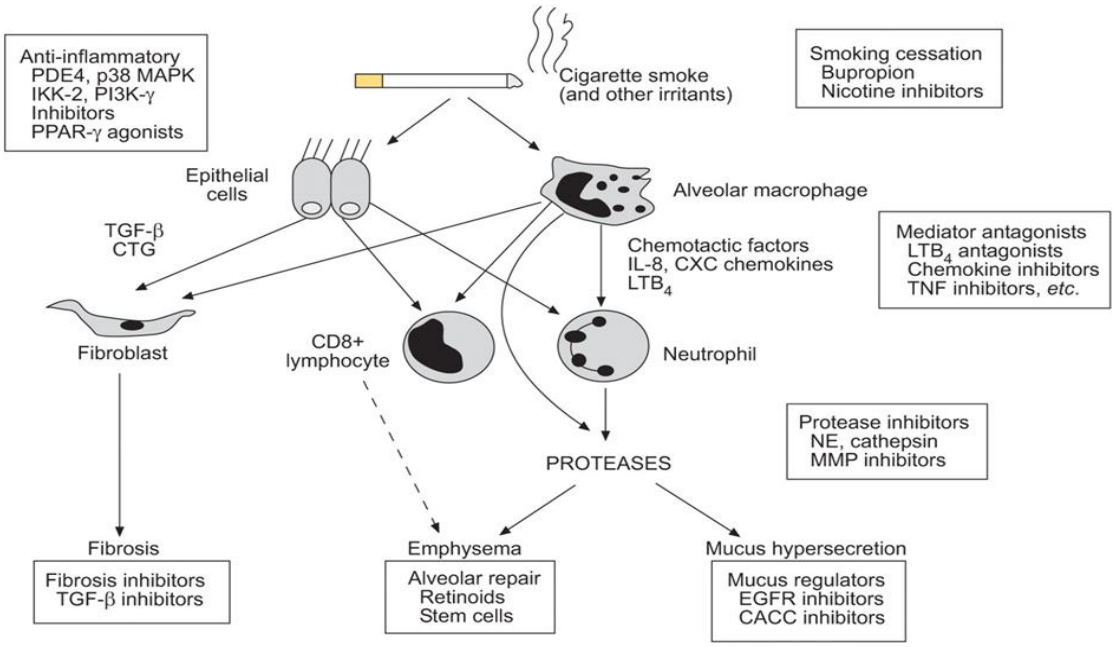


DIAGRAM: CIGARETTE SMOKING AND EMPHYSEMA

Protease inhibitor deficiency:

"α_{1}- Antitrypsin(α_{1}-AT) or α_{1}-protease inhibitor (α_{1}-Pi) is a polymorphic glycoprotein that is responsible for the majority of the antiprotease activity in the serum. It is synthesized in hepatocytes and increases in concentration rapidly as part of the acute phase response. In 1963, Laurell and Eriksson became the first ones to describe the association between α_{1}-AT deficiency and the development of early onset emphysema"[(27)].

The serum levels of α_{1}-AT in α_{1}-AT deficiency is around 20% of the normal level. The minimum point for an increased risk of development of emphysema is a level around 27% of normal. This has been considered as a strong genetic risk factor for the development of emphysema. It also forms the basis of proteolytic theory of the pathogenesis of emphysema.

Occupation:

The relationship between the development of airways obstruction and the exposure to dust at the workplace is controversial[(28)]. Many confounding factors add to the aetiology. Despite the fact that smoking is the eminent risk factor in development of COPD, the irony is only 20% of smokers go to develop the disease. But the prevelance of the same is increased when compounded with exposure to dust at work implicating an interplay between smoking and exposure to dust. Many studies have shown that workers exposed to coal, welding fumes, and cadmium developed COPD.

Chronic bronchopulmonary infection:

Acute bronchopulmonary infection in a setting of COPD showed an acute decline in lung functions, which may persist for several weeks but recovers completely.However,"Studies in general population and in smokers failed to

demonstrate a strong association between the annual rate of decline in FEV_1 and recurrent bronchopulmonary infection, and it was mainly studied in smokers with mild impairment of lung function.""Indeed a study in Salt Lake City did find an association between lower respiratory tract infection and an accelerated decline FEV_1 in a group of patients who had an established COPD"[29].

Growth and nutrition:

There are several studies to suggest the effect of nutrition on both the growth and decreased ventilatory function. "In a study done among men born in Hertfordshire, lung function in adult life and mortality from chronic respiratory diseases correlated inversely with the birth weight and weight at 1 year of age"[30].

Asthma and Airway Hyperresponsiveness:

Asthma has been implicated as a risk factor for development of chronic airflow limitation and COPD."Tucson Epidemiological Study of Airway Obstructive Disease reported that adults with asthma have a twelve-fold higher risk of acquiring COPD over time to those without asthma, after adjusting for smoking"[31].

In multiple population studies, airway hyper-responsiveness without the presence of asthma in the individual has been demonstrated as an independent predictor of COPD and respiratory mortality.

PATHOLOGY OF COPD IN ELDERLY:

The pathological changes in patients with COPD are complex and occur in both large and small airways, and in the alveolar compartment. There is still no clarity regarding the mode of fixed airway obstruction in COPD. It can either be due to inflammation and scarring in small airways which would result in airway lumen narrowing or due to the loss of support to the airways because of loss of alveolar walls in emphysema.

The pathology of COPD can be studied in a simple manner by considering the three sides at which the pathological changes occurs in the airway system among smokers. These are:

a) The bronchi where chronic bronchitis develops
b) The alveolar compartment where emphysema develops
c) The more peripheral airways, where small airways disease develops.

CHRONIC BRONCHITIS:

The increase in the volume of the sub mucosal glands and an increase in the number and change in distribution of the goblet cells in the surface epithelium is the pathological basis behind the hypersecretion of mucus. "In chronic bronchitis, the hypertrophy of the mucus secreting glands was thought to be largely a consequence of irritant action of cigarette smoke"[(32)]. The hypertrophy of mucus glands is prominent in the larger bronchi and it is distributed equallyin whole of the lung[(33)]."Reid index is the ratio of distance between the basement membrane of airway epithelium and the cartilage to the thickness of the gland layer and it is normally 3:1"[(34)]. The hypertrophy of the mucus gland is assessed by Reid index.

"Normally goblet cells are predominantly present in the proximal airways and decrease in number in more distal airways, being normally absent in terminal or

respiratory bronchioles. In smokers, goblet cells not only increase in number but extend more peripherally. The metaplastic and dysplastic changes in the surface epithelium in smokers may replace the goblet cells of normal respiratory epithelium resulting in decrease in the goblet cells"[35]. As the amount of submucosal glands is more than that of goblet cells, a direct relationship exists between the total mass of submucosal glands and the amount of sputum produced [29].

EMPHYSEMA:

Emphysema is defined as "a condition of the lung characterised by abnormal, permanent enlargement of the airspaces distal to the terminal bronchiole, accompanied by destruction of their walls and without obvious fibrosis. "

There is little information about the collagen framework in emphysema and if there is an increase or decrease in collagen and elastin in the early stages of emphysema. Histological examination of the emphysematous reveals increased amount of collagen when compared to less emphysematous or non-emphysematous area of the lung[36].

Classification of emphysema:

Four types are recognised and classified according to the distribution of the abnormally large air spaces within the acinar unit[37][38].

a) Panacinar emphysema, in which the abnormally large air spaces are found evenly distributed across the acinar unit.
b) Centriacinar or proximal acinar emphysema, in which the abnormal air spaces are found initially in association with the respiratory bronchioles.
c) Periacinar or paraseptal emphysema, in which the abnormal air spaces run along the edge of the acinar unit where it abuts a fixed structure such as the pleura, a septum or a vessel.

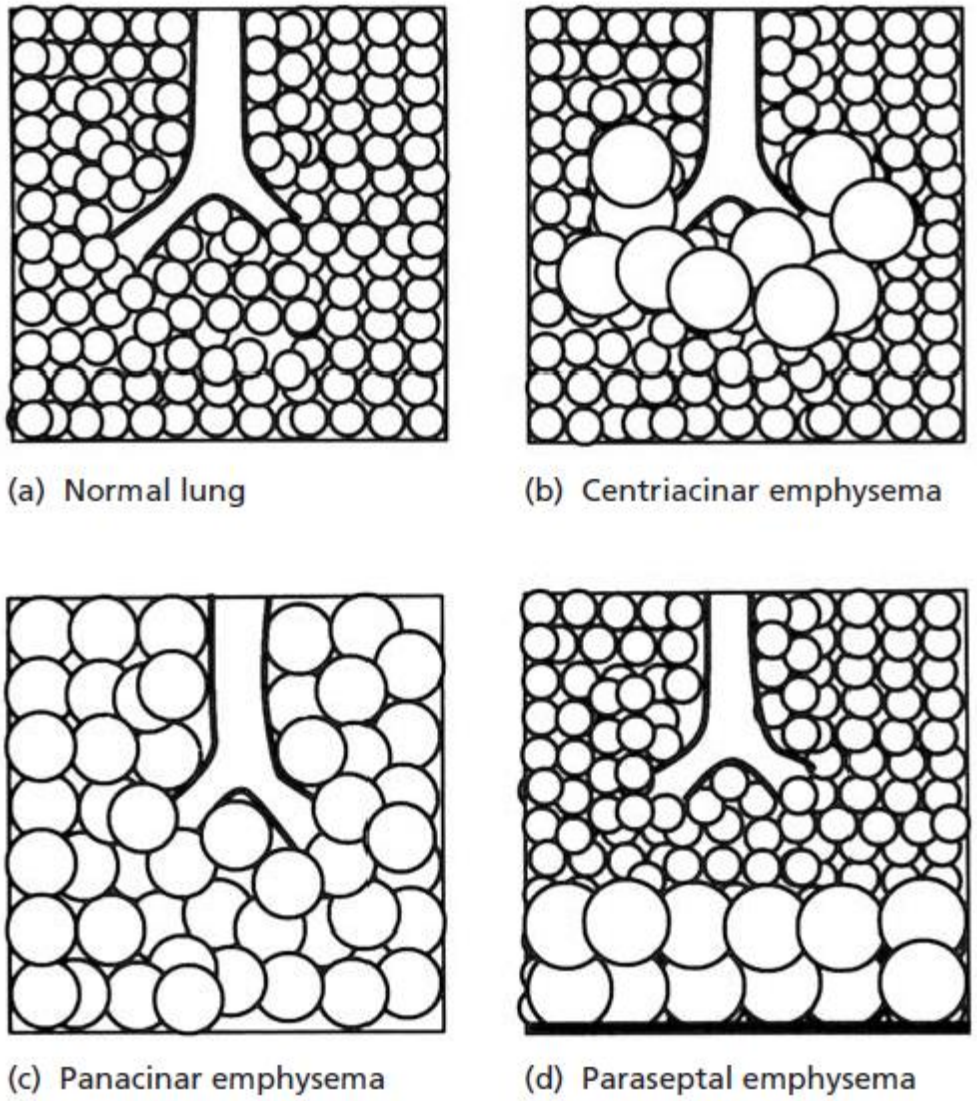
d) Scar or irregular emphysema found around the margin of the scars in the lung and not related to the architecture of the acinus because the scars themselves are irregularly distributed.

The different patterns of emphysema may occur singly or together in the same lung. Although both Centriacinar and Panacinar emphysema are related to smoking, they have different distributions in the lung. These two types of emphysema have different distribution within the lungs. Centriacinar emphysema is more common in the upper zones of the upper and lower lobe, whereas panacinar emphysema may be formed anywhere in the lungs but is more prominent at the bases and may be associated with alpha-antitrypsin deficiency.

Bullae represent localised areas of emphysema that are over distended and are more than 1cm in diameter. The terms bulla, cyst, cavity and pneumatocele are often used interchangeably.

"Bullae have been classifies according to their size and position"[39].

a) Type 1 bullae having narrow neck, attached to a mushroom like expansion into the pleural space[39].
b) Type 2 having a broader neck, represent distension of a moderate area of emphysema[39].
c) Type 3 occurring in area of severe emphysema within the lung and having no pleural reflection[39].



DISTRIBUTION OF ABNORMAL AIRSPACES WITHIN THE ACINAR UNIT IN DIFFERENT TYPES OF EMPHYSEMA

Small airway disease:

Hogg, Macklem and Thurlbeck introduces the concept of 'small airways disease', by using,"A retrograde catheter through which they were able to show that the increased flow resistance in the lungs of the patients with COPD largely occurred in the small airways at the periphery of the lungs"[(40)].

Pathology of severe COPD:

Severe macroscopic emphysema is the most prominent feature at autopsy in patients dying with end stage COPD[41]. "Centriacinar or panacinar emphysema may predominate, or there may be mixture of both. Centriacinar emphysema is more extensive and the lesions are larger in end-stage COPD than those seen in smokers without airways obstruction"[34].

The Centriacinar lesions are more conspicuous in the upper zone but they can be found in all the lobes in extensive lesions. Mucous plugging and areas of bronchopneumonia are a common finding at autopsy of cases of severe COPD.

Pulmonary vasculature:

The development of chronic alveolar hypoxia in patients with COPD produces characteristic remodelling of the pulmonary arteries that consist of three components.

1) Extension of the medical muscle into the pulmonary arterioles, which normally have no muscle in their walls[42][43].
2) Presence of longitudinal smooth muscle in the intima of the small pulmonary arteries. The muscle may become progressively thicker and may eventually occlude the vascular lumen.
3) Small pulmonary arteries,where they develop inner muscular tubes.

Heart:

"Right ventricular hypertrophy and pulmonary hypertension are commonly found in patients in COPD who have chronic hypoxemia"[44].

PATHOGENESIS OF COPD IN ELDERLY:

"As COPD encompasses at least these pathologies conditions, chronic bronchitis, emphysema and small airways disease or respiratory bronchiolitis, it is a difficult task to encompass these diverse pathologies in our simple pathogenic mechanism"[34].

Several important studies and observations suggest,"The basis of the protease-antiprotease theory of the pathogenesis of emphysema". The hypothesis states that,"In healthy lungs the release of proteolytic enzymes from inflammatory cells does not cause lung disease because of inactivation of these proteolytic enzymes by an excess of inhibitors. An imbalance develops between proteinases and antiproteases in favour of proteinases in conditions of excessive enzyme load or where there is an absolute or functional deficiency of antiprotease resulting in uncontrolled enzyme activity and degradation of lung connective tissue in alveolar walls, leading emphysema."

α_1- Antitrypsin/ α_1- protease inhibitor:

"α_1- AT is a potent inhibitor of serine proteases and has greatest affinity for the enzyme neutrophil elastase"[45]."It is a glycoprotein that is synthesized in the liver and it increases from its usual plasma concentration as a part of acute-phase response.

α_1 –AT found in the lung is almost derived from plasma and in minor from the monocytes and macrophages"[34].

α_1–AT protein is encoded by a single 12.2 kb gene present on chromosome 14[46].

Emphysema develops in the absence of α_1 –AT deficiency by:

1) An increase in the proteinase burden, due to either the presence of increased number of inflammatory leucocytes in the airspaces or the release of excess protease from the leucocytes
2) A functional deficiency of protease inhibitors.
3) A combination of both the above-mentioned pathways.
4) An abnormality in the repairs mechanisms for lung connective tissue.

Pathogenesis of emphysema in patients without α_1-AT:

In these cases, pathogenic mechanisms are more complex and the clearest association is with cigarette smoking. There are several other mechanisms whereby cigarette smoke can alter the elastase-antielastase balance in the lungs, assuming that neutrophil elastase and α_1–AT are the main players in the protease- anti protease imbalance[34].

To the surprise only 20% of smokers go on develop COPD. So, the question of susceptibility for the causation of COPD among smokers.These variable factors include the cellular response to tobacco, bronchial hyper activity, variations in neutrophil macrophage protease activity, protease inhibitor function and lung matrix injury and repair.

Overall, the mechanisms for the development of emphysema can be conveniently described under there major heading:

1) Increased protease burden
2) Decreased anti protease function
3) Decreased synthesis of elastin

Increase in protease burden:

Several studies have now provided evidence supporting a role of neutrophil elastase in the development of emphysema[47].

The several processes by which the elastase burden could be in increased in cigarette smokers include:

1) Increased sequestration and migration of neutrophils in to the lungs on smokers
2) Neutrophils from susceptible smokers may contain increased amounts of elastase compared with non-susceptible smokers or control subjects.
3) Neutrophil, once recreated may show enhanced degradation, leading to more connective tissue injury.

Decreased Antiprotease Function:

"In the protease ant protease theory of the pathogenesis of emphysema, the concept is the functional deficiency of Alpha –AT in the airspaces produced by smoking due to oxidation of the methionine-358 residue at the active site of α_1 –AT molecule. It can be due to a direct oxidative effect of cigarette smoke or by oxidants released from activated airspace leucocytes"[48][49]."Along with that the direct oxidant effect of cigarette smoke, both macrophages and neutrophil from cigarette smokers release more reactive oxygen species than cells obtained from non-smokers and inactivate α_1–AT in vitro"[50][51]. In contrary to this measurement of α_1 –AT in BAL from healthy smokers and non-smokers have failed to find any difference.

Many explanations have been preferred to explain this somewhat unclear picture.

1) Other anti-elastases may contribute to the anti-protease shield in the lungs, in addition to α_1–AT.
2) More subtle mechanisms may reduce the inhibitory activity of Alpha –AT.

3) The protease anti protease imbalance occurs in micro environment or the lung interstitium, which is not sampled by BAL.

Decrease Elastin Resynthesis:

"Many studies have attempted to measure products of elastin degradation as a reflection of the excess proteolytic activity which is thought to occur in emphysema. The concentration of the elastin cross-linking peptide desmosine and elastin peptides is increased in experimental emphysema in smokers and in patient with COPD"[52][53]. It has been postulated that further factors leading to the development of emphysema is a defect in elastin re synthesis. An enzyme, lysyl oxidase is required for cross linking of elastin fibred and so is necessary for the formation of normal tissue elastin. There is a subtle evidence to suggest that lysyl oxidase activity is reduced by cigarette smoking and it may contribute to emphysema by preventing elastase repair.

PATHOPHYSIOLOGY OF COPD IN ELDERLY:

A good understanding has now been acquired regarding the underlying disease process in COPD which leads to the characteristic physiological abnormalities and symptoms.

Airflow limitation and gas trapping:

"The extent to which there is presence of inflammation, fibrosis, and luminal exudates in the small airways correlates with the reduction in FEV_1 and FEV_1/FVC ratio, and probably with the accelerated decline in FEV_1 that is characteristic of COPD. The peripheral airway limitation progressively traps gas during expiration, resulting in hyperinflation. Static hyperinflation reduces the inspiratory capacity and is commonly associated with dynamic hyperinflation during exercise leading to increased dyspnoea and limitation of exercise capacity"[12]. Bronchodilators which act on the peripheral airways reduce gas trapping, which in turn reduces the lung volume and improves the symptoms and exercise capacity.

Gas exchange abnormalities:

Gas exchange abnormalities results in hypoxemia and hypercapnia, and have several mechanisms in COPD. As the disease progresses, "Gas transfer for oxygen and carbon dioxide worsens. Increased dead space ventilation or reduced ventilatory drive may lead to carbon dioxide retention when it is combined with reduced ventilation, due to increased effort to breathe because of severe limitation and hyperinflation coupled with ventilatory muscle impairment"[12].

Pulmonary hypertension:

Pulmonary hypertension develops in the later stages of the disease and hypoxic vasoconstriction in the small pulmonary arteries which would result in the

various structural changes. The structural changes include intimal hyperplasia and smooth muscle hyperplasia combined with hypertrophy.

In COPD an inflammatory response is seen in vessels which is similar to that observed in the airways, along with evidence of endothelial cell dysfunction. "The loss of pulmonary capillary bed in emphysema in turn further contributes to increased pressure in the pulmonary circulation. Progressive pulmonary hypertension may lead to right ventricular hypertrophy and eventually to right cardiac failure"[(12)].

CLINICAL PRESENTATION IN ELDERLY:

Most clinical symptoms occur during the fifth and sixth decade of life. However, the onset of COPD symptoms may be delayed to the seventh decade and beyond in smokers who stopped smoking in midlife. The main symptoms of COPD are breathlessness on exertion and/or cough with or without sputum, reflecting the symptoms of both emphysema and chronic bronchitis.

Breathlessness is the most important reason for medical consultation in COPD, noticed first during physical exertion such as climbing stairs, or during an acute bronchial exacerbation. The symptom of breathlessness usually implies severe impairment of pulmonary function with, with the forced expiratory volume in 1 second(FEV1) less than 50% of predicted(54).Breathlessness is particularly affected by environmental factors such as cold air, dust, fumes, and tobacco smoke and breathlessness aggravates with complications such as pneumothorax, pneumonia or bronchial exacerbations[(55)(56)].

Persistent or intermittent chronic cough, with or without sputum production is the most frequent symptom reported by patients with COPD. Cough usually appears first in the early morning, particularly in the winter. Cough productive of sputum occurs in up to 50% of cigarette smokers, usually within 10years of starting smoking.

Later, cough extends throughout the year. The sputum is usually mucoid, but becomes purulent during infection. Even cough without sputum production('dry cough'), cough with explosive bouts and cough syncope occur but they are uncommon[57].

Haemoptysis occurs occasionally, particularly in acute exacerbations, but should always suggest another cause such as bronchiectasis or lung cancer.

Severe chest pain is not a feature of COPD and its presence should suggest complications (pneumothorax, pleuritic pain in pneumonia) or other conditions that frequently coexist with COPD, such as ischemic heart disease or gastroesophageal reflex. Anorexia and weight loss are common as the disease progression occurs and it is indicative of worse prognosis[58].

The social history reveals that the majority of patients with COPD are cigarette smokers or ex-smokers. Calculation of 'pack years' provide a semi-quantitative but useful estimate of smoking intensity (1 pack year is equivalent to 20 cigarettes smoked each day for 1 year).

THE MISLEADING SYMPTOMS IN ELDERLY:

The chronobiology of symptoms changes from patient to patient in elderly as also highly variable is the presentation of exacerbations. Comorbidity and disability of various origins contribute to make the recognition of COPD problematic. "To add to the problem, cognitive impairment, mainly of verbal memory and constructive ability, and depression may dominate the clinical scene in subjects with hypoxemia and hypercapnia"[19].

Comorbidity and disability contribute to make symptoms a true puzzle in elderly.

A) Relationship between symptoms and phenotype: Two extreme phenotypes persist, the one being bronchitic and the other the emphysematous. Other various

phenotypes co-exist, e. g. the asthma-like and the Combined Pulmonary lower lobe Fibrosis and upper lobe emphysema coexists[59].

B) Chronobiology of symptoms: An important contributor to the clinical phenotype, the circadian rhythm of symptoms would deserve much more attention than currently paid to. Several varieties of symptoms have been reported and contribute to shape a clinical phenotype. "Nocturnal symptoms have been reported in about 60% of COPD patients and wheezing is the most common of these[60][61], Insomnia is highly prevalent in elderly COPD patients and its prevalence increases for increasing age from 65 to over 90 years, whereas such an increase is not evident in patients with chronic non-respiratory diseases[62]. "Chest tightness which is usually suggestive of coronary artery disease has been reported by about one out of four COPD patients"[63].

C) Frequency and clinical presentation of the exacerbations: Having two or more exacerbations in a year would define such a new phenotype irrespective of which is the dominant symptoms. The clinical presentation of exacerbation dramatically changes from patient to patient. Dyspnoea was the hallmark of typical presentation whereas atypical presentations included leg oedema secondary to severe hypoxia and hypercapnia, chest tightness simulating a cardiac attack, dizziness and postural instability due to hypoxemia and fatigue.

D) Impact of comorbidity and disability on symptoms: Disability frequently limits the physical activity and, then, prevents the patient from reaching the threshold of dyspnoea. Accordingly, alternative symptoms such as fatigue, dizziness, non-specific malaise, defective attention and concentration may dominate the clinical scenario[64].

COPD AS A SYSTEMIC DISEASE IN ELDERLY:

COPD has important manifestations beyond the lungs, the so-called systemic effects in elderly. These include the unintentional weight loss, skeletal muscle dysfunction, an increased risk of cardiovascular disease, osteoporosis, and depression, among others. Low grade, chronic systemic inflammation is one of the key mechanisms underlying these systemic effects. Because these extra-pulmonary manifestations of COPD are common and/or may have significant implications for the patient well-being and prognosis, they warrant systemic screening and appropriate management in order to provide optimal medical care.

Cardiovascular diseases (including ischemic heart disease, heart failure, atrial fibrillation, and hypertension) is a major comorbidity in COPD and probably both the most frequent and most important disease coexisting with COPD. Benefits of cardio selective beta-blocker treatment in heart failure outweigh potential risk even in patients with severe COPD.

Osteoporosis and anxiety/depression are often under-diagnosed and associated with poor health status and prognosis.

Lung cancer is frequent in patients with COPD; the most frequent cause of death in patients with mild COPD. Serious respiratory infections are especially frequent.

Asthma-COPD overlap syndrome (ACOS)is a term that has recently been used. It is characterized by persistent airflow limitation with several features usually associated with asthma and several other features usually associated with COPD. ACOS is therefore identified by the features that it shares with both asthma and COPD.

PHYSICAL SIGNS IN ELDERLY:

Many patients with COPD show little abnormality on physical examination in early stages. Hence a diagnosis of COPD cannot be excluded due to the mere presence of normal physical examination. Many times, signs manifest only during an acute exacerbation or with respiratory distress following physical exertion. In cases of severe COPD, physical signs are more specific and sensitive and should be actively elicited.

In the later stages in elderly patients, there will be emaciation, cyanosis, polycythaemia, oedema, raised jugular venous pressure, if there is associated cor-pulmonale and heart failure.

Barrel shaped chest with kyphosis, increased antero-posterior diameter, ribs being set more horizontally, prominent sternal angle and wide subcostal angle are the commonest signs observed in elderly. These changes are permanent. Due to the elevation of sternum, the distance between the suprasternal notch and the cricoid cartilage is reduced from the normal 3-4 finger breadths.

On inspection, severely dyspnoeic patients frequently sit leaning forward with the arms resting on a stationary object, thus supporting the upper body and stabilising the shoulder girdle(coachman's seat). Some patients develop 'pursed-lips' breathing during expiration, which has the effect of preventing respiratory collapse of the intrathoracic airways. Hypercapnia is usually present if the respiratory rate is 25 cycles per minute(65). In advanced disease,there will be barrel shaped chest deformity, which reflects hyperinflation and diaphragm descent and paradoxical in drawing of the lower ribs during inspiration(Hoover's sign)(66).

Percussion of the chest is not very helpful in patient with COPD. The finding of apparently increased resonance is neither sensitive nor specific.

On auscultation, the intensity of the vesicular breath sounds is decreased, correlating with the degree of hyperinflation of the lung. In addition, prolonged expiration, reflecting airflow limitation, crackles on inspiration, best heard at lung bases and reflecting secretions in large airways, must be elicited. Auscultation of the lungs is helpful to differentiate COPD from left heart failure and fibrotic lung disease. In these 2 conditions, end-inspiratory fine crackles can be heard.Because of hyperinflation, apex beat is difficult to feel. Loud pulmonary component of the second heart sound is audible in patients with pulmonary hypertension.

DIAGNOSIS AND INVESTIGATIONS OF COPD IN ELDERLY:

The diagnosis of 'COPD' is usually presumptive: airway obstruction has to be documented by objective tests and other diseases, associated especially with tests and other diseases, associated especially with dyspnoea and cough, need to be ruled out. Spirometry testing is required to confirm the diagnosis and to determine the severity of the disease. Though most of the older people can perform spirometry adequately, some patients may be unable to perform this test. Therefore, in the large majority of patients diagnosis of COPD will need to be made by clinical assessment. COPD is usually accompanied by chronic and age-related diseases, including cardiovascular, metabolic, osteoskeletal and neurologic diseases.

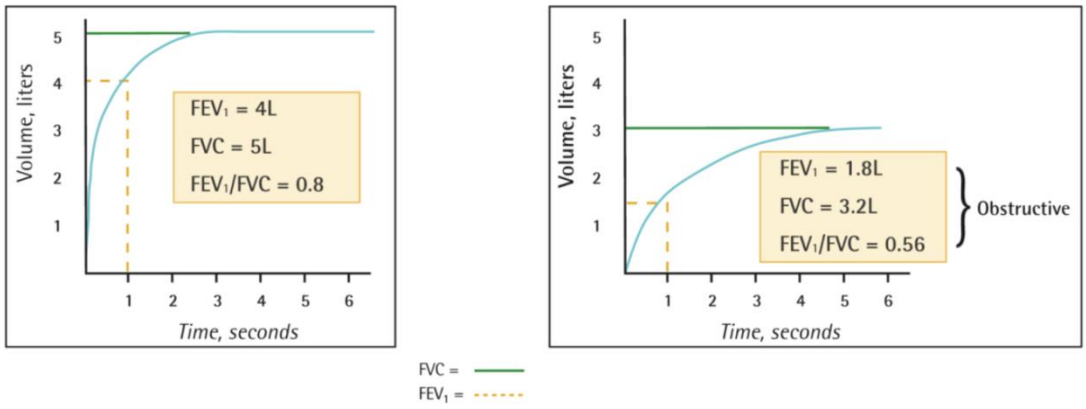
Respiratory function tests:

Pulmonary function tests play a key role in COPD, encompassing diagnosis, assessment of severity, immediate response to therapy, prognosis and aetiology. The dominant functional abnormality is airway obstruction.

Spirometry:

Spirometer is one of the most reproducible and objective measurement of airflow limitation which is non-invasive and readily available test. Spirometry should

measure the volume of air forcibly exhaled from the point of maximal inspiration (forced vital capacity, FVC) and the volume of air exhaled during the first second of this manoeuvre (forced expiratory volume in one second, FEV_1), and the ratio of these two measurements (FEV_1/FVC) should be calculated. Spirometry measurements are evaluated by comparison with reference valuesbased on age, height, sex and race. Patients with COPD typically show a decrease in both FEV_1 and FVC.



SPIROMETRY-NORMAL TREESPIROMETRY-OBSTRUCTIVE TREE

The spirometric criterion for airflow limitation remains a post-bronchodilator fixed ratio of FEV_1/FVC < 0.70. This criterion is simple and independent of reference values, and has been used in numerous clinical trials that form the evidence base from which most of our treatment recommendations are drawn.

Classification of airflow limitation severity in COPD (Based on post-bronchodilator FEV_1):

GOLD 1	Mild	FEV_1>/= 80% predicted
GOLD 2	Moderate	50% </= FEV_1 <80% predicted
GOLD 3	Severe	30% </= FEV_1 <50% predicted
GOLD 4	Very severe	FEV_1<30% predicted

Other pulmonary function tests:

Exercise testing may have a useful role in selecting patient undergoing surgery or pulmonary rehabilitation and to assess the response to treatment. It can be performed with a wide spectrum of techniques from a simple 6-minute walk test with or without pulse oximetry to sophisticated bicycle spirometry.

Diagnostic Difficulty in Older Patients Related to Spirometry Testing:

"Spirometry can be performed adequately in most of the elderly COPD patients. However, in a proportion of patients, particularly aged above 75 years do not perform full spirometry reliably owing to impairment of cognitive, ideo-motor, and executive functions, all of which affect inhaler technique"[(67)(68)]."For testing cognitive function, the mini-mental state examination (MMSE) and its intersecting pentagon copying component (IP) has high specificity but with moderate sensitivity"[(69)]. Patient with a MMSE score of < 24/30 or inability to copy overlapping pentagon are rarely able to perform adequate spirometry

Whole body plethysmography:

Using the whole-body plethysmography, airway resistance during quiet breathing, lung volumes, as well as complete spirometry including flow-volume curves, can be obtained within a few minutes very elegantly and non-invasively.

PATIENT UNDERGOING PULMONARY FUNCTION TEST

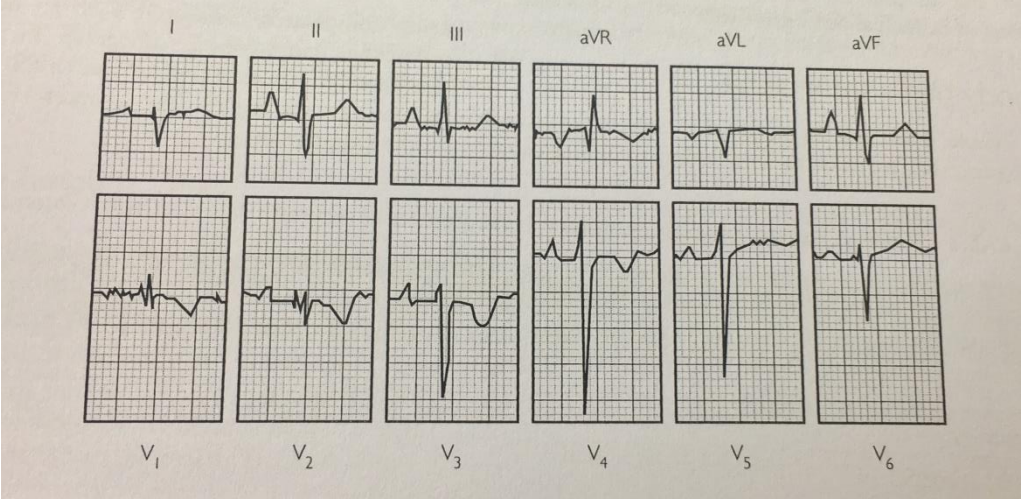
Arterial blood gas analysis:

In stable COPD cases, there is a good direct correlation between FEV1 and PaO2 begins to increase in patient with moderate or severe disease. In severe exacerbations of COPD, drop in pH is observed with rising PaCO2 and it is an important prognostic factor[(70)].

ECG Changes:

Electrocardiography may show signs of right atrial or right ventricular hypertrophy in advanced COPD with pulmonary hypertension.

The following electrocardiogram is of the patient who is a case of severe COPD and cor pulmonale. P Pulmonale can be noted (best seen in leads 2, 3 and aVF), dominant R wave in V1, dominant S wave in V4-6 and T wave inversion in V1-4.The features are those of right ventricular and right atrial hypertrophy.



ECG CHANGES

Laboratory tests:

For diagnostic purposes, the laboratory tests play a minor role in COPD. Serum alpha1-antitrypsin level can be measured, usually in younger patients with emphysema, and in case the serum level is decreased, phenotype should be identified[71].Laboratory tests are not of much value for monitoring the course of disease. In exacerbations, the C-reactive protein can increase, while the erythrocyte sedimentation rate and peripheral blood leukocyte count are often unaffected.

Erythrocytosis may be an indicator of hypoxemia in COPD patients but the correlation is poor between, for example, PaO2 and haematocrit, perhaps because the resting PaO2 is not necessarily representative, since intermittent hypoxemia (exercise,sleep) may stimulate erythropoietin production.

Sputum examination:

Inspection of the sputum is helpful from the point of view of recognising the pathogen if it is responsible for the exacerbation and for administration of timely and required treatment.

Routine sputum culture can yield pathogens in about 50% of cases. An important part of sputum examination is cytology and gram staining.

In stable COPD, microscopic examination reveals mainly alveolar macrophages and a few bacteria. In purulent sputum and during exacerbations, neutrophils dominate, and on Gram staining, Gram positive diplococcic and/or fine pleomorphic gram-negative rods may be seen in large numbers.

Imaging techniques:

The diagnosis of COPD is not made by chest imaging techniques but based upon pulmonary function testing. The main indication for imaging is to support the diagnosis and to exclude other conditions that produce similar signs and symptoms.

Chest Radiography:

The sensitivity of Chest X-Ray for diagnosis of COPD is poor. However, it is useful to rule out alternative diagnosis, and to identify other comorbidities and/or complications. On chest radiography, the lung is over-inflated with flattened diaphragms and tubular heart. The maximum curvature of the right diaphragmatic dome is less than 1.5 cm and it is placed low above which the posterior portions of the 11^{th} or even 12^{th} ribs may be visible. The hilar vessels are enlarged in advanced cases with cor pulmonale. Peripheral vascular shadows are thin, straight, or even lost as they are deranged or destroyed by advancing emphysema. Presence of radiological hyperluncency (bullae) and vascular attenuation are confirmatory of emphysema.

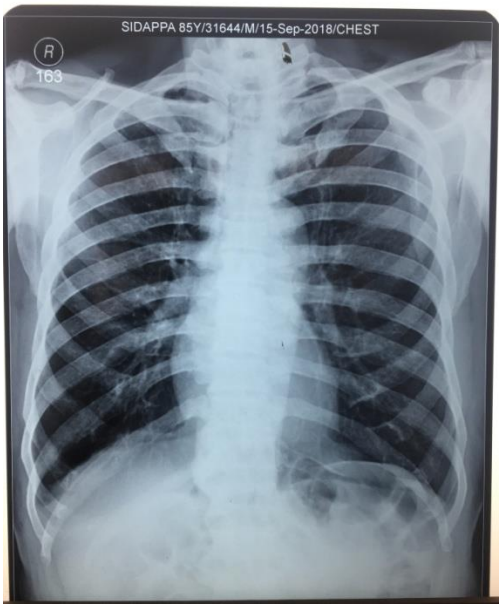
Bullae are identified by fine hair-like margins and lack of vascular shadows. The bullae may also rupture giving rise to secondary pneumothorax.

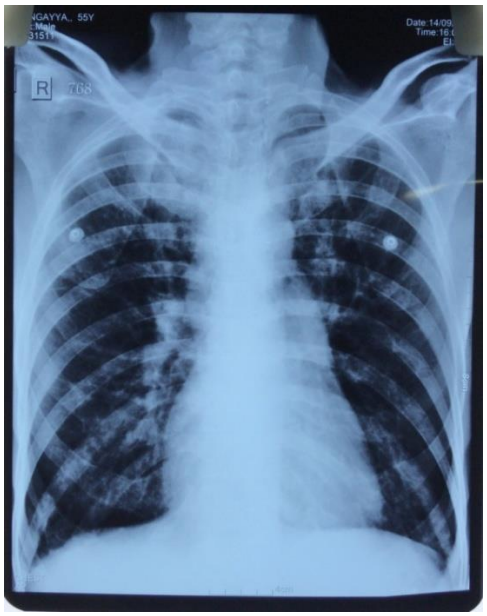
On a lateral chest radiograph, there will be large retrosternal air space; 3 cm below the manubrium the horizontal distance from the posterior surface of the aorta to the sternum exceeds 4.5 cm.

Four radiologic criteria have been described to diagnose emphysema. They are:

1) A retrosternal space (greatest distance from the sternum to the anterior heart silhouette)more than 2.54 cm (lateral radiograph)
2) Regular or irregular hyperluncency of lung fields reflecting attenuated pulmonary vessels
3) Low (mid diaphragm below tenth posterior intercostal space) and flat (for two thirds of their length) diaphragm on posteroanterior radiograph
4) Bullae- one or more thin walled hyperlucent lesions.

Radiologic emphysema is considered to be present when the two criteria are present.





CHEST X-RAY CHANGES IN COPD

Computed tomography:

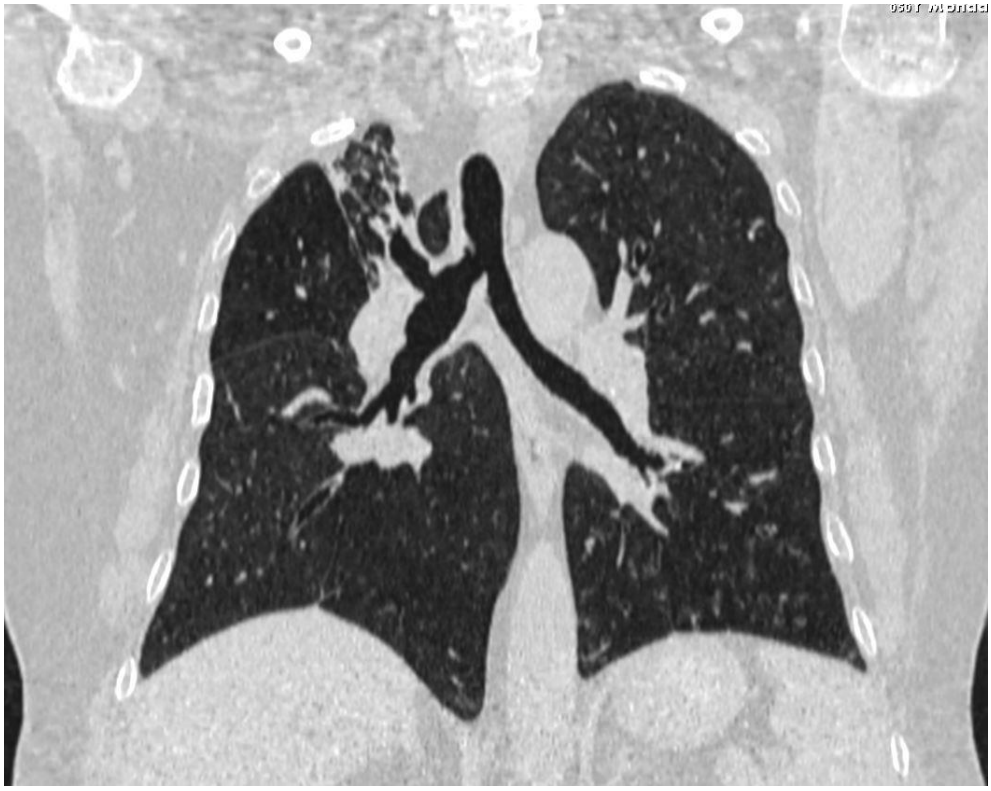
Computed tomography has a greater accuracy than plain radiography in diagnosing pulmonary emphysema and bullous disease in COPD and in assessing the central pulmonary vessels. A visual assessment of emphysema on CT reveals:

1. Areas of low attenuation without obvious margins or walls:
2. Attenuation and pruning of vascular tree:
3. Abnormal vascular configurations

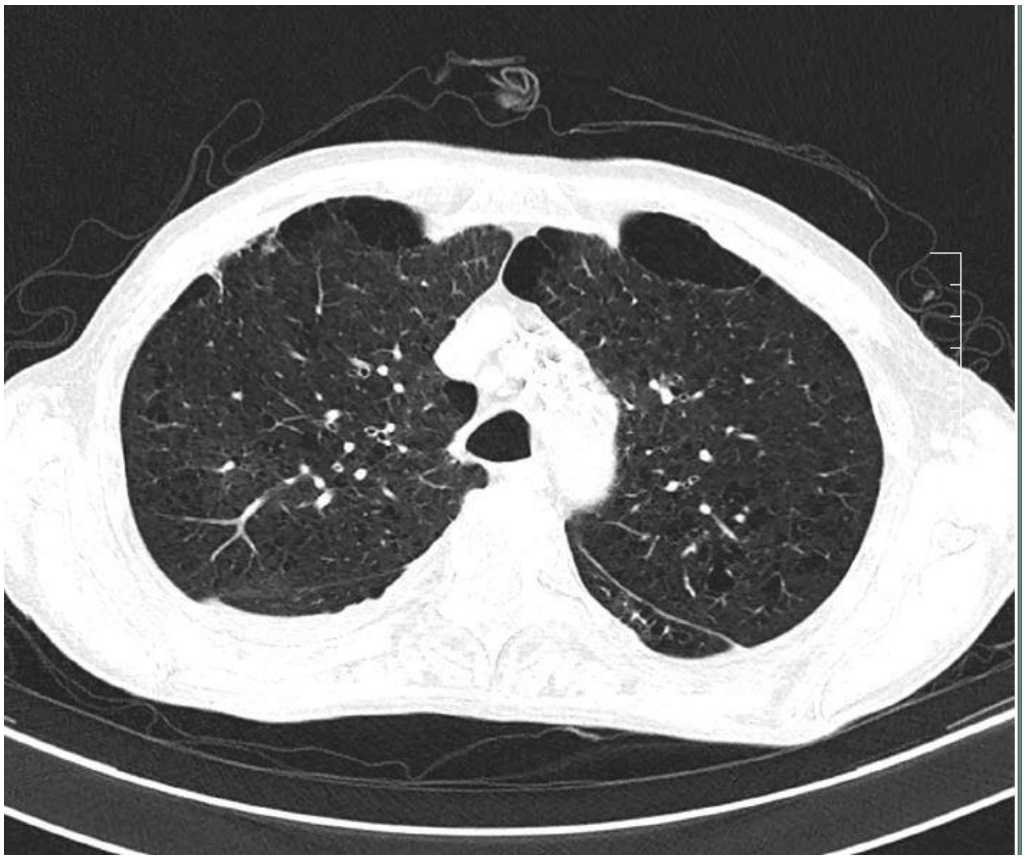
Changes can range from small focal areas of distribution with normal surrounding lung(centrilobular emphysema) to frank destruction (panacinar or advanced centrilobular emphysema)[72].

Scintigraphic imaging:

Perfusion and ventilation scintigraphy can detect early changes in COPD;in chronic obstructive bronchitis without emphysema, marked V/Q disturbance can be observed before lung function becomes abnormal. In cases of clinically evident emphysema, perfusion scintigraphy shows more or less large, non-segmental defects(Swiss cheese pattern) matched by similar defects of ventilation. Many thoracic surgeons are now using perfusion scan as the most appropriate method of selecting patients for lung volume reduction surgery and identify the 'target zones' for resection[73].



COMPUTED TOMOGRAPHY CHANGES IN COPD



ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE (AECOPD) IN ELDERLY:

COPD is usually characterized by the slowly progressive impairment of airflow and these symptoms are usually not exhibited until the age of 55 years, and mortality usually occurs after the age of 66 years.The prevalence of COPD dramatically increases with age and it also accounts for most of the people on long term oxygen therapy, that is on average a population aged over 70 years[17].Exacerbation and concomitant chronic diseases increases symptoms, especially in elderly.

The progression of COPD is associated with increasing frequency and severity of exacerbations. "Such exacerbations are associated with short term and long term reductions in quality of life and lung function, as well as increased risk of death"(74)(55)."The average patient with COPD experiences two episodes of AECOPD per year, and 10% of these episodes require hospitalization. The average duration of an episode is 7 days, although it may take several months for the patient to return to normal functional status"[75].

In some patients, exacerbations result in prolonged activity limitation and can quickly reverse the hard-won benefits of exercise training programmes. Exacerbations of COPD have short- and long-term clinical implications. The clinical diagnosis of COPD exacerbations is currently made on the basis of sustained worsening of the common respiratory symptoms. An acute exacerbation of COPD was defined in the GOLD 2014 update as "an acute event characterized by worsening of the patient respiratory symptoms that is beyond normal day-to-day variations and; leads to change in medication"[1].

The presentations of episodes of exacerbations vary from patient to patient and it depicts the multiple factors involved in the pathophysiology of COPD. "Expiratory flow limitation (EFL), as a consequence of airway inflammation, is the pathophysiological hallmark of COPD. The exacerbations in the patients with COPD basically reflect acute worsening of EFL, and there is evidence for both increased airway inflammatory activity and worsening airway obstructions as plausible explanations"[(76)]. It is reasonable to assume that worsening airway inflammation is the primary inciting event of COPD exacerbations and may be caused by bacteria, viruses, or environmental pollutants, including cigarette smoke.

Aetiology of Acute Exacerbations:

It is estimated that 70-80% of COPD exacerbations are due to primary respiratory infections, either bacterial or viral. The remaining 20-30% is due to environmental pollution or has an unknown aetiology[(77)].Sometimes the presence of congestive heart failure and pneumonia may be difficult to distinguish from acute exacerbations because, in severe disease, the characteristic radiological features of all these entities is difficult to distinguish from one another.

Viral Infection:

Viruses can be detected in one-third to two-thirds of exacerbations using culture, serology, and polymerase chain reaction (PCR)-based methods. The most common viruses associated with exacerbations of COPD are rhinoviruses. Influenza, parainfluenza, coronavirus, and adenovirus are also common during exacerbations[(78)]. Respiratory syncytial virus and human metapneumovirus were more recently associated with exacerbations[(79)(80)].

Identification of a virus in the sputum sample of a patient having an exacerbation of COPD does not mean the virus caused the exacerbation. This is

supported by the observation that viral nucleic acids can be detected by sensitive PCR-based assays in up to 15% of sputum samples from patients with stable COPD[81][82].The pathologic significance of a very low titre infection is uncertain.

The mechanisms by which viruses induce exacerbations have been partially elucidated. Viral infection of the airway epithelial cells induces inflammation[83]. This causes airway epithelial damage, muscarinic receptor stimulation, and induction of inflammatory mediators (eg: cytokines, chemokines). Airway eosinophilia is associated with viral mediated exacerbations, which highlights the importance of the host response to infection and its impact on both inflammation and symptoms[84].

Bacterial Infection:

Bacterial infections appear to trigger one-third to one-half of COPD exacerbations. Nontypeable *Haemophilus influenzae, Moraxella catarrhalis,* and *Streptococcus pneumoniae* are the bacteria most frequently isolated bronchoscopically from patients having an exacerbation of COPD[85][86].*Pseudomonasaeruginosa* and *Enterobacteriaceae* are also isolated, particularly from patients with severe COPD.

"Exacerbations of COPD are strongly associated with acquisition of a new strain of *H. influenzae, M. catarrhalis, S. pneumoniae, or P. aeruginosa"*[87]. As a result, it has been proposed that acquisition of a new bacterial strain plays a central role in the pathogenesis of an exacerbation. This hypothesis is supported by the following observations: Exacerbations with new bacterial strains are more likely to be associated with a humoral immune response.

"In one study, exacerbations with a new strain of *Haemophilus influenzae* were significantly more likely to be associated with a humoral immune response than exacerbations with pre-existing strains of *H.influenzae* (61 versus 21 percent)"[88]. The new antibodies were strain specific. *Moraxella catarrhalis* and *Streptococcus*

pneumoniae also induce an antibody response that is measurable following an exacerbation of COPD[89]. Exacerbations with new bacterial strains are associated with a more robust inflammatory response. Exacerbations of COPD with a new strain of bacteria have been associated with more intense neutrophilic airway inflammation and systemic inflammation than exacerbations with pre-existing bacterial strains or without pathogenic bacteria. Resolution of the airway inflammation is related to eradication of pathogenic bacteria from sputum and resolution of clinical symptoms. "In an animal model, new strains of *Haemophilus influenzae* that were known to be associated with COPD exacerbation caused significantly more airway neutrophil recruitment than colonizing strains of *Haemophilus influenzae"*[90].

Most of the human studies were performed in patients with COPD who had chronic bronchitis because expectorated sputum could be obtained easily. Thus, the degree to which the data can be generalized to exacerbations in patients with COPD who do not have chronic bronchitis is unknown.

"The idea that exacerbations of COPD are due to acquisition of a new strain of bacteria has largely replaced the older hypothesis that increases in the concentration of colonizing bacteria are the primary cause of exacerbations. The older theory was largely disproven by a comprehensive analysis of the relationship among sputum bacterial concentrations, exacerbation occurrence, and new pathogen acquisition"[91]. The analysis demonstrated that an increase in bacterial load is not a cause of exacerbation.

Atypical Bacteria:

There are conflicting data regarding the incidence of atypical bacterial infection in patients having an exacerbation of COPD. This is related, in large part, to the varying criteria used to diagnose exacerbation and infection. The incidence of

Chlamydophila pneumoniae in exacerbations of COPD appears to be 3 to 5 percent (*Mycoplasma pneumoniae and Legionella spp.* are even more rare) if one considers only studies with rigorous methodology that excluded pneumonia and defined infection as a strict fourfold increase in titer or a positive culture[92].

COINFECTION

"Coinfection is increasingly being considered in studies looking at the pathogenesis of COPD exacerbation. Such studies categorize exacerbations of COPD due to respiratory infection as being caused by viral infection alone, bacterial infection alone, or both. Exacerbations were equally distributed across the three categories in one study"[84].

Coinfection appears to increase the severity of COPD exacerbations. In a study of inpatients, "Coinfection was associated with a greater decrement of lung function and longer hospitalization"[84]. In a similar study of outpatients, coinfection was associated with more symptoms, a larger fall in the forced expiratory volume in one second (FEV_1), higher bacterial loads, and systemic inflammation[93].

PATHOPHYSIOLOGY OF ACUTE EXACERBATIONS

"EFL (Expiratory Flow Limitation) is the pathophysiological hallmark of COPD. Patients with COPD are said to be flow limited when the expiratory flow they generate during tidal respiration represents the maximal possible flow that they can generate at that volume. In flow limited patients the time available for lung emptying (expiratory time) during spontaneous breathing is often insufficient to allow End Expiratory Lung Volume (EELV) to decline to its natural relaxation volume leading to lung over inflation"[94].

Thus, in flow limited patients, EELV becomes dynamically rather than statically determined, and essentially becomes a continuous variable that fluctuates

widely depending on the extent of EFL and the prevailing ventilatory demand. Dynamic hyperinflation (DH) refers to acute and variable increase in EELV above its baseline value.

"DH occurs during exercise in flow limited patients as inspired tidal volume increases and expiratory time decreases, and is associated with severe mechanical constraints on ventilation and perceived respiratory discomfort. DH also occurs during acute bronchoconstriction in asthma. In this setting, the reduction in inspiratory capacity (IC), which reflects the increase in EELV, correlates strongly with the perception of inspiratory difficulty"[95][96].

"During COPD exacerbations airways resistance is abruptly increased (due to bronchospasm, mucosal oedema, and sputum inspissations) and this worsens EFL. The time constant for lung emptying (given by the product of resistance and compliance) is therefore prolonged and EELV is dynamically increased. Furthermore, during an exacerbation, patients tend to adopt a rapid shallow breathing pattern which further limits the time available for lung emptying, thus promoting greater DH in a vicious cycle. In fact, any acute increase in ventilation (such as occurs with anxiety or transient hypoxemia) can be associated with DH in flow limited patients. There is abundant evidence that acute DH may be life threatening during severe exacerbations of asthma or COPD"[97].

NEGATIVE MECHANICAL EFFECTS OF DYNAMIC HYPERVENTILATION

Severe DH imposes a "restrictive" mechanical constraint on the respiratory system, where tidal volume expansion is limited in the face of increasing inspiratory effort. “The net effect of this increased loading and functional weakness of the inspiratory muscles is that the effort required for tidal inspiration represents a relatively high fraction of the maximal possible effort that the patient can develop at that lung volume. This increased effort may be directly perceived (via central corollary discharge) as unpleasant if it exceeds a certain threshold. The neural drive to breathe is usually preserved in COPD (even in many patients with chronic compensated hypercapnic acidosis) and actually increases during times of physiological stress such as during exercise or exacerbations”[98]. Central drive increases further in the presence of critical arterial oxygen desaturation, carbon dioxide retention, or acidosis, and is also stimulated by fever or increased sympathetic nervous system activation.

However, “During COPD exacerbations the mechanical output of the flow limited respiratory system may not increase in proportion to neural drive, resulting in neuromechanical dissociation or uncoupling of the respiratory system. This disparity between central drive and the mechanical response as a consequence of acute DH has been implicated in the genesis of dyspnoea (or its dominant qualitative dimensions) in COPD patients during exercise, and in asthmatics during acute bronchoconstriction”[96]. It is reasonable to assume that similar mechanisms explain dyspnoea during COPD exacerbations.

In a recent study, Stevenson et alevaluated changes in spirometric parameters during recovery in 22 patients with COPD exacerbations who required admission to

hospital[99]. Compared with values obtained at the time of admission, the mean post-bronchodilator FEV_1 improved by 0.20l and the mean IC improved by 0.42l after 42 days of follow up. Furthermore, there was no change in the FEV_1/FVC ratio during the follow up period and the authors concluded that favourable changes in volume during recovery resulted in improved expiratory flows.

"The magnitude of change in IC (approximately 20% of baseline value) found in this study may have important clinical consequences. There is evidence that in flow limited patients with reduced resting IC (<80% predicted), further acute reductions in IC as a result of DH lead to a limited ability to increase VT and ventilation when demand suddenly increases as, for example, in exercise"[100][101].

Clinical Recognition:

Increased shortness of breath, increased cough and increased sputum volume or prevalence are most common symptoms patients with exacerbations present with. Additional symptoms, such as malaise, body ache, decreased exercise tolerance, fluid retention, increased fatigue and confusion can also be present depending upon the disease severity as well as the extent of physiological derangements.

'Common colds', sore-throat, runny nose, and cough increase significantly during the prodromes, suggesting that respiratory viruses are important exacerbation triggers. The clinical severity of AECOPD varies widely. It may be managed in outpatient setting but may be severe enough to require hospitalizations. When exacerbations are complicated by respiratory failure, intensive care monitoring including ventilatory support, non-invasive or invasive may be required.

Staging of AECOPD:

The severity of AECOPD without respiratory failure can be classified according to several staging systems;"The traditional one being used is the Winnipeg

criteria, which were derived from a double blind, placebo-controlled trial that evaluated the role of antibiotics in patients with COPD with acute exacerbations"[102].

THE WINNIPEG CRITERIA:

TYPE of AECOPD	CRITERIA
Type 1	All three of the following symptoms: increase in sputum volume, increase in sputum purulence, Increase in shortness of breath
Type 2	Any two of the following symptoms: increase in sputum volume, increase in sputum purulence, Increase in shortness of breath
Type 3	Any one of the following symptoms: increase in sputum volume, increase in sputum purulence, increase in shortness of breath plus at least one of the following: upper respiratory tract infection lasting for 5 days, fever; increase in wheezes, increase in cough, increase in heart rate >20%

IMPACTS OF EXACERBATIONS OF COPD IN ELDERLY:

An acute exacerbation may be mild and require only an unscheduled visit to the physician and outpatient management or may be severe enough to require emergency room, in patient or even intensive care.

Economic costs:

"Hospitalizations during the episode of AECOPD are the main reasons for the use of health care resources and these costs are attributed to the small proportions of patients with repeated exacerbations"[103].

Exacerbations account for about 70% of the total costs of COPD management[104].The estimated costs of exacerbations varied widely across many studies and it can be related to differences, in geographic locations, treatment patterns, local health delivery systems and patient populations.

Health related Quality of Life:

"Health status has been regarded as one of the major outcome measures in COPD. A vast majority of population suffer a sharp decline in the Quality of life (QoL) after acute exacerbations. A prospective cohort study which was followed for six months showed that only 26% of the patients were both alive and able to report a good, very good, or excellent QoL"[105].

Lung function and disease progression:

COPD is usually accompanied by a progressive decline in the lung function. "The rate of decline in FEV_1 has varied individually considerably both in observational cohorts and intervention trials from 150ml to 200ml per year and few patients may even show increase of up to approximately 159 ml per year. The frequency of exacerbations is one of the determinants of rate of decline"[106].Recovery of lung function after an exacerbation is usually less than complete. Smoking and exacerbations have an interactive effect on the progression of COPD, with continued smoking having a worse prognosis.

Physical activity:

AECOPD episode aggravates peripheral muscle weakness. A sharp fall in outdoor activity is seen with exacerbations can lead to a major decline in the time spent outdoors[107].Physical inactivity in turn carries unfavourable prognostic factors which include cardiorespiratory deconditioning which can lead to increase dyspnoea and fatigability, increased risk of venous thromboembolism, worsening of osteoporosis and neuropsychiatric comorbidity.

Osteoporosis:

"Approximately two-thirds of patients with COPD have osteoporosis or osteopenia and it can be correlated with the extent of emphysema"[108].Multiple

factors contribute to the development of osteoporosis which include age, smoking, physical activity, corticosteroid use and systemic inflammation.

Neuro-psychiatric complications:

"Depression is quite common in patients with COPD. The ECLIPSE study found a prevalence of symptom defined depression in 26% of patients compared to 12% of controls that increased with disease severity"[109]. Depression has been a major factor contributing to decreased physical activity, deconditioning and worsening of symptoms, and also adversely impacts adherence, compliance and utilisation of health care.

TREATMENT OF COPD EXACERBATIONS IN ELDERLY:

The management of elderly patient with COPD should encompass a multidisciplinary approach. In addition to the assessment of lung ventilatory performance and functional impairment, nutritional status and mental health should be evaluated. Underlying comorbidities should also be evaluated and treated. Therapy for COPD should start with cessation of tobacco smoking.

Elderly patient with COPD requires special attention because of high susceptibility of older people to disease, medication is more and the number of drugs to be taken daily increases progressively with age. Prescribing medication for older subjects is a complex issue as their behaviour towards medications and their effects vary according to the health of the patient, the route of drug metabolism/elimination, and its intrinsic safety. The process of ageing can influence pharmacodynamics responses as well as pharmacokinetics (absorption, distribution, metabolism, and excretion of drugs).

The goal of treatment is to minimise the negative impact of the current exacerbation.

Beta agonists and anticholinergics:

Short acting inhaled β_2 agonists and short acting anticholinergics are the initial treatment of COPD exacerbations[(9)(110)]."Prior to the discharge of the patient, maintenance with long acting antimuscarinic agonists (LAMA) tend to have a greater effect on exacerbation than long acting β_2 agonists"[(111)].

Corticosteroids:

Systemic corticosteroids have been used as standard treatment for exacerbations for a long time[(112)]."They have been proved and shown to improve lung function and oxygenation, to shorten recovery time and duration of hospitalisation and to reduce treatment failures. The European Respiratory Society (ERS)/ American

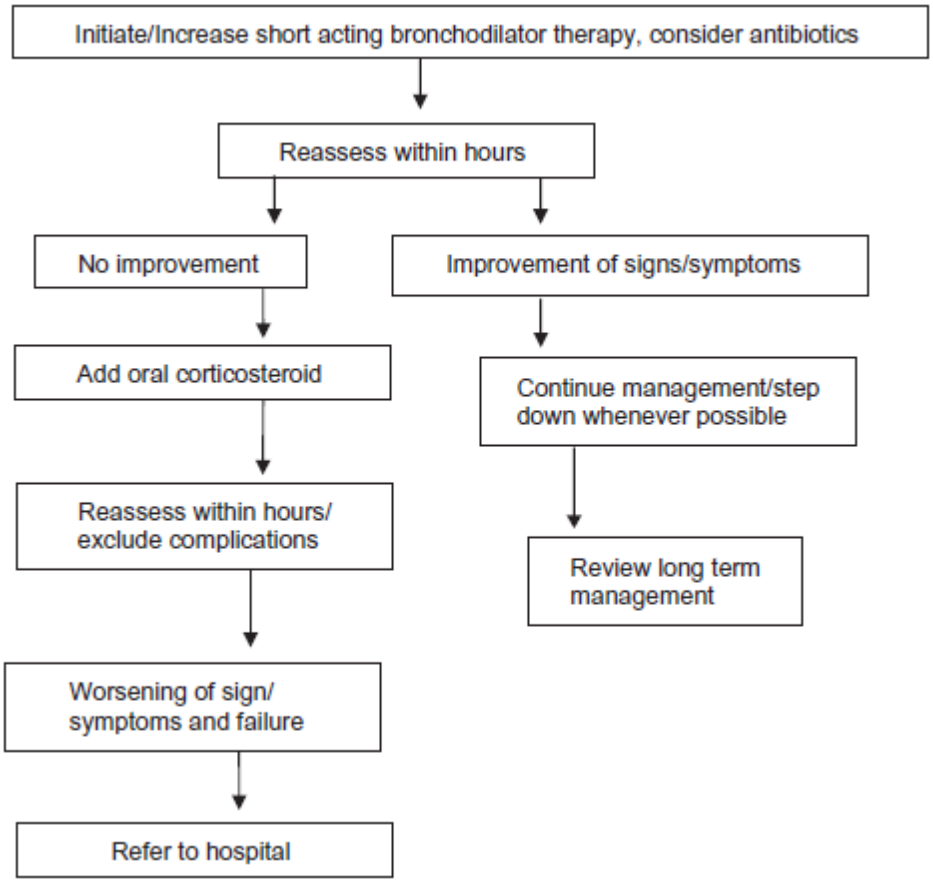
Thoracic society (ATS) guidelines for the management of COPD exacerbations suggest a short course of 14 days of oral corticosteroids for ambulatory patients with an exacerbation of COPD"[113].For patients who are admitted to hospitals with acute exacerbations, administration of oral corticosteroids is preferred over intravenous corticosteroids.

Antibiotics:

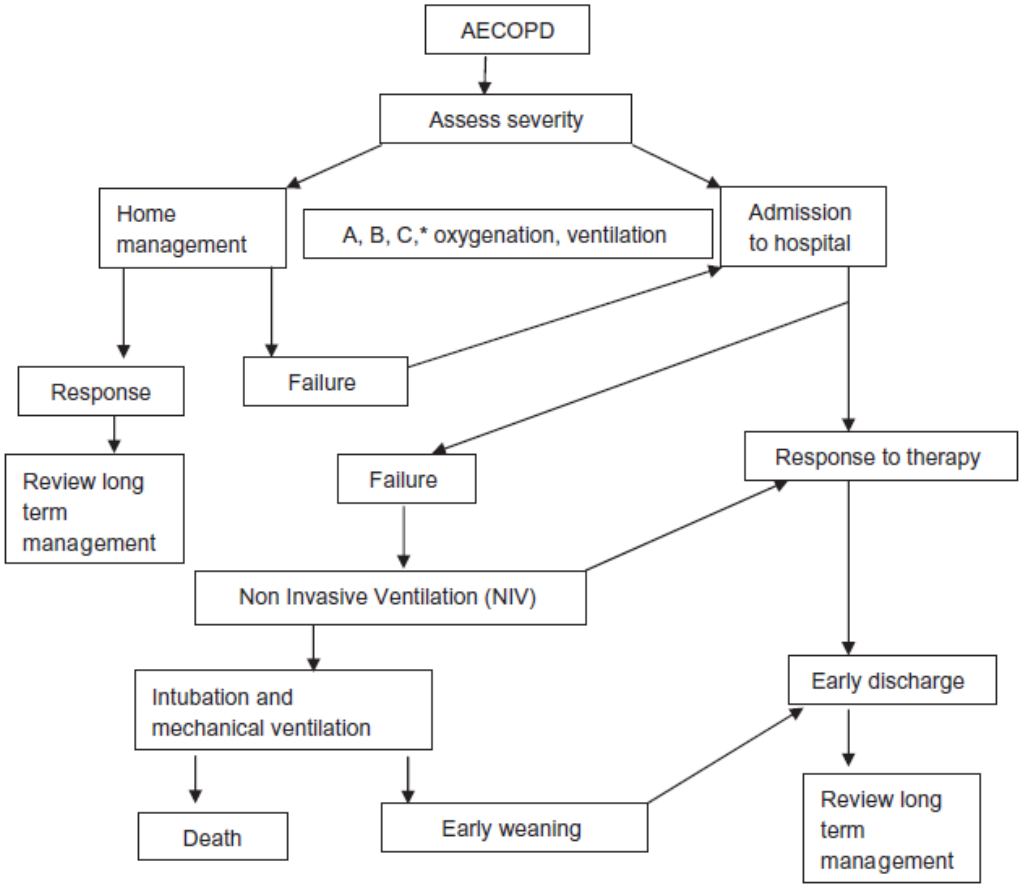
Review of all the COPD guidelines revealed that criteria for treatment with antibiotics were mainly an increase in respiratory symptoms[113]."Studies suggest that antibiotics should only be given in patients with presumed bacterial infection. In order to differentiate between chronic colonisation and acute infection, procalcitonin levels can be assessed as a marker for antibiotic treatment"[114][115].

Non-invasive ventilation:

A meta-analysis conducted in 2003 concluded that non-invasive ventilation (NIV) is the first line intervention in patients with COPD exacerbation in addition to the usual medical care[116].



FLOW CHART FOR HOME MANAGEMENT OF AECOPD



FLOW CHART FOR HOSPITAL MANAGEMENT OF AECOPD

POLYPHARMACY IN ELDERLY:

As a result of advancing age and increasing number of chronic diseases, older people have become the major consumers of drugs. The factors which predispose to such polypharmacy include poorer health, multiple chronic disease, multiple prescribing physicians, therapeutic advances, and expectations of the patient, education, increasing demands for health care, supplemental insurances, and reluctance to discontinue old medications. A population-based cohort study showed that 200% of ambulatory older adults were presented at least 1 inappropriate drug per year.

"Inappropriate medications are detected according to various screening tool for the assessment of quality and safety of prescriptions, for example the screening tool of older persons potentially inappropriate prescription (STOPP) and the screening tool to alert doctors to the right treatment, (START)"[(117)].

Inappropriate prescription for the patients with COPD; criteria for the screeining toolto alert doctors to the right treatment (START) and the screening tool of older persons's prescriptions (STOPP)

STOPP	START
Drug prescriptions potentially inappropriate in persons aged > 65 years	***Medications for people aged >65 years with the following conditions when no contraindication to prescription exists:***
1) Theophylline as monotherapy for COPD	1) Regular inhaled beta-2-agonist or anti-cholinergic agent for mild-to-moderate asthma or COPD
2) Systemic corticosteroids instead of inhaled corticosteroids for maintainance therapy in modertae-to-severe COPD	2)Regular inhaled corticosteroid for moderate-to-severe asthma or COPD when FEV_1 is <50% predicted
3)Nebulised ipratropium with glaucoma	3)Continous oxygen at home with documented chronic type 1 or type 2

Mode of therapy:

Inhaled bronchodilator therapy is the mainstay of treatment in the management of COPD, although it is available in various formulations (metered dose inhaler [pMDI] / dry powder inhaler [DPI] or nebulised), the MDI is the most commonly prescribed[118]."Therapeutic benefit depends on adequate airway drug deposition. Inhaler technique is crucial, but it is suboptimal in many elderly patient groups"[119]."Arthritis, weakness, poor manual dexterity and visual limitations are potential problems affecting inhaler use in the elderly"[120]. Nebulisers are frequently used to deliver bronchodilators in elderly patients. Elderly patients are more able to

inhale the medications from these devices than from MDIS or PDIs supplemental oxygen therapy.

Supplemental oxygen for >/= 15hrs per day reduces the mortality in patients with COPD[121]. Medicine guidelines recommended that oxygen therapy should be initiated in stable patients if the resting arterial partial pressure of oxygen saturation is <88% long term oxygen therapy increases survival in COPD patients with respiratory failure and severe resting hypoxemia.

Nutrition support:

European society for parenteral and enteral nutrition guidelines suggests enteral nutrition in combination with exercise and anabolic pharmacotherapy for COPD patients. This is to improve nutritional status and function in COPD patients[122].

Palliative and end of life care:

People suffering from life-threatening illnesses, such as advanced COPD, should receive palliative care in order to improve their own and their families' quality of life. Palliative care focuses on the prevention and relief of suffering by means of early identification, impeccable assessment and treatment of all physical, psychosocial and spiritual issues affecting the patient and their relatives.

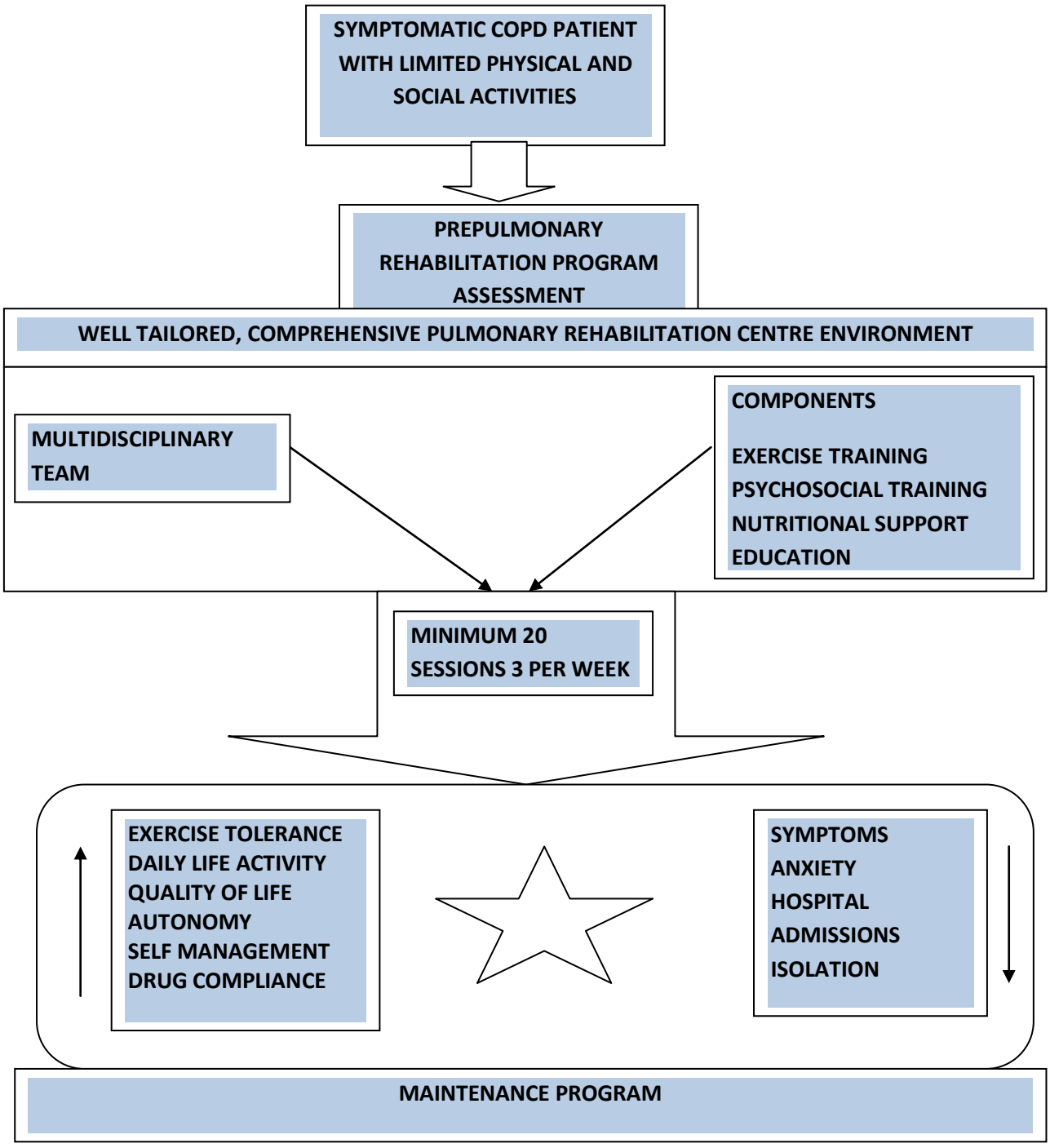
Any palliative care provided within the last 12 months of life is considered as end-of-life care, the last phase of palliative care. Smoking cessation and long-term oxygen therapy improve survival as well as quality of life in COPD patients. Non-invasive positive pressure ventilation delivered through nasal or face mask avoids the risk associated with mechanical ventilation and is an alternative to it for symptom relief in end stage COPD[123].

Pulmonary rehabilitation:

Since long, the point of focus in treatment in patients with COPD has been the pharmacological improvement of airway obstruction. Pulmonary rehabilitation (PR) plays a very pivotal role in the management of symptomatic patients with COPD in elderly, by breaking the vicious circle of dyspnoea–decreased activity–deconditioning–isolation. PR has been shown to be the most effective non-pharmacological intervention for improving health status in COPD patients and has become a standard of care for COPD patients[124].

"Pulmonary rehabilitation is a comprehensive intervention based on a thorough patient assessment followed by patient-tailored therapies, which include, but are not limited to, exercise training, education and behaviour change, designed to improve the physical and emotional condition of people with chronic respiratory disease and to promote the long-term adherence of health-enhancing behaviours"[125].

"PR helps in establishing a personalized and global treatment for the symptomatic COPD patient. A PR program is not a stand-alone therapy, but rather, should be integrated into a management program in which the general practitioner as well as the patient's pulmonary specialist takes an active part. By using a holistic approach centered on the patient, PR aims to reverse the systemic manifestations of COPD as well as to relieve the fears and anxiety associated with social and exterior activities, thereby leading to a change in the patient's day-to-day life"[126].



SUMMARY OF THE STEPS AND BENEFITS OF PULMONARY REHABILITATION

THERAPEUTIC COMPLIANCE IN ELDERLY PATIENTS WITH COPD:

The problems of therapeutic adherence are very frequent in the elderly. Compliance to drug therapy in COPD is much lower than that of other common diseases such as diabetes, osteoporosis, and hypertension[127].

Data from the international literature shows that adherence to treatment in COPD is less than 50% including drug therapy, O2-therapy and rehabilitation[128].

Poor adherence to therapy includes:

1. "Overuse" (typical of exace0rbations);
2. "Underuse" (typical of mild-moderate COPD in which low intensity of symptoms, besides progressive reduction in physical activity, induces the patient to do without therapy);
3. "Improper use" (typical of elderly patient and often due to difficulties in devices management).

"Major predictors of poor adherence to medication are presence of psychological problems, presence of cognitive impairment, treatment of asymptomatic disease, inadequate follow-up or discharge planning, side effects of medication, patient's lack of belief in benefit of treatment, patient's lack of insight into the illness, poor provider patient relationship, presence of barriers to care or medications, missed appointment, complexity of treatment, cost of medication, co-payment or both"[129].

Number of daily administration and rapid onset of the effect of the drugs may affect compliance with therapy.

Comorbidity can affect adherence to therapy because more factors may interfere with drugs assumption (mental impairment, depression, visual impairment, functional limitations related to arthritis, cerebrovascular disease, Parkinsonism).

Polypharmacy can also adversely affect compliance.

Another factor that significantly influences therapeutic compliance is the devices management.

CONCLUSION

Chronic Obstructive Pulmonary Disease (COPD) is a preventable and treatable respiratory disease which is a major cause of chronic morbidity and mortality throughout the world, represents the fourth leading cause of death in the world. The prevalence of COPD dramatically increases with age. Aging causes decline in lung function, reduced chest wall compliance, reduced diaphragmatic strength, degeneration of the elastic fibres resulting in air trapping, and all these results in increased prevalence of COPD in elderly.

Aging, cigarette smoking, occupational exposure, environmental pollution, genetic factors and socioeconomic factors are the major risk factors in the development of COPD. Most clinical symptoms occur during the fifth and sixth decade of life. The main symptoms are breathlessness on exertion and/or cough with or without sputum, reflecting the symptoms of both emphysema and chronic bronchitis.

COPD is rarely presenting alone in elderly patients. Co-morbidity and disability of various origins contribute to make the recognition of COPD problematic. COPD has important manifestation beyond the lungs, the so-called systemic effects in elderly. The diagnosis of COPD is usually presumptive airway obstruction has to be documented by objective test i.e. spirometry and other diseases, associated especially with dyspnoea and cough, need to be rule out. Spirometry can be performed adequately in most of the elderly COPD patients. However, in a proportion of patients, particularly aged above 75 years do not perform full spirometry reliably owing to impairment of cognitive, ideo-motor, and executive functions, all of which affect inhaler technique.

The progression of COPD is associated with increasing frequency and severity of exacerbation in elderly. The average patient with COPD experiences two episodes of AECOPD per year and 10% of these bacterial or viral. *Haemophilus influenza, Moraxella catarrhalis, and Streptococcus pneumonia* are the bacteria most frequently isolated from patients having exacerbation of COPD.

An acute exacerbation may be mild and require only an unscheduled visit to the physician and outpatient management or may be severe enough to require emergency room, in patient or even intensive care. It is estimated that 70-80% of COPD exacerbations are due to primary respiratory infections, either bacterial or viral. The remaining 20-30% is due to environmental pollution or has an unknown aetiology.

An acute exacerbation may be mild and require only an unscheduled visit to the physician and outpatient management or may be severe enough to require emergency room, in patient or even intensive care. A vast majority of population suffer a sharp decline in the Quality of life (QoL) after acute exacerbations. Depression is quite common in patients with COPD.

The management of elderly patient with COPD should encompass a multidisciplinary approach. Elderly patient with COPD requires special attention because of high susceptibility of older people to disease, medication is more and the number of drugs to be taken daily increases progressively with age. Prescribing medication for older subjects is a complex issue as their behaviour towards medications and their effects vary according to the health of the patient, the route of drug metabolism/elimination, and its intrinsic safety.

People suffering from life-threatening illnesses, such as advanced COPD, should receive palliative care in order to improve their own and their families' quality

of life. Pulmonary rehabilitation (PR) plays a very pivotal role in the management of symptomatic patients with COPD in elderly, by breaking the vicious circle of dyspnoea–decreased activity–deconditioning–isolation.

MATERIALS AND METHODS

METHOD OF COLLECTION OF DATA:

Information will be collected through prepared proforma from each patient. All patients will be interviewed as per the prepared proforma and then complete clinical examination and laboratory findings will be done.

Inclusion Criteria

Age > 60yrs,irrespective of sex. Clinical symptoms like increased cough, increased purulence and/or volume of expectorations, increased severity of dyspnoea supported by pulmonary function test.

Previously diagnosed patients of COPD on the basis of exposure to risk factors, clinical history and examination supported by pulmonary function test.

Exclusion Criteria

a) Active pulmonary tuberculosis
b) Lung malignancies
c) Bronchiectasis
d) Patients who are already on antibiotic treatment
e) Acute severe asthma
f) Pneumonia

TYPE OF STUDY – Prospective study

SAMPLE SIZE:

The prevalence of COPDin individuals aged above 65 years is 14.2% , at 95% confidence interval and at 5% precision the sample size worked out is 66.

$$n=\frac{Z \times P \times (100 - P)}{e^2}$$

Z – Z value at 95% CI

P- Prevalence rate

e – Margin of error

Statistical Analysis

- Mean ± SD
- Chi-square test (if necessary)

RESULTS

The present study was conducted at BLDEDU's Shri. B. M. Patil Medical College, Hospital and Research Centre, Vijayapura. This study is a prospective study carried out in 66 cases of Acute Exacerbation of Chronic Obstructive Pulmonary Disease aged more than 60 years. A detailed history was taken, clinical examination was carried out, relevant blood investigations, chest x ray, Pulmonary function test,sputum examination consisting of Gram staining, Ziehl-Neelsen staining and Culture/Sensitivity pattern were studied. The results and observations of the study are as follows.

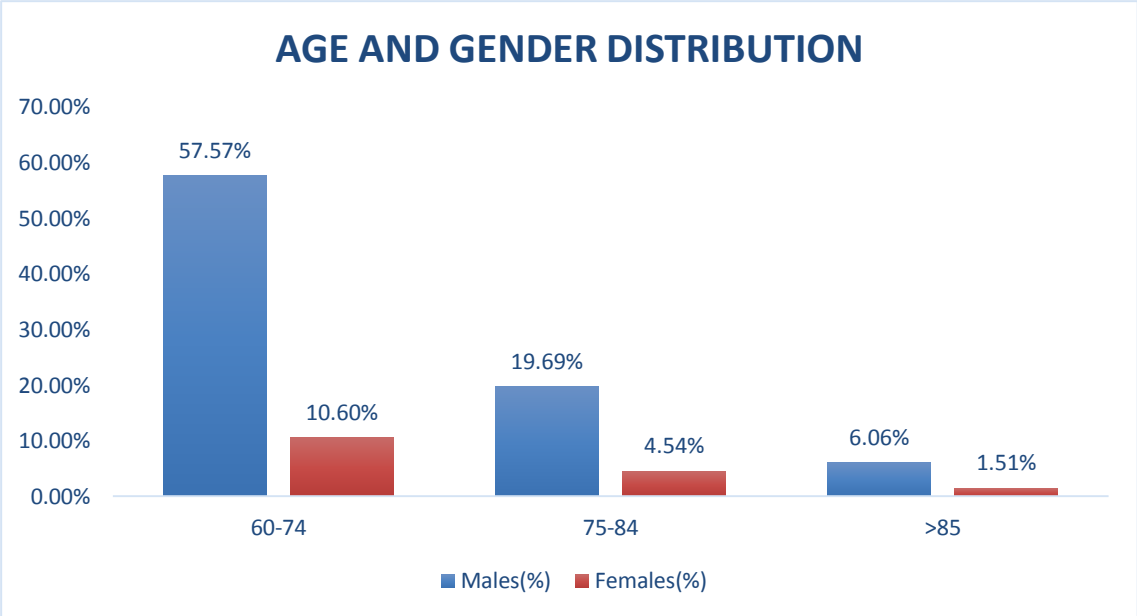
AGE AND GENDER DISTRIBUTION:

In this study, the age group of patients varied from 60 to 91 years. The oldest was 91-year-old male patient. Mean age was 70.63 years. Majority of the patients (45) were young old, in the age group of 60-74 years. Out of 66 patients, 55(83%) were males and 11(17%) were females. The details of age and gender distribution is shown in the table and diagram.

TABLE 1: (AGE AND GENDER DISTRIBUTION)

Age/Gender	Male	Percentage(%)	Female	Percentage (%)	Total	Percentage (%)
60-74 (Young old)	38	57.57	7	10.60	45	68.18
75-84 (Old old)	13	19.69	3	4.54	16	24.24
>85 (Very old)	04	6.06	1	1.51	5	7.57
Total	55	83.33	11	16.66	66	100

DIAGRAM 1: AGE AND GENDER DISTRIBUTION



CHIEF COMPLAINTS:

The patients presented with both the typical and atypical symptoms of AECOPD. Among the typical symptoms, cough was present in 66(100%) patients, followed by expectoration of sputum in 65(98.5%) patients, breathlessness in 65 (98.5%), and fever was present in 35(53.1%) patients. Among the atypical complaints chest pain was present in 1 patient, altered sensorium, hiccups and giddiness and reduced appetite, each seen in 1 patient (1.5%).

TABLE 2 AND 3: DISTRIBUTION ACCORDING TO THE COMPLAINTS:

Typical Complaints	No. of patients	Percentage
Fever	35	53.1
Breathlessness	65	98.5
Cough	66	100.0
Expectoration	65	98.5

Other complaints	No of patients	Percentage
Altered Sensorium	1	1.5
Chest pain	1	1.5
Dribbling of urine	1	1.5
Giddiness;Hiccups	1	1.5
Loose stools	1	1.5
Lower limb swelling	1	1.5
Reduced Appetite	1	1.5
None	59	89.39

DIAGRAM 2: DISTRIBUTION ACCORDING TO CHIEF COMPLAINTS

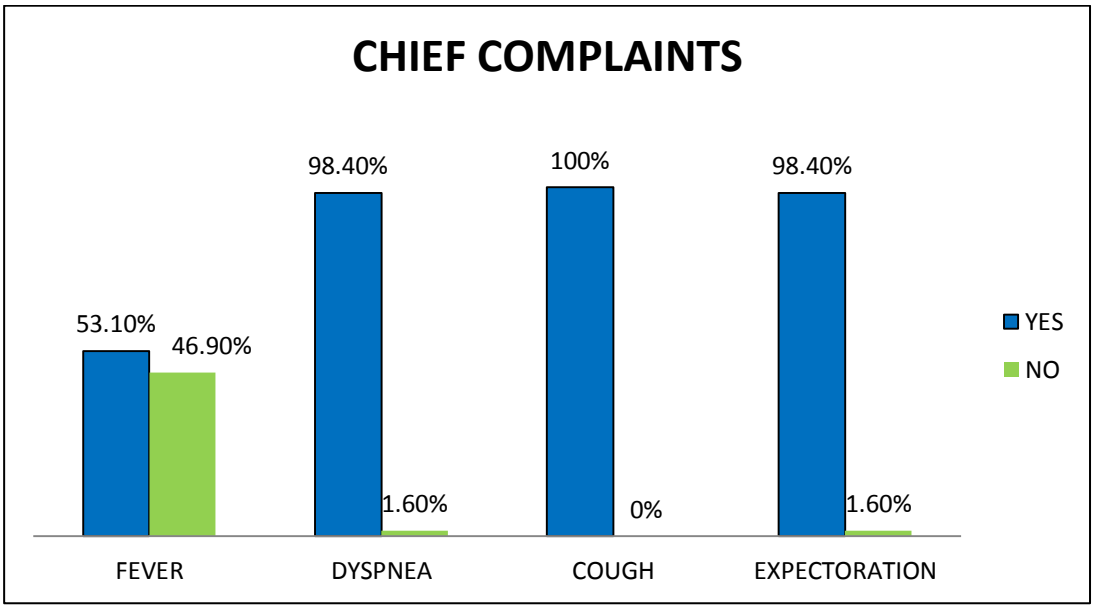
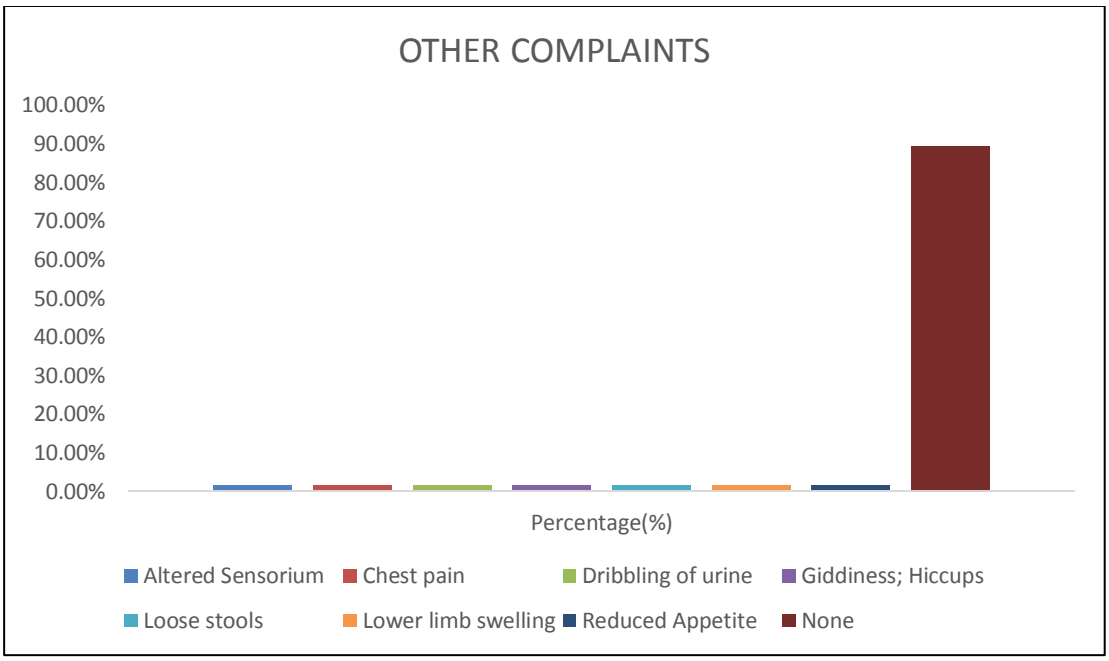


DIAGRAM 3: DISTRIBUTION ACCORDING TO OTHER COMPLAINTS



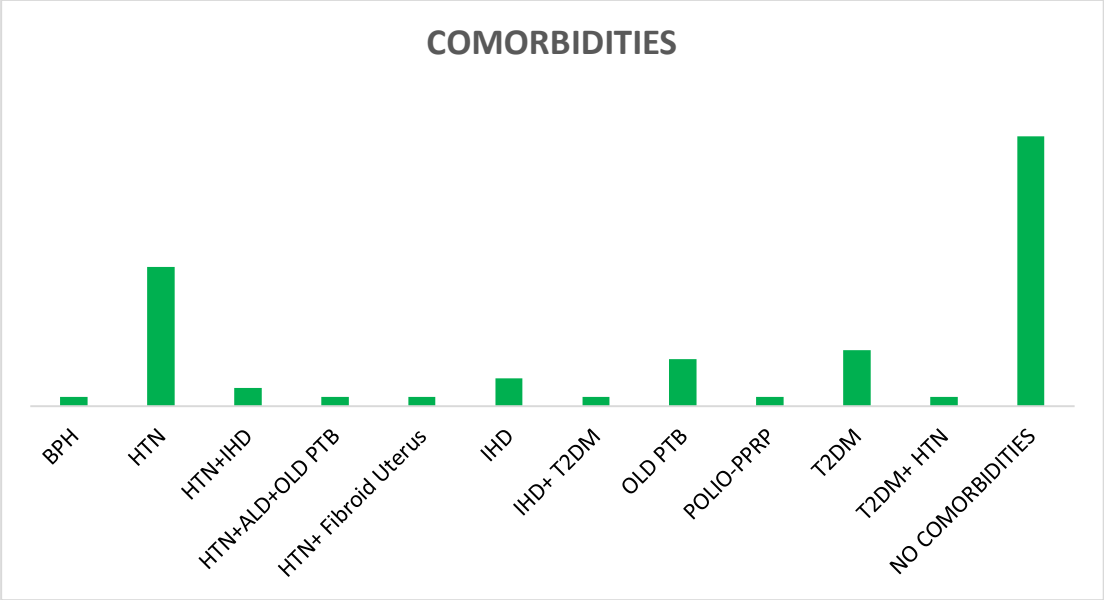
COMORBID CONDITIONS:

Among the comorbid conditions, Hypertension was the most common, noted in 15(23%) patients, followed by Type 2 Diabetes Mellitus seen in 6(9%). Old Pulmonary Tuberculosis was seen in 5(8%) patients and Ischemic Heart Disease in 3(4.5%) patients. Multiple comorbidities were noted in 6(9%).

TABLE 4: DISTRIBUTION ACCORDING TO COMOBIDITIES:

Co morbidities	No. of patients	Percentage
BPH	1	1.5
HTN	15	22.7
HTN+IHD	2	3
HTN+ALD+OLD PTB	1	1.5
HTN+ Fibroid Uterus	1	1.5
IHD	3	4.5
IHD+ T2DM	1	1.5
OLD PTB	5	7.6
POLIO-PPRP	1	1.5
T2DM	6	9.1
T2DM+ HTN	1	1.5
NO COMORBIDITIES	29	43.9
Total	66	100.0

DIAGRAM 4: DISTRIBUTION ACCORDING TO COMOBIDITIES:



BPH: Benign Prostatic Hypertrophy, HTN: Hypertension, IHD: Ischemic Heart Disease, ALD: Alcoholic Liver Disease, OLD PTB: Old Pulmonary Tuberculosis, T2DM: Type 2 Diabetes Mellitus, POLIO-PPRP: Polio-Post Polio Residual Paralysis

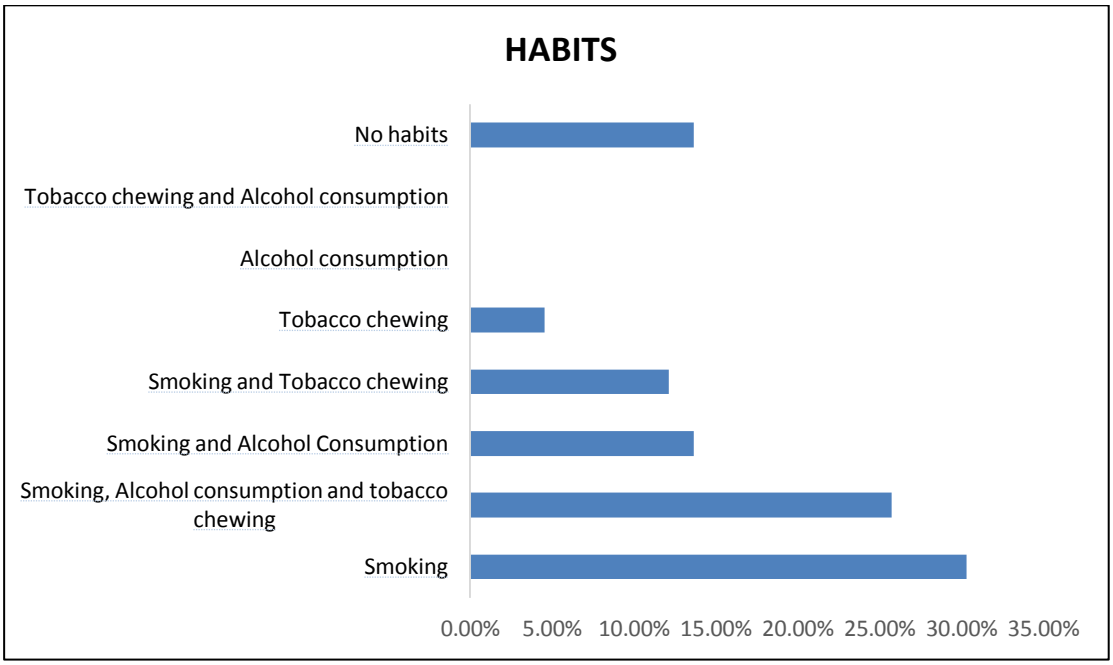
DISTRIBUTION ACCORDING TO HABITS:

Among habits, alone smoking only was the predominant and was noted in 20 patients (30%), tobacco chewing was seen in 3 (4%) patients. Multiple habits like smoking, tobacco chewing and alcohol consumption altogether was seen in 17(26%) patients, smoking and alcohol consumption in 9(13%), smoking and tobacco chewing in 8(12%) patients. Nine (13.6%) patients did not have any habits.

TABLE 5: DISTRIBUTION ACCORDING TO HABITS:

Habits	No of Patients	Percentage (%)
Smoking	20	30.30
Smoking, Alcohol consumption and tobacco chewing	17	25.75
Smoking and Alcohol Consumption	9	13.63
Smoking and Tobacco chewing	8	12.12
Tobacco chewing	3	4.54
Alcohol consumption	0	0
Tobacco chewing and Alcohol consumption	0	0
No habits	9	13.63
Total	66	100

DIAGRAM 5: DISTRIBUTION ACCORDING TO HABITS:



IMMUNIZATION:

All the patients 66(100%) in the study had not been immunised with pneumococcal and influenza vaccines in the past.

TABLE 6: DISTRIBUTION ACCORDING TO IMMUNIZATION

Immunization	**No of Patients**	**Percentage (%)**
No immunization	66	100
Total	66	100

VITAL SIGNS:

In this study, tachycardia defined as pulse rate>100/min was noted in 17(26%), tachypnoea defined by respiratory rate >16/min was observed in 62(94%), and increased temperature defined as temperature>37^0 was noted in 39 patients.

TABLE 7: VITAL PARAMETERS

Vitals	No of patients	Percentage (%)
PR		
60-100	49	74.24
>100	17	25.76
RR		
12-16	4	6.0
>16	62	94.0
Temperature		
<37 degree	27	40.9
>37 degree	39	59.1
Total	66	100

DIAGRAM 6: PULSE RATE

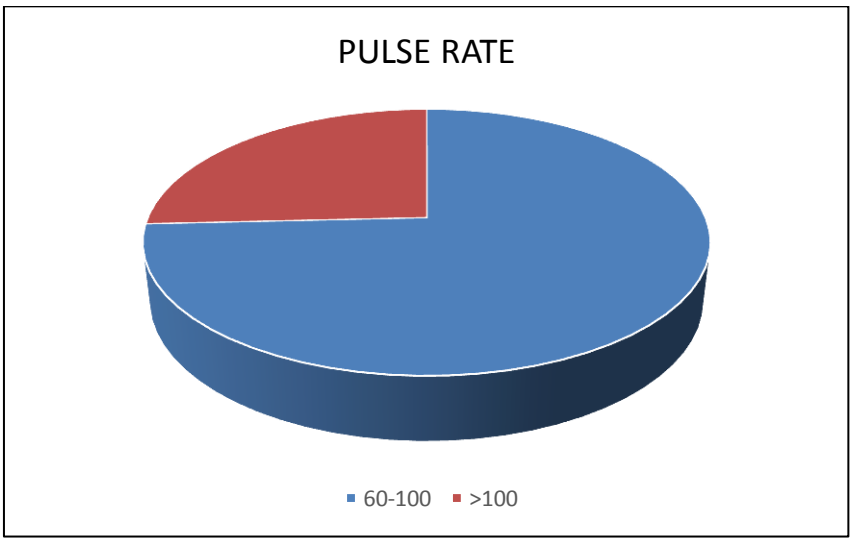


DIAGRAM 7: RESPIRATORY RATE

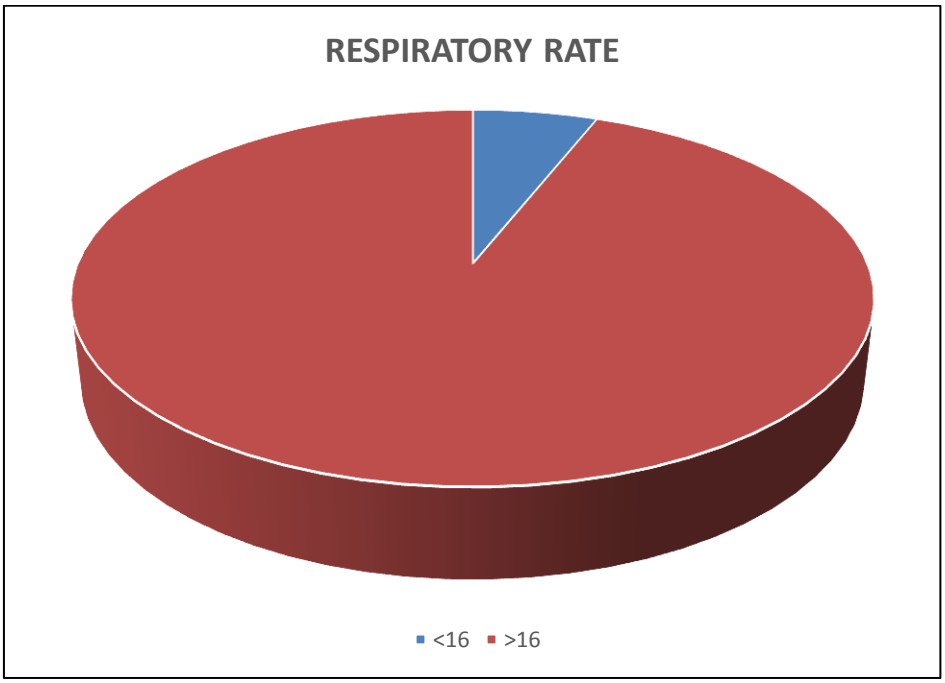
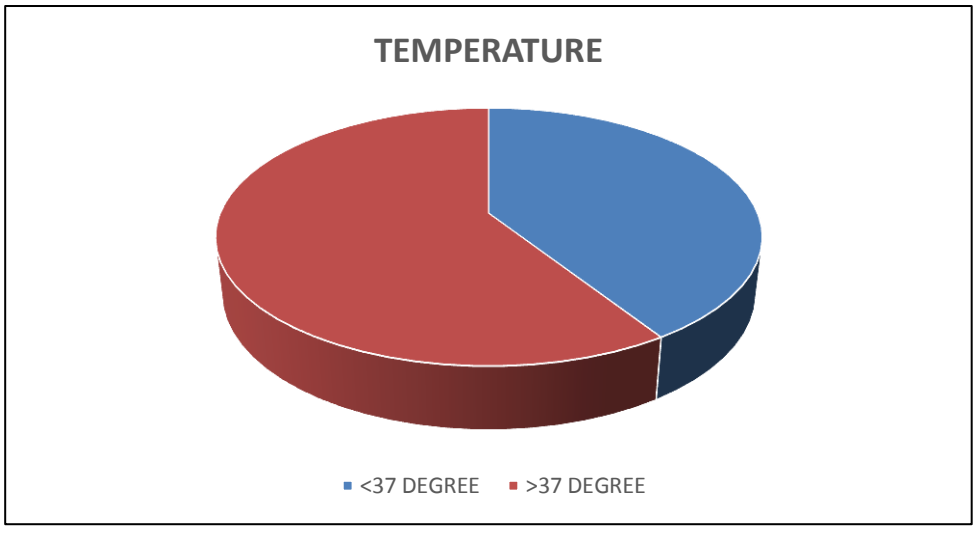


DIAGRAM 8: TEMPERTAURE



RADIOLOGICAL FINDINGS:

On Chest-X Ray, it was noticed that all the patients (100%) had emphysematous chest.

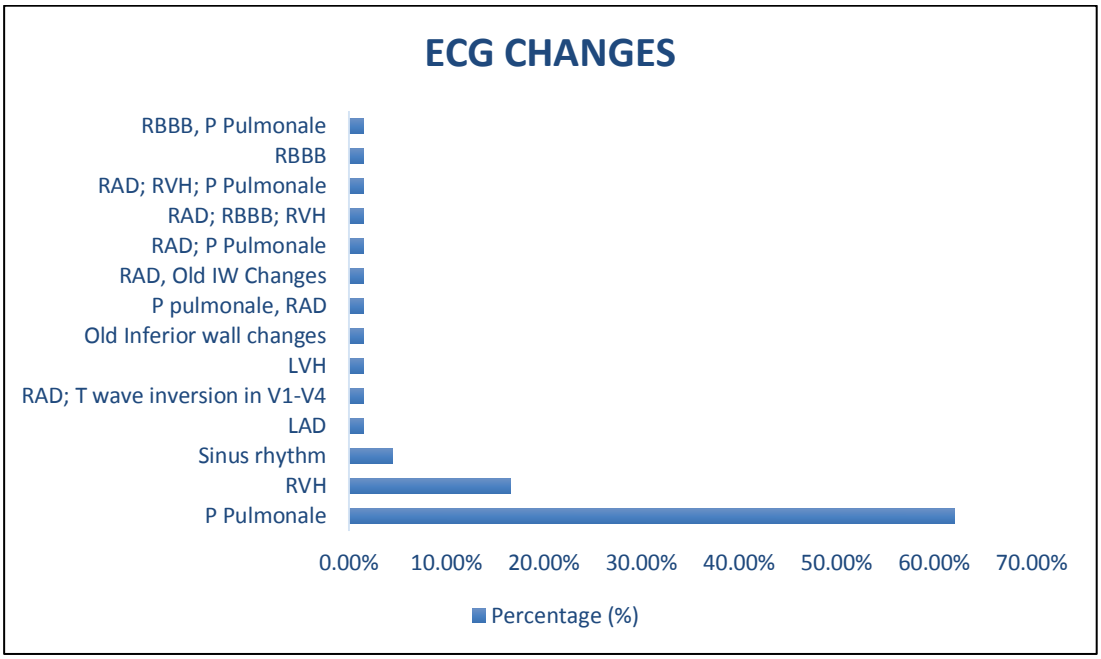
ECG CHANGES:

Among all the patients, P Pulmonale was the most common change observed which was seen in 41(62%) patients followed by Right ventricular hypertrophy seen in 11(17%) patients. Right axis deviation with T wave inversion in anterior chest leads was seen in 1 patient, right axis deviation with right ventricular hypertrophy with P pulmonale was seen in 1 patient. The ECG changes have been depicted in the table and diagram to follow.

TABLE 8: ECG CHANGES IN COPD PATIENTS

ECG	No. of patients	Percentage (%)
P Pulmonale	41	62.1
RVH	11	16.6
Sinus rhythm	3	4.5
LAD	1	1.5
RAD; T wave inversion in V1-V4	1	1.5
LVH	1	1.5
Old Inferior wall changes	1	1.5
P pulmonale, RAD	1	1.5
RAD, Old IW Changes	1	1.5
RAD; P Pulmonale	1	1.5
RAD; RBBB; RVH	1	1.5
RAD; RVH; P Pulmonale	1	1.5
RBBB	1	1.5
RBBB, P Pulmonale	1	1.5
Total	66	100.0

DIAGRAM 9: ECG CHANGES IN COPD PATIENTS



LABARATORY CHARACTERISTICS:

Leucocytosis defined as total leucocyte count >11,000/cum was the most common haematological change noted in 42(63.7%) patients. Mean total leucocyte count was 14,427.03. Increased haemoglobin defined as Hb>14gm/dL was noted in 15(22.7%) patients, mean Hb was 12.41gm/dL. ESR>20mm at 1 hour was noted in 61(92.4%) patients. Mean ESR was 26.43mm.

TABLE 10: LABARATORY CHARACTERISTICS

Variables	N	Minimum	Maximum	Mean	Std. Deviation
TC	66	4340	44890	14427.03	7708.590
Hb	66	5.0	18.4	12.413	2.4793
ESR	66	5	125	47.97	26.438

TABLE 11: LABARATORY CHARACTERISTICS

Lab Characters	No. of patients	Percentage (%)
TC		
4000-11000	24	36.3
>11000	42	63.7
Hb		
10	7	10.6
10-14	44	66.6
>14	15	22.7
ESR		
0-20	5	7.6
>20	61	92.4
Total	64	100

DIAGRAM 10: TOTAL LEUCOCYTE COUT

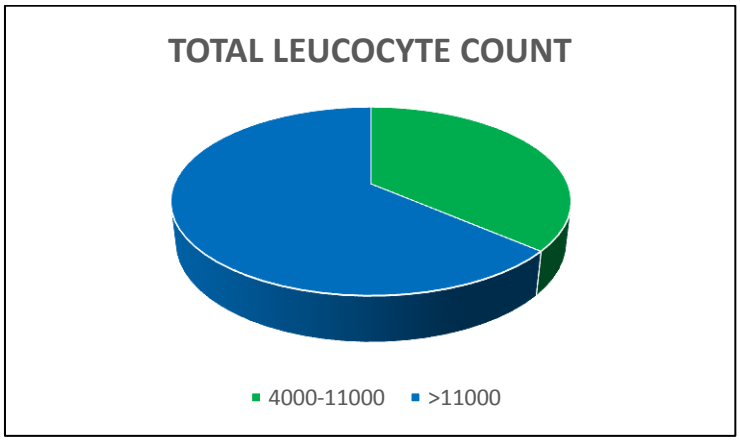


DIAGRAM 10: ERYTHROCYTE SEDIMENTATION RATE

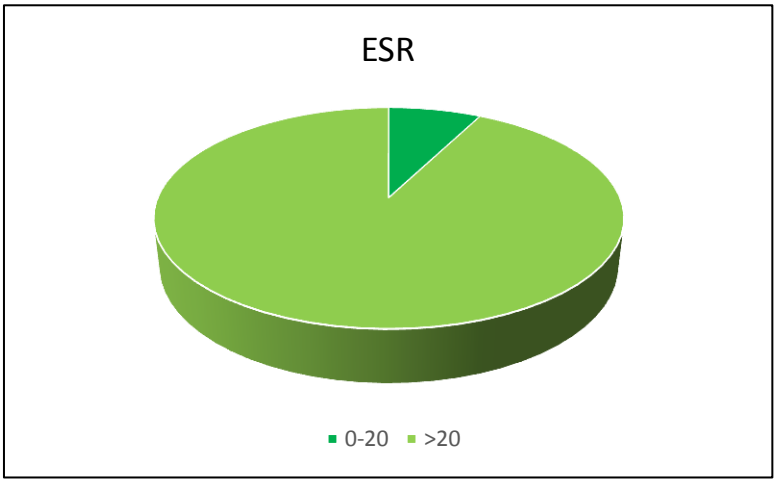
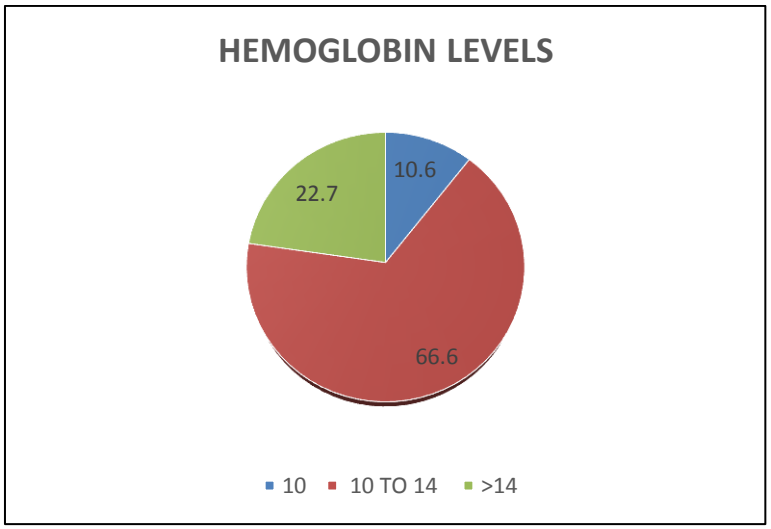


DIAGRAM 11: HEMOGLOBIN LEVELS



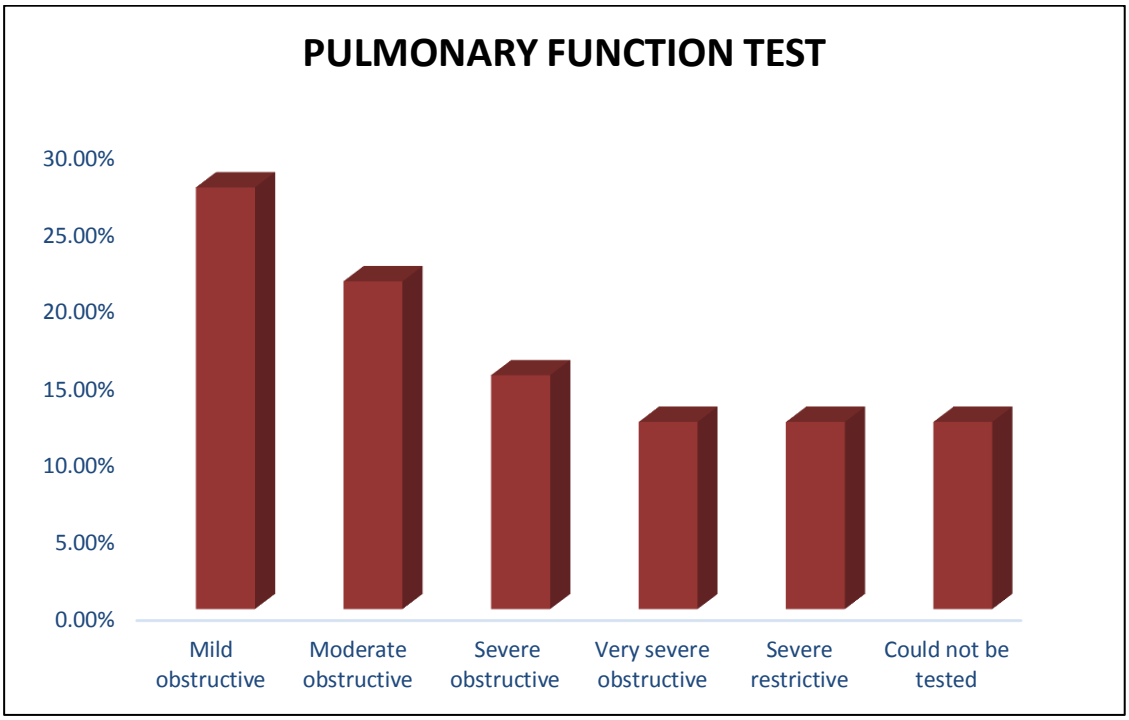
PULMONARY FUNCTION TEST:

Pulmonary function test (PFT) was done in 58 patients. It could not be done in 8 patients; 4 among them were ventilated initially and later after extubation patients refused owing to the seriousness of the illness and 4 were unable to complete the procedure of PFT. The PFT revealed mild obstructive pattern in 18(27.7%) patients, moderate obstructive pattern in 21%, severe obstructive in 15.15% and very severe obstructive pattern in 12.12% patients. This was classified according to the GOLD 2017 Classification of severity of airflow limitation. In our study 8(12.12%) patients had severe restrictive pattern.

TABLE 12: PULMONARY FUNCTION TEST

Pulmonary Function Test	No. of patients	Percentage%
Mild obstructive	18	27.27
Moderate obstructive	14	21.21
Severe obstructive	10	15.15
Very severe obstructive	8	12.12
Severe restrictive	8	12.12
Could not be tested	8	12.12
Total	66	100.0

DIAGRAM 12: PULMONARY FUNCTION TEST



RESULTS OF SPUTUM GRAM STAINING:

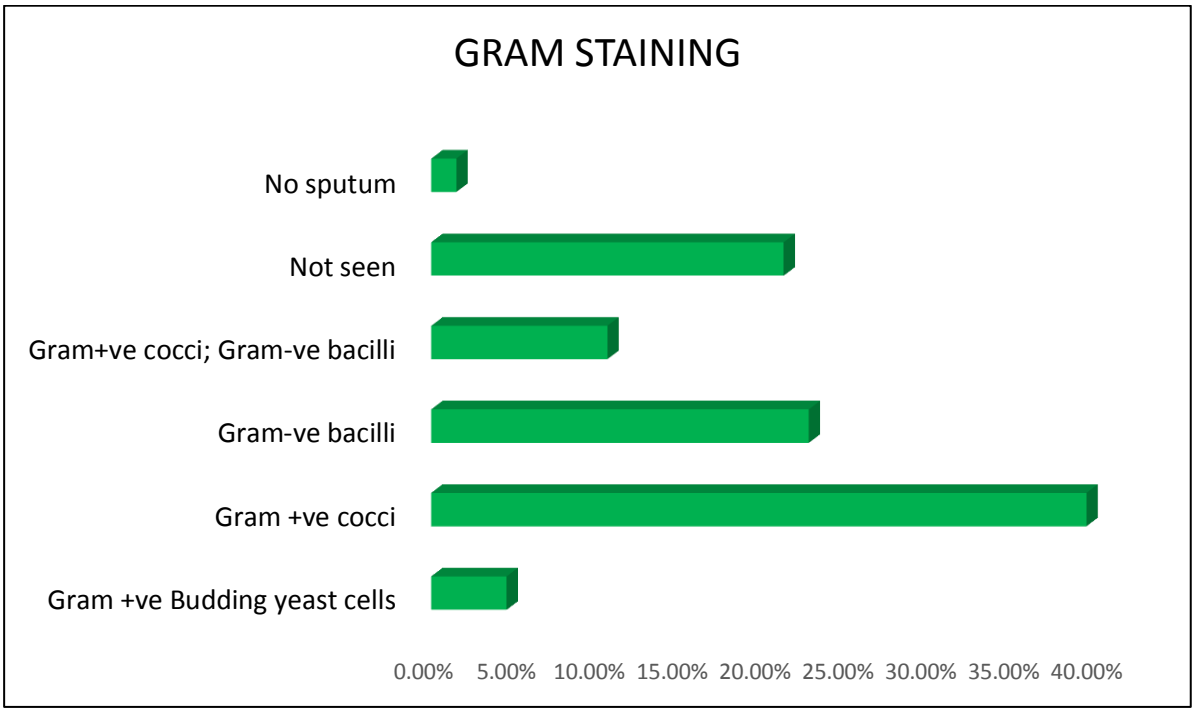
On Gram staining, Sputum sample showed the presence of Gram positive cocci predominantly in 26(39.39%) patients, Gram negative bacilli in 15(22.72%) patients, both Gram positive cocci and Gram-negative bacilli in 7(10.60%), and budding yeast cells in 3(4.5%) patients. No organisms were obtained in 14(21.21%) patients and 1 patient, cough was not associated with expectoration and hence no sputum was given for examination.

This is shown the table below,

TABLE 13: DISTRIBUTION ACCORDING TO SPUTUM EXAMINATION - GRAM STAINING:

SPUTUM EXAMINATION	No. of patients	Percentage (%)
Gram +ve Budding yeast cells	03	4.54
Gram +ve cocci	26	39.39
Gram-ve bacilli	15	22.72
Gram+ve cocci; Gram-ve bacilli	07	10.60
Not seen	14	21.21
No sputum	01	1.51
Total	66	100.0

DIAGRAM 13: SPUTUM EXAMINATION – GRAM STAINING



All the patients with expectoration, sputum examination was negative for acid fast bacilli on Zeil-Neelsan staining.

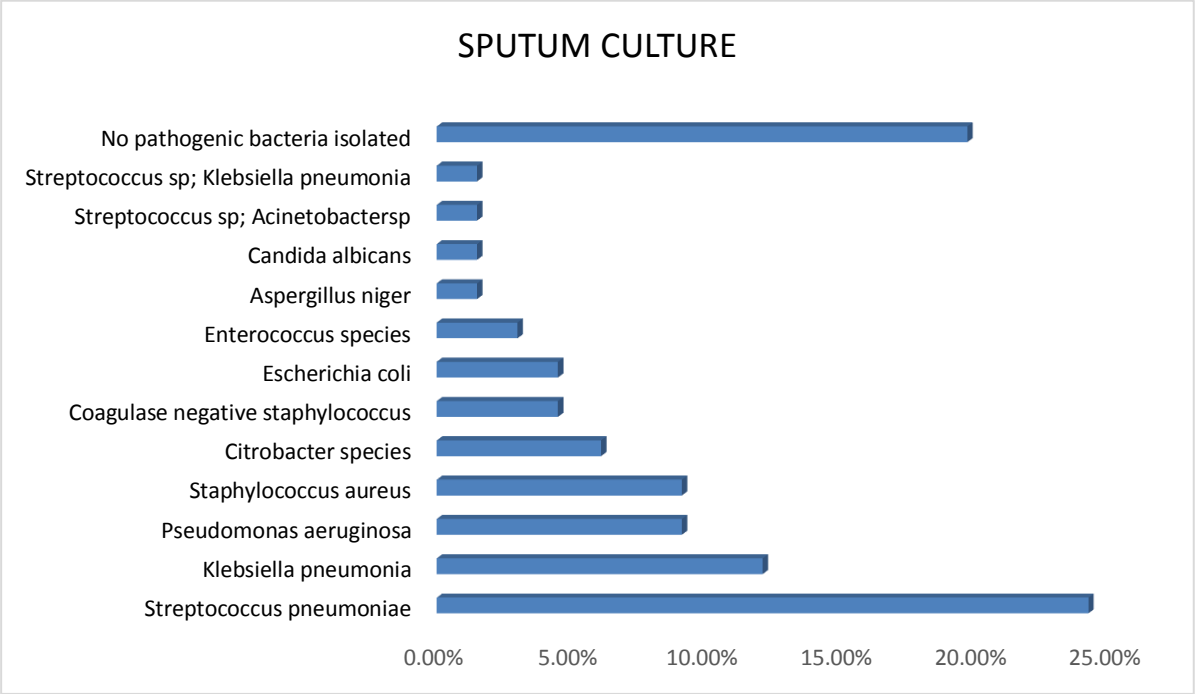
RESULTS OF SPUTUM CULTURE:

The commonest organism isolated was *Streptococcus pneumoniae* 16(24.2%) followed by *Klebsiella pneumonia* in 8(12.1%), *Pseudomonas aeruginosa* and *Staphylococcus aureus* each in 6(9.1%) patients, *E coli* in 3(4.5%) patients. No pathogenic bacteria were isolated in 13(19.7%) patients. This is shown in the table.

TABLE 14: DISTRIBUTION ACCORDING TO SPUTUM EXAMINATION - SPUTUM CULTURE

Sputum Culture	No. of patients	Percentage(%)
Streptococcus pneumonia	16	24.2
Klebsiella pneumonia	8	12.1
Pseudomonas aeruginosa	6	9.1
Staphylococcus aureus	6	9.1
Citrobacter species	4	6.1
Coagulase negative staphylococcus	3	4.5
Escherichia coli	3	4.5
Enterococcus species	2	3
Aspergillus niger	1	1.5
Candida albicans	1	1.5
Streptococcus sp; Acinetobactersp	1	1.5
Streptococcus sp; Klebsiella pneumonia	1	1.5
No pathogenic bacteria isolated	13	19.7
Total	66	100.0

DIAGRAM 14: SPUTUM EXAMINATION – SPUTUM CULTURE



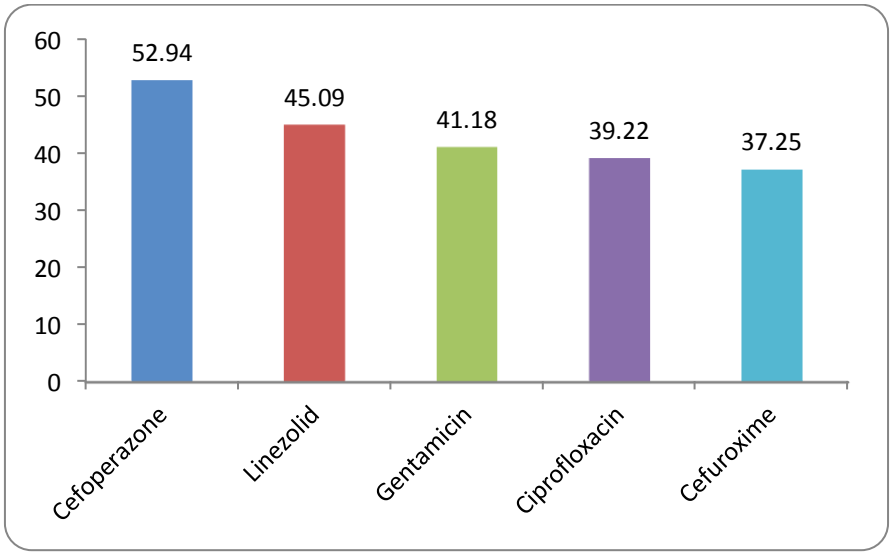
ANTIBIOTIC SENSITIVITY PATTERN:

Out of 66 patients, pathogenic bacteria were isolated in 51(77.27%) patients. Sensitivity pattern was tested for all these patients. Among all the tested antibiotics for various organisms isolated, maximum numbers of patients were sensitive to Cefoperazone (53%), 45% of the patients were sensitive to Linezolid. These were followed by Gentamicin in 21(41%) patients, Ciprofloxacin in 20(39%) patients.

TABLE 15: ANTIBIOTIC SENSITIVITY PATTERN (N=51)

Sensitive Drug	No. of patients	Parentage
Cefoperazone	27	52.94
Linezolid	23	45.09
Gentamicin	21	41.18
Ciprofloxacin	20	39.22
Cefuroxime	19	37.25

DIAGRAM 15: ANTIBIOTIC SENSITIVITY PATTERN



ANTIBIOTIC SENSITIVITY PATTERNS OF THE ISOLATES:

The sensitivity pattern of the four most common bacteria isolated was studied. Streptococcus pneumoniae, which was the most common isolate, was sensitive to Cefoperazone, Linezolid, Piperacillin and Clindamycin in decreasing frequency. *Klebsiella pneumoniae* isolates were sensitive to Amikacin, Ciprofloxacin, Gentamicin and Cefuroxime. In our study *Pseudomonas aeruginosa* isolates were sensitive to Amikacin, Cefoperazone, and Piperacillin. *Staphylococcus aureus* isolates were sensitive Cefoperazone, Cefuroxime, Clindamycin and Gentamicin.

TABLE 16: ANTIBIOTIC SENSITIVITY PATTERN OF THE ISOLATES

Isolated organism	*Streptococcus Pneumoniae* (16)	*Klebsiella pneumoniae* (8)	*Pseudomonas aeruginosa* (6)	*Staphylococcus aureus* (6)
Amikacin	NT	5(62.5%)	5(83.3%)	NT
Amoxiclav	6(37.5%)	1(20%)	2(33.3%)	NT
Azithromycin	4(25%)	NT	1(16.6%)	1(16.6%)
Cefoperazone	16(100%)	NT	5(83.3%)	4(66.6%)
Cefuroxime	12(75%)	3(37.5%)	NT	4(66.6%)
Ciprofloxacin	5(31.25%)	5(62.5%)	5(83.3%)	2(33.3%)
Clindamycin	7(43.75%)	NT	NT	5(83.3%)
Gentamicin	4(25%)	4(50%)	5(83.3%)	3(50%)
Levofloxacin	NT	NT	5(83.3%)	1(16.6%)
Linezolid	14(87.5%)	NT	NT	1(16.6%)
Piperacillin	8(50%)	1(20%)	5(83.3%)	1(16.6%)

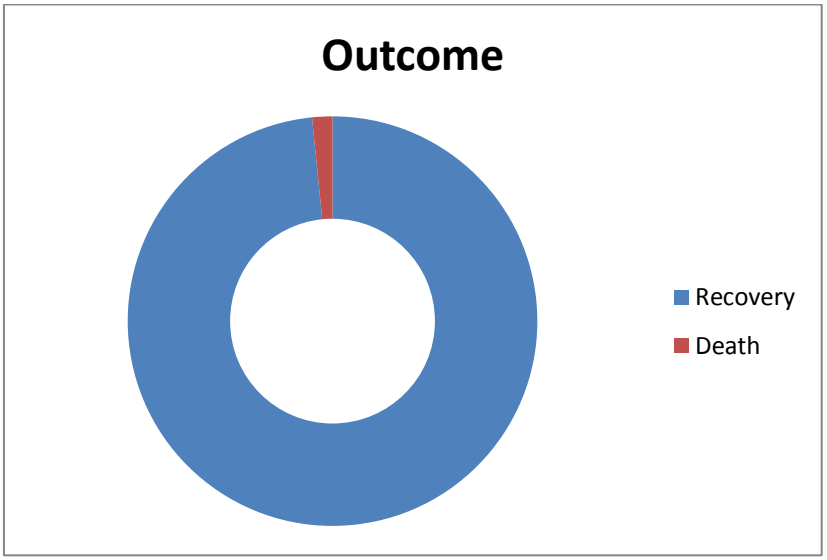
OUTCOME:

In this study, out of 66 patients, 65(98.4%) patients recovered, mortality was seen in 1 patient (1.6%).

TABLE 17: OUTCOME

Outcome	No of patients	Percentage (%)
Recovery	65	98.5
Death	1	1.5
Total	66	100

DIAGRAM 16: OUTCOME



DISCUSSION

Chronic obstructive pulmonary disease is a chronic non-communicable disease and its prevalence dramatically increases with age and leads to decreased quality of life in elderly. COPD exacerbations are the leading cause of morbidity and mortality and early introduction of empirical antibiotics, can improve outcome and reduce mortality[130].

Knowledge of local bacteria implicated the sensitivity patterns of AECOPD in patients at this geographical area that would facilitate an early introduction of a proper antibiotic, which would reduce the mortality, morbidity and improve the prognosis and Quality of Life among the elderly patients.

In the present study, 66 patients with AECOPD aged more than 60 years were included and their bacteriological profile and culture pattern were studied. The results of study which has been described are discussed below.

AGE DISTRIBUTION

In this study, the age group of patients varied from 60 to 91 years. Mean age was 70.63 years. Majority of the patients (45) were in the age group of 60-74 years, which constituted 68.2 % of the total patients. It is similar to the study conducted by Babu D *et al.* [131]where 74.5% of the patients were between 60-79 years.

SEX DISTRIBUTION

In this study out of 66 patients, 55(83%) were males and 11(17%) were females, which depicts that males were affected much more compared to females. It is similar to the study conducted by Shashibhushan B. L*et al.* [132] where 84% of the patients were males and 16% females. Increased incidence of AECOPD in males is observed.

PRESENTING COMPLAINTS

The characteristic symptoms of exacerbations of COPD include either increased shortness of breath or breathlessness, increased cough, which is often but not always productive; that is increased sputum volume or purulence, all these being accompanied by fever. Patients can also present with other additional symptoms such as increased fatigue, decreased exercise intolerance, malaise, body aches and confusion which all depend on the severity of the disease and the extent of physiological derangements.

In our study, cough with expectoration, that is increased sputum production were the commonest symptoms seen in 100% and 98.5% of patients respectively, which is similar to the study conducted by S. B. Lal*et al.* [133]and Arora. N*et al.* [134].

Breathlessness was the second most common symptom in our study, which was seen in 98.4% of the patients. It is similar to the study conducted by N. Arora *et al.* [134] where 98.2% patients presented with varying degree of breathlessness.

Fever was seen in 53.1% of the patients in our study. It is contradicting to the similar studies conducted by Arora. N.*et al.* [134]and Kulkarni G *et al.* [135].

HABITS

Among habits, alone smoking only was predominant in 30.3% of the patients. Multiple habits like smoking, tobacco chewing and alcohol consumption altogether were seen in 26% patients and smoking and tobacco chewing together in 12.1% patients. In total, 82% of patients in the present study were smokers. It is similar to the study conducted by Arshi Syed*et al.* (136) where 85% of the patients were smokers and S. B. Lal *et al.* [133] where 95% of the patients were smokers. No history of smoking was reported by female patients similar to the observations in the study by Arshi Syed *et al.* [136].

VITALS

In our study, tachycardia was seen in 26% patients, tachypnoea in 94% of the patient and increased temperature in 59% patients.

LABORATORY CHARACTERISTICS

Leucocytosis was observed in 63.7% patients in our study. Raised ESR was observed in 92.4% patients in our study. These observations were similar to the one made in the study by Kulkarni G *et al.* [135].

ECG CHANGES:

In our study, P Pulmonale was the most common ECG finding observed in 62% of the patients followed by right ventricular hypertrophy in 16.6% of the patients. T wave inversion in V1-V4 was seen in one patient. P Pulmonale with right ventricular hypertrophy with right axis deviation was seen in one patient. These observations are similar to the standard ECG changes observed in all the patients with emphysema.

CHEST X-RAY FINDINGS:

All the patients in the study had features of emphysematous chest on chest radiography. Findings observed in our study were low flattened diaphragm, bronchial wall thickening, increased inter-coastal space, and tubular heart and hyperinflated lung fields. The findings are similar to the observations in the study by Arora. N.*et al.* [134].

PULMONARY FUNCTION TEST

In our study 8(12.1%) patients had severe restrictive pattern. This could be attributed as pseudo-restrictive pattern as these patients had clinical features and suggestive of AECOPD and history repeated exacerbations and exposure to risk factors and these patients did not have other conditions which contributed to the

restrictive pattern. It was observed these patients had very low Forced Vital Capacity (FVC), which can explain pseudo-restriction which is characterised by increased residual volume due to prominent air trapping with normal or slightly increased TLC, thereby reducing the FVC.

GRAM STAINING

On gram staining of the sputum, Gram positive cocci were isolated from 39.39% of the patients, Gram negative bacilli in 22.72% of the patients, and mixed in 10.6% of the patients in our study. This finding is contrary to other studies reported by Sharan. H.*et al.* [137], Aleemullah.M. F.*et al.* [138], and Babu. D.*et al.* [131]where gram negative bacteria were isolated predominantly.

SPUTUM CULTURE

In our study, predominantly isolated organism was *Streptococcus pneumoniae* in 24.2% of the patients, followed by *Klebsiella pneumoniae* in 12.1% patients, *Pseudomonas aeruginosa* and *Staphylococcus aureus* in 9.1% patients each. It is similar to the studies conducted by, Arora. N.*et al.* [134], Shashibhushan B. L.*et al.* [132], Patel A. K.[130], and Arshi Syed*et al.* [136] where *Streptococcus pneumoniae* was the most common bacteria isolated. Contrary to this, the studies conducted by Babu. D.*et al.*[131], Sharan. H.*et al.* [137], and Narayanagowda D. S*et al.* [139] found out *Klebsiella pneumoniae* to be the most common bacteria causing exacerbations.

In, 2 patients, fungi were isolated, *Candida albicans* in one and *Aspergillus niger* in the other patient. *Candida albicans* was isolated in 2.9% of the patients in the study by Arshi Syed*et al.* [136]. Other gram-negative bacteria that were isolated were *Citrobacter species* (6%) and *Escherichia coli* (4.5%).

No pathogenic bacteria were isolated in 13 (19.7%) patients in our study. This was less when compared to the studies done by Narayanagowda D. S.*et al.* [139] where 63% yielded no bacteria, Babu. D.*et al.* [131] where 57% yielded no bacteria.

Multiple organisms were isolated from 2 patients, *Streptococcus pneumoniae* and *Acinetobacter species* in one patient and *Streptococcus pneumoniae* and *Klebsiella pneumoniae* in the other patient.

ANTIBIOTIC SENSITIVITY PATTERN

In our study, antibiotic sensitivity pattern was tested for all the patients in whom pathogenic bacteria were isolated. Among all the tested antibiotics for various gram negative and gram-positive organisms, maximum number of patients were sensitive to Cefoperazone that is in 53% of patients, Linezolid in 45% of patients, Gentamicin in 41% of patients and Ciprofloxacin in 39% of patients. The study conducted by Patel A. K.*et al.* [130] found that Piperacilline+Tazobactum was the most sensitive drug against all organisms, followed by quinolones.

ANTIBIOTIC SENSITIVITY PATTERNS OF THE ISOLATES

Streptococcus pneumoniae, which was the most common isolate, was sensitive to cefoperazone, linezolid, Piperacillin and clindamycin in decreasing frequency. The study conducted by Gauri kulkarni[5] found 1st generation cephalosporin, 2nd generation cephalosporin, 3d generation cephalosporin and fluoroquinolones.

Klebsiella pneumoniae isolates were sensitive to Amikacin, ciprofloxacin, Gentamicin and cefuroxime. In the study done by Narayanagowda D. S. *et al.* [139]*Klebsiella pneumoniae* was sensitive to Ampicillin, Ciprofloxacin and Netilmicin.

A study by S. B. Lal*et al.* [133] study demonstrated sensitivity to a combination of Levofloxacin and Gentamicin.

In our study, *Pseudomonas aeruginosa* isolates were sensitive to Amikacin, Cefoperazone, and Piperacillin. It is similar to the study conducted by Narayanagowda D. S.*et al.* [139]where it was mainly sensitive to Piperacillin, Amikacin and Gentamicin. In the study conducted by Kulkarni G.*et al.* [135], the isolates were sensitive to Amikacin, Cefoperazone-Sulbactam, Cefotaxime, Gentamicin, Levofloxacin and Ciprofloxacin.

Staphylococcus aureus isolates were sensitive Cefoperazone, Cefuroxime, Clindamycin and Gentamicin. The study by Narayanagowda D. S.*et al.* [139] study found *Staphylococcus aureus* to be sensitive to Amoxyclavulinate, Penicillin, Erythromycin, Gentamicin, Amikacin, Netilmicin and co-trimoxazole.

OUTCOME

All case mortality in this study was 1.5%. It is contrary to the study done by Gaude G S*et al.* [140] where 12% mortality was observed and Reddy MR*et al.*[141]where 14.5% mortality was observed.

CONCLUSION

Chronic obstructive pulmonary disease is a chronic non-communicable disease and its prevalence dramatically increases with age and leads to decreased quality of life in elderly. Exacerbations of COPD in elderly result in substantial worsening of the general condition of them and depression in quality of life. Elderly patients with exacerbations can present with both typical and atypical complaints. Breathlessness, cough with expectoration are the most common typical symptoms whereas tightness of chest, loss of appetite, altered sensorium and giddiness are the common atypical symptoms. None of the elderly COPD patients had either received pneumococcal or influenza vaccine in past nor had the awareness regarding it. Elderly COPD patients usually cannot perform Pulmonary function test fully owing to the decreased physical capacity and cognitive impairment.

Bacterial infection is the most common triggering factor for exacerbations of COPD in elderly. Streptococcus pneumoniae was the most common bacteria isolated in our study. Most of the organisms isolated in our study were sensitive to Cefoperazone. Knowledge of the local bacteria with their sensitivity pattern resulting in exacerbations in the local geographical area would help in prompt management of them. Adequate awareness regarding the immunization among the elderly COPD patients, their caregivers and the treating doctor would prevent many exacerbations and hence improved quality of life.

The management of elderly patient with COPD should encompass a multidisciplinary approach. Elderly patient with COPD requires special attention because of high susceptibility of older people to disease, medication is more and the number of drugs to be taken daily increases progressively with age.

SUMMARY

1) This prospective observational cross-sectional study was conducted in Shri B M Patil Medical College Hospital and Research centre, BLDEU, Vijayapura. A total of 66 patients aged more than 60 years diagnosed with acute exacerbation of chronic obstructive pulmonary disease were included in the study.
2) The age group of patients varied from 60 to 91 years with a mean age of 70.63 years. 55(83%) of the patients were males and 11(17%) were females.
3) Most of the patients presented with typical complaints of exacerbations, that is increased breathlessness and cough which was productive in nature. More than half of the patients presented with fever also. Atypical symptoms such as history of altered sensorium, reduced appetite and chest pain were present in very few patients.
4) Most of the patients had associated co-morbid conditions like hypertension, diabetes mellitus, old pulmonary tuberculosis, and ischemic heart disease. Of this hypertension was the most commonly seen comorbidity, present in 23% of patients.
5) Common signs which were observed include tachycardia in 26% patients, tachypnoea in 94% of the patient and increased temperature in 59% patients. Barrel shaped chest, decreased vocal fremitus and resonance, hyper-resonant note on percussion, decreased vesicular breath sounds and added sounds like crepitations were observed in most of the patients.
6) Raised ESR was the most common laboratory finding noted in 59(92.4%) patients followed by leucocytosis in 40(63.7%) patients.

7) P Pulmonale was the most common finding [39(62.1%) patients] noted in ECG followed by right ventricular hypertrophy.
8) All the patients in the study had features of emphysematous chest on chest radiography.
9) Pulmonary function test was conducted in 58 patients in the study. Among them 50(75.7%) patients showed obstructive and 8(12.3%) showed pseudo restrictive pattern.
10) On gram staining of the sputum, Gram positive cocci were isolated from 39.4% of the patients, Gram negative bacilli in 22.7% of the patients, and mixed in 11% of the patients.
11) Bacteriological isolation by sputum culture showed *Streptococcus pneumoniae* as the most common isolated organism [16(24.2%) patients], followed by *Klebsiella pneumoniae* in 8(12.1%) patients, and *Pseudomonas aeruginosa* and *Staphylococcus aureus* in 6(9.1%) patients. Other organisms which were isolated include *Citrobacter species* in 4(6.1%), *Escherichia coli* and *Enterococcus species* in 3(4.5%) each. Multiple organisms were isolated from 2 patients, *Streptococcus pneumoniae* and *Acinetobacter species* in one patient and *Streptococcus pneumoniae* and *Klebsiella pneumoniae* in the other patient.
12) No pathogenic bacteria were isolated in 13(19.69%) patients.
13) Among all the tested antibiotics for various gram negative and gram-positive organisms, maximum number of patients were sensitive to Cefoperazone that is in 53% of patients, Linezolid in 45% of patients, Gentamicin in 41% of patients and Ciprofloxacin in 39% of patients.
14) *Streptococcus pneumoniae*, which was the most common isolate, was sensitive to Cefoperazone, Linezolid, Piperacillin and Clindamycin in decreasing

frequency.*Klebsiella pneumoniae* isolates were sensitive to Amikacin, Ciprofloxacin, Gentamicin and Cefuroxime. In our study *Pseudomonas aeruginosa* isolates were sensitive to Amikacin, Cefoperazone, and Piperacillin. *Staphylococcus aureus* isolates were sensitive Cefoperazone, Cefuroxime, Clindamycin and Gentamicin.

15) All case mortality in this study was seen in 1(1.5%) patient.

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ANNEXURE –I

ETHICAL COMMITTEE CLEARANCE CERTIFICATE

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 04-10-2016 at 3-00pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "Bacteriological profile & antibiotic sensitivity pattern in Sputum culture of elderly patients with acute exacerbations of chronic obstructive pulmonary disease"

Name of P.G. student Dr Jayanth. S. S
Dept of Medicine

Name of Guide/Co-investigator Dr Anand. P. Ambali
Prof of Medicine

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

ANNEXURE –II

INFORMED CONSENT FORM

BLDEU'S SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR- 586103

TITLE OF THE PROJECT -

BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SENSITIVITY PATTERN IN SPUTUM CULTURE OF ELDERLY PATIENTSWITH ACUTE EXACERBATIONS OF CHRONICOBSTRUCTIVE PULMONARY DISEASE

PRINCIPAL INVESTIGATOR - Dr JAYANTH S S

P.G. GUIDE NAME - Dr. ANAND P AMBALI

PROFESSOR OF MEDICINE

CHAIRMAN ETHICAL COMMITTEE

All aspects of this consent form are explained to the patient in the language understood by him/her.

I) **INFORMED PART**

1) PURPOSE OF RESEARCH:

I have been informed about this study. I have also been given a free choice of participation in this study.

2) PROCEDURE:

I am aware that in addition to routine care received I will be asked series of questions by the investigator. I have been asked to undergo the necessary investigations and treatment, which will help the investigator in this study

3) RISK AND DISCOMFORTS:

I understand that I may experience some pain and discomfort during the examination or during my treatment. This is mainly the result of my condition and the procedure of this study is not expected to exaggerate these feelings that are associated with the usual course of treatment

4) BENEFITS:

I understand that my participation in this study will help to patients survival and better outcome.

5) CONFIDENTIALITY:

I understand that the medical information produced by this study will become a part of Hospital records and will be subject to the confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file and identified only by a code number. The code-key connecting name to numbers will be kept in a separate location.

If the data are used for publication in the medical literature or for teaching purpose, no name will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand that I may see the photographs and videotapes and hear the audiotapes before giving this permission.

6) REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about the study at anytime .Dr. JAYANTH S S is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of the study, which might influence my continued participation.

If during the study, or later, I wish to discuss my participation in or concerns regarding this study with a person not directly involved, I am aware that the social worker of the hospital is available to talk with me. A copy of this consent form will be given to me to keep for careful reading.

7) REFUSAL OR WITHDRAWAL OF PARTICIPATION:

I understand that my participation is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice to my present or future care at this hospital. I also understand that Dr. JAYANTH S S may terminate my participation in the study after he has explained the reasons for doing so

and has helped arrange for my continued care by my own physician or physical therapist, if this is appropriate.

8) INJURY STATEMENT:

I understand that in the unlikely event of injury to me resulting directly from my participation in this study, if such injury were reported promptly, the appropriate treatment would be available to me, but no further compensation would be provided. I understand that by my agreement to participate in this study I am not waiving any of my legal rights.

I have explained to _____the purpose of the research, the procedures required and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Dr.JAYANTH S S Date :

(Investigator)

ANNEXURE –III

BLDEDU'S SHRI B.M. PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA

Name: CASE NO:

Age: IP NO:

Sex: DOA:

Religion: DOD:

Past Occupation:

Present Occupation:

Residence:

Chief complaints:

History of present illness:

Fever

Breathlessness

Cough

Expectoration

Past History:

COPD/ IHD/ tuberculosis /diabetes mellitus/ lung malignancy/hypertension / Bronchial Asthma

History of immunization:

Personal History:

Diet/appetite:

Sleep:

Bladder and bowel habits :

Smoking/Tobacco chewing/Snuff Inhalation/alcohol:

Family History:

TB: Asthma: Malignancy: DM: HTN:

Treatment History:

General Physical Examination

Height :

Weight:

Body Mass Index :

Vitals

PR:

BP:

RR:

Temp:

Head to toe examination:

SYSTEMIC EXAMINATION.

Respiratory System

Upper respiratory tract:

Lower respiratory tract:

A. INSPECTION:

1. Shape of chest:

2. Drooping of shoulder:

3. Lye of ribs:

4. Trachea:

5. Apex beat:

6. Chest movements:

7. Any engorged veins:

8. Visible pulsations/scars:

9. Spine

B. PALPATION:

1. Trachea:

2. Apex beat:

3. Chest movements:

4. Tactile vocal fremitus:

	Right	Left
Supraclavicular		
Infraclavicular		
Mammary		
Inframammary		
Axillary		
Infraaxillary		
Suprascapular		
Interscapular		
Infrascapular		

5.Measurements:

AP diameter:

Transverse diameter:

Right hemithorax:

Left hemithorax:

Circumference:

On inspiration:

On expiration:

Expansion:

C. PERCUSSION:

Resonant/ Dull/ Hyperresonant:

Site:

D.AUSCULTATION:

1. Air entry:
2. Breath sounds:
3. Rhonchi
4. Crepitations:
5. Wheeze:
6. Pleural rub:
7. Bronchophony:
8. Egophony:
9. Whispering pectoriloquy:
10. Vocal resonance:

	Right	Left
Supraclavicular		
Infraclavicular		
Mammary		
Inframammary		
Axillary		
Infraaxillary		
Suprascapular		
Interscapular		
Infrascapular		

Cardiovascular System

Central Nervous System

Per abdomen

INVESTIGATIONS

HAEMATOLOGY –

Hemoglobin	gm. %
Total WBC counts	Cells/mm^3
Differential counts -	
Neutrophils	%
Lymphocytes	%
Eosinophils	%
Monocytes	%
Basophils	%
ESR	mm after 1 hour

Sputum for Gram stain:

AFB:

Sputum bacteriological profile:

Sputum antibiotic sensitivity pattern:

Chest X-ray:

ECG:

PULMONARY FUNCTION TEST:

BIOCHEMISTRY:

Serum electrolytes:

Serum creatinine:

URINE EXAMINATION -

Albumin	
Sugar	
Microscopy	

FINAL DIAGNOSIS

MASTER CHART

SL NO	NAME	AGE	SEX	IP NO	DOA	CHIEF COMPLAINTS					COMORBIDITIES	HABITS			GPE				RESPIRATORY S				TC	Hb	ESR	
						FEVER	DYSPNEA	COUGH	EXPECTORATION	OTHERS		SMOKING	TOBACCO	ALCOHOL	PR(bpm)	BP(mmHg)	RR(cpm)	TEMP(℃)	TVF	VR	BS	AS				GRAM STAIN
1	Tulujappa Neelappa Koulagi	82	M	6769	23/02/2018	Y	Y	Y	Y	NONE	NIL	Y	Y	N	90	130/80	16	37.8	I	I	D	Crepts	8160	8.9	40	Not seen
2	Dundappa Shivamurti Kumbar	91	M	15755	05/04/2018	Y	Y	Y	Y	NONE	IHD	Y	N	N	90	140/80	18	37.6	I	I	D	None	6330	10.6	40	Gram +ve Budding yeast cells
3	Guruprasad Annappa Mali	65	M	7536	03/02/2018	Y	N	Y	Y	NONE	NIL	Y	N	N	98	144/90	16	38.1	I	I	D	Crepts	5730	12.2	25	Gram +ve cocci
4	Guranna Basavaraj Yevoor	65	M	15623	05/09/2018	N	Y	Y	Y	Altered Sensorium	NIL	Y	N	Y	88	160/90	20	37.8	ND	ND	D	Crepts	12460	18.3	10	Gram+ve Cocci;Gram-ve Bacilli
5	Gadigeppa Mallappa Jamakhandi	82	M	4266	02/03/2018	Y	Y	Y	Y	Reduced Appetite	NIL	Y	N	Y	98	158/90	18	37.6	I	I	D	Crepts	6500	12.3	60	Gram +ve cocci
6	Nagappa Malkappa	85	M	4722	02/07/2018	N	Y	Y	Y	NONE	NIL	Y	N	N	80	168/90	16	38.1	I	I	D	Ronchi	11250	13.9	40	Gram+ve Cocci;Gram-ve Bacilli
7	Pirappa Sangappa Haranal	65	M	16704	17/05/2018	N	Y	Y	Y	NONE	NIL	Y	Y	Y	100	114/80	14	37.9	I	I	D	None	25860	14.1	60	Gram-ve Bacilli
8	Shivanna Annappa Talikota	68	M	9829	20/03/2018	N	Y	Y	Y	NONE	NIL	Y	N	N	92	134/70	18	36.7	I	I	D	Crepts	18430	11.8	60	Gram-ve Bacilli
9	Sonubai Bhagwanrao Asteku	78	F	9069	14/03/2018	N	Y	Y	Y	NONE	HTN	N	N	N	108	160/70	30	36.6	I	I	D	Crepts	7580	14.2	20	Gram +ve Budding yeast cells
10	Ramrao Basavantrao Kulkarni	65	M	7886	15/03/2018	Y	Y	Y	Y	NONE	HTN,IHD	Y	N	N	104	102/60	18	37.8	I	I	D	Wheeze	12210	14.8	10	Gram +ve cocci
11	Sharanappa Shivappa Kondaguli	78	M	3408	28/01/2018	N	Y	Y	Y	Lower limb swelling	NIL	Y	N	N	120	100/70	28	36.6	I	I	D	Crepts	4340	7.8	30	Gram +ve cocci
12	Shanthamma Mallappa Sajjan	65	F	3567	29/01/2018	N	Y	Y	Y	NONE	HTN;Fibroid Uterus	N	N	N	80	110/80	18	36.7	I	I	D	Crepts	12200	12	40	Not seen
13	Mainibai Pujari	70	F	35539	18/10/2017	N	Y	Y	Y	NONE	NIL	N	Y	N	80	110/70	24	36.5	I	I	D	Wheeze	8350	13.7	60	Not seen
14	Ningamma	78	F	34105	07/10/2017	Y	Y	Y	Y	NONE	NIL	N	Y	N	84	120/80	18	37.8	I	I	D	Wheeze	15920	10.3	40	Gram+ve Cocci;Gram-ve Bacilli
15	Ramanna Kalappa Halki	75	M	1493	12/01/2018	Y	Y	Y	Y	NONE	NIL	Y	Y	Y	90	130/80	14	37.8	I	I	D	Crepts	9910	16.1	40	Gram-ve Bacilli
16	Bapugouda S Patil	60	M	10257	31/03/2017	N	Y	Y	Y	NONE	NIL	Y	N	N	90	100/80	18	36.6	I	I	D	Wheeze	15810	8.3	80	Gram +ve cocci
17	Revansiddappa	77	M	38802	23/11/2016	N	Y	Y	Y	NONE	NIL	Y	Y	N	84	124/80	16	36.7	I	I	D	Crepts	20820	12.2	75	Gram+ve Cocci;Gram-ve Bacilli
18	Basamma	70	F	3632	01/02/2017	N	Y	Y	Y	NONE	NIL	N	N	N	78	124/80	18	36.6	I	I	D	Crepts	8190	11.3	30	Not seen
19	Sharanappa Gowda	80	M	3768	02/02/2017	N	Y	Y	Y	NONE	NIL	Y	Y	N	80	114/80	18	36.8	I	I	D	Ronchi	9980	10.2	10	Gram-ve Bacilli
20	Basamma B Kumar	90	F	5326	12/02/2017	N	Y	Y	Y	NONE	NIL	N	N	N	80	120/70	16	36.6	I	I	D	Crepts	12310	11.9	25	Not seen
21	Sangappa Siddappa Bellulli	66	M	4705	11/02/2017	Y	Y	Y	Y	NONE	HTN	Y	Y	N	78	136/80	16	37.9	I	I	D	Crepts	12210	14.4	35	Gram +ve cocci
22	Irappa Basappa Laslangi	75	M	40179	05/12/2016	Y	Y	Y	Y	NONE	NIL	Y	N	Y	80	130/80	18	37.7	I	I	D	Wheeze	17480	10.8	100	Gram+ve Cocci;Gram-ve Bacilli
23	Shrimantharao Bhimrao Patil	80	M	7404	01/03/2018	N	Y	Y	Y	NONE	HTN	Y	Y	N	90	130/80	18	36.6	I	I	D	Crepts	9900	14.6	40	Not seen
24	Bhimanna Krishnappa Dharnalli	65	M	1899	16/01/2018	N	Y	Y	Y	NONE	OLD PTB	Y	N	N	96	90/60	22	36.7	I	I	D	Crepts	17700	13.3	70	Gram +ve cocci
25	Revansiddappa r Bagali	80	M	10559	26/03/2018	Y	Y	Y	Y	NONE	NIL	Y	Y	Y	104	130/80	18	38.2	I	I	D	Wheeze	27630	11.3	50	Gram-ve Bacilli
26	Santosh Babugoda Biradar	65	M	4434	06/02/2018	Y	Y	Y	Y	NONE	T2DM	Y	N	Y	100	134/80	18	37.9	I	I	D	Crepts	14040	13.6	40	Gram +ve cocci
27	Shrishail Shivappa Chigeri	65	M	10218	23/03/2018	N	Y	Y	Y	NONE	HTN	Y	N	N	98	116/80	18	36.6	I	I	D	Wheeze	16590	11.7	105	Gram +ve Budding yeast cells
28	Sangappa Ningappa Bhurusi	74	M	5826	16/02/2018	y	y	y	y	NONE	IHD	Y	Y	Y	98	138/90	24	37.8	I	I	D	Wheeze	12490	15	30	Gram-ve Bacilli
29	Irappa Gangappa Badiger	65	M	7813	05/03/2018	Y	Y	Y	Y	NONE	HTN;ALD;OLD PTB	Y	Y	Y	88	144/90	16	37.7	I	I	D	Crepts	33750	10.5	40	Gram-ve Bacilli
30	Mahadevappa Alabanna talawar	70	M	12694	13/04/2018	Y	Y	Y	Y	NONE	HTN	Y	N	Y	78	140/80	16	37.8	I	I	D	Crepts	32210	14	70	Gram +ve cocci
31	Shankerappa Gunappa Kanal	60	M	15257	2/5/2018	Y	Y	Y	Y	NONE	T2DM	Y	N	Y	96	128/80	20	37.9	I	I	D	Crepts	6360	14.1	45	Not seen
32	Basagondappa Venkappa Jirali	90	M	17859	28/5/2018	Y	Y	Y	Y	NONE	IHD;HTN	Y	N	N	90	110/80	18	37.8	I	I	D	Wheeze	9310	13.7	30	Gram +ve cocci
33	Gollalappa B Halagond	70	M	8798	12/3/2018	Y	Y	Y	Y	NONE	OLD PTB	Y	Y	Y	98	114/70	16	37.9	I	I	D	Wheeze	11870	14.3	40	Gram+ve cocci;Gram-ve bacilli
34	Bashir Murtiya Feerzade	65	M	34279	10/10/2017	N	Y	Y	Y	Giddiness;Hiccups	POLIO-PPRP	Y	N	N	90	160/110	16	36.6	I	I	D	Crepts	18400	14.6	60	Gram-ve Bacilli
35	Hanamnth Malakappa Pujeri	80	M	34358	9/10/2017	Y	Y	Y	Y	NONE	NIL	Y	N	N	88	130/80	18	37.8	I	I	D	Crepts	16470	15.6	35	Gram +ve cocci
36	Ninganagouda S Patil	70	M	37023	29/10/2017	Y	Y	Y	Y	NONE	HTN	Y	Y	Y	88	136/80	17	37.9	I	I	D	Wheeze	22120	11	40	Gram +ve cocci
37	Basanagouda M Patil	78	M	37163	30/10/2017	N	Y	Y	Y	NONE	NIL	Y	Y	Y	84	140/90	18	36.7	I	I	D	Crepts	13200	14	35	Gram +ve cocci
38	Revaneppa Shivappa Takkalaki	70	M	33074	30/9/2017	Y	Y	Y	Y	NONE	IHD	Y	Y	N	88	134/80	18	37.8	I	I	D	Wheeze	7460	8.7	40	Gram-ve Bacilli
39	Balachandara Bhimaraya Hugar	60	M	33316	2/10/2017	Y	Y	Y	Y	NONE	HTN	Y	Y	Y	72	100/70	18	37.9	I	I	D	Wheeze	28960	12.5	50	Not seen
40	Yamanappa Basappa Huggi	65	M	33781	5/10/2017	Y	Y	Y	Y	NONE	T2DM	Y	Y	Y	80	140/90	20	37.8	I	I	D	Crepts	14350	13	40	Gram +ve cocci
41	Vilas Khandappa Mane	60	M	39570	16/11/2017	N	Y	Y	Y	NONE	T2DM	Y	Y	Y	80	130/80	22	36.6	I	I	D	Crepts	14620	10.8	110	Not seen
42	Kantabai B Pattanashetti	82	F	39983	20/11/2017	Y	Y	Y	Y	NONE	T2DM	N	N	N	88	110/70	16	37.8	I	I	D	Crepts	22460	10.7	50	Gram +ve cocci
43	Hanamanth S Wajantri	65	M	41153	28/11/2017	Y	Y	Y	Y	NONE	HTN	Y	Y	Y	102	114/80	18	37.9	I	I	D	Crepts	13540	12.5	45	Gram +ve cocci
44	Ravindra K Avadani	76	M	41866	5/12/2017	Y	Y	Y	Y	NONE	NIL	Y	N	Y	112	124/80	18	37.8	I	I	D	Crepts	8910	10.6	40	Gram+ve cocci;Gram-ve bacilli
45	Yallamma Basappa Kuri	60	F	42428	9/12/2017	Y	Y	Y	Y	NONE	NIL	N	N	N	94	130/80	16	37.9	I	I	D	Crepts	14100	11.3	40	Gram-ve Bacilli
46	Girmalla Kamagond mote	65	M	44074	23/12/2017	Y	Y	Y	Y	NONE	T2DM	Y	N	N	86	146/90	19	37.8	I	I	D	Crepts	13350	13.3	70	Gram +ve cocci
47	Sidamma Gundappa Devareddi	65	M	18723	12/6/2018	N	Y	Y	Y	NONE	T2DM;HTN	N	N	N	88	134/80	16	36.8	I	I	D	Crepts	7210	12.9	45	Gram +ve cocci
48	Pharisappa H Daddi	85	M	44468	27/12/2017	N	Y	Y	Y	Dribbling of urine	BPH	Y	Y	N	98	160/90	20	36.6	I	I	D	Crepts	10720	9.2	30	Gram +ve cocci
49	Channappa S Biradar	75	M	12590	12/4/2018	N	Y	Y	Y	NONE	IHD;T2DM	Y	N	N	98	144/80	20	36.7	I	I	D	Crepts	44890	10.7	5	Gram +ve cocci
50	Devakemma G Patil	65	F	11666	5/4/2018	N	Y	Y	Y	NONE	NIL	N	N	N	104	110/70	22	36.6	I	I	D	Wheeze	27880	12.7	20	Gram-ve Bacilli
51	Ningammagoudati A M	70	F	9970	27/3/2018	Y	Y	Y	Y	NONE	HTN	N	N	N	104	144/80	16	37.8	I	I	D	Crepts	16440	11.8	30	Gram +ve cocci
52	Lakshmibai B Talikoti	68	F	7434	3/3/2018	N	Y	Y	Y	NONE	NIL	N	Y	N	90	134/80	22	36.6	I	I	D	Wheeze	16120	12.8	45	Gram +ve cocci
53	Basavanthrayagond T Biradar	68	M	6785	24/2/2018	N	Y	Y	Y	Chest pain	OLD PTB	y	N	N	82	130/80	16	36.6	I	I	D	Wheeze	13080	6.2	125	Gram +ve cocci
54	Gaddeppa K Matageri	68	M	4442	7/2/2018	Y	Y	Y	Y	NONE	HTN	Y	N	Y	98	144/80	18	38	I	I	D	Crepts	5610	5	110	Gram-ve Bacilli
55	Annappa V Honawad	64	M	4433	5/12/2018	N	Y	Y	Y	NONE	OLD PTB	Y	N	N	110	104/70	24	36.5	I	I	D	Crepts	14040	13.6	40	Gram +ve cocci
56	Bhashasab K Jamadhar	60	M	4092	3/2/2018	N	Y	Y	Y	NONE	HTN	Y	N	N	102	110/70	30	36.6	I	I	D	Crepts	9570	18.4	25	Gram +ve cocci
57	Shankaragouda B Tangadagi	67	M	24305	18/7/2018	Y	Y	Y	Y	NONE	NIL	Y	Y	N	88	136/80	16	37.8	I	I	D	Crepts	7360	15.1	10	Gram-ve Bacilli
58	Salikram N Rajaput	68	M	25944	1/8/2018	Y	Y	Y	Y	NONE	HTN	Y	Y	Y	102	110/70	18	37.9	I	I	D	Crepts	10670	12.4	60	Gram +ve cocci
59	Neelkanth H Bandiwaddar	65	M	24661	21/7/2018	Y	Y	Y	Y	NONE	OLD PTB	Y	N	N	88	164/80	16	37.8	I	I	D	Crepts	11330	16.8	40	Not seen
60	Shivappa M chinagundi	60	M	18327	30/5/2018	N	Y	Y	Y	Loose stools	NIL	Y	N	Y	102	126/78	16	36.6	I	I	D	Crepts	7590	12.4	60	Gram-ve Bacilli
61	Jagannath B Kamali	63	M	17588	16/5/2018	Y	Y	Y	N	NONE	NIL	Y	N	N	98	118/80	18	37.8	I	I	D	Crepts	9070	10.3	105	Not seen
62	Ramachandra B Pawar	65	M	27772	17/8/2018	N	Y	Y	Y	NONE	HTN	Y	Y	Y	104	124/80	16	36.6	I	I	D	Crepts	10500	12.8	70	Not seen
63	Basagonda M Badiger	60	M	20168	14/6/2018	N	Y	Y	Y	NONE	HTN	Y	Y	Y	94	130/80	18	36.6	I	I	D	Crepts	25050	13.2	85	Not seen
64	Ishwarappa D Umarai	74	M	6436	21/2/2018	Y	Y	Y	Y	NONE	NIL	Y	Y	Y	102	118/86	24	37.8	I	I	D	Wheeze	14380	13.3	20	Gram-ve Bacilli
65	Basagonda Manappa Badiger	60	M	20168	6/21/2018	Y	Y	Y	Y	NONE	NIL	Y	N	N	104	110/80	24	37.8	I	I	D	Wheeze	11650	13.6	35	Not seen
66	Siddappa Basappa Handiganur	60	M	15704	5/17/2018	N	Y	Y	Y	NONE	NIL	Y	N	N	106	114/86	28	37.9	I	I	D	Wheeze	13650	12.8	40	Not seen

SPUTUM			PFT	CXR-PA	ECG	DIAGNOSIS	Outcome
Zn STAIN	C/S	SENSITIVITY PATTERN					
		SENSITIVE					
Negative	No Pathogenic bacteria isolated	NOT DONE	Mild Obstructive	Emphysema	LAD	AECOPD,IHD	Discharged
Negative	Streptococci pneumoniae	Tetracycline;Cefaperazone;Cefuroxime;Cotrimoxazole;Erythromicin;Linezolid;Penicillin	Moderate Obstructive	Emphysema	RAD, Old IW Changes	AECOPD,IHD,T2DM,PAH	Discharged
Negative	Staphylococcus aureus	Cefoperazone;Cefuroxime;Clindamycin;Cloxacillin;Cotrimaxazole;Linezolid	Mild Obstructive	Emphysema	P Pulmonale	AECOPD,HTN	Discharged
Negative	Klebsiella pneumoniae	Cephalexin;Ciprofloxacillin;Cotrimoxazole;Gentamycin;Levofloxacin;Netilmycin;Piperacillin;Tobramycin	Not Done	Emphysema	P Pulmonale	AECOPD,Cor Pulmonale	Discharged
Negative	Staphylococcus aureus	Cefaperazone;Cefuroxime;Cephalexin;Clindamycin;Cloaxacillin;Gentamicin;Linezolid;Tetracycline	Severe Obstructive	Emphysema	RAD	AECOPD	Discharged
Negative	Streptococci pneumoniae	Cefaperazone;Cefuroxime;Clindamycin;Linezolid	Mild Obstructive	Emphysema	P pulmonale,RAD	AECOPD;T2DM;HTN	Discharged
Negative	Pseudomonas aerruginosa	Amikacin;Carbenicillin;Cefaperazone;Ceftazidine;Ciprofloxacin;Gentamicin;Levofloxacin;Norfloxacin;Piperacillin	Moderate Obstructive	Emphysema	P pulmonale	AECOPD	Discharged
Negative	Citrobacter species	Imipenem;Meropenem	Moderate Obstructive	Emphysema	P PULMONALE	AECOPD,T2DM	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Not Done	Emphysema	RBBB,P Pulmonale	AECOPD,HTN	Discharged
Negative	Streptococci pneumoniae	Azithromycin;Cefaperazone;Cefuroxime;Cephalexin;Ciprofloxacin;Clindamycin;Cloaxacillin;Erythromycin;Gentamicin;Linezolid	Mild Obstructive	Emphysema	Old Inferior wall changes	AECOPD;HTN;IHD	Discharged
Negative	Streptococci pneumoniae	Cefaperazone;Cefuroxime;Clindamycin;Linezolid;Piperacillin	Not Done	Emphysema	P Pulmonale	AECOPD;IHD;PAH	Discharged
Negative	Candida albicans	NOT DONE	Not Done	Emphysema	LAD;T wave inversion in V1-V4	AECOPD;IHD	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Moderate Obstructive	Emphysema	Sinus rhythm	AECOPD	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Mild Obstructive	Emphysema	RBBB	AECOPD	Discharged
Negative	Klebsiella pneumoniae	Amikacin;Ampicillin;Ceftriaxone;Cefuroxime;Cephalexin;Gentamycin;Lomefloxacin;Netilmycin;Tetracycline;Tobramycin	Moderate Obstructive	Emphysema	RAD	AECOPD	Discharged
Negative	Streptococci pneumoniae	Cefaperazone;Cefuroxime;Gentamycin;Linezolid;Pefloxacin;Pencillin;Piperacillin;Tetracycline	Mild Obstructive	Emphysema	Sinus rhythm	AECOPD;Anemia	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Severe Obstructive	Emphysema	RAD;RBBB;RVH	AECOPD	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Not Done	Emphysema	LVH	AECOPD	Discharged
Negative	Klebsiella pneumoniae	Amikacin;Amoxyclav;Cotrimoxazole;Netilmicin	Severe Restrictive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Mild Obstructive	Emphysema	RAD	AECOPD	Discharged
Negative	Streptococci pneumoniae	Amoxyclav;Azithromycin;Cefoperazone;Cefuroxime;Erythromycin;Linezolid;Penicillin;Piperacillin;Tetracycline	Severe Obstructive	Emphysema	RAD	AECOPD;HTN	Discharged
Negative	Pseudomonas aerruginosa	Amoxyclav;Azithromycin;Tobramycin;Cotrimoxazole;Netilmicin;Penicillin;Piperacillin	Severe Restrictive	Emphysema	Sinus rhythm	AECOPD	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Mild Obstructive	Emphysema	RAD	AECOPD;Lower lobe Bronchiectasis;HTN	Discharged
Negative	Streptococci pneumoniae	Amoxyclav;Cefoperazone;Cotrimoxazole;Erythromycin;Gentamicin;Linezolid;penicillin;Tetracycline	Mild Obstructive	Emphysema	RAD	AECOPD	Discharged
Negative	Klebsiella pneumoniae	Amikacin;Ceftriaxone;Cefuroxime;Ciprofloxacillin;gentamicin;Lomefloxacin;Netilmicin;Tetracycline;Tobramycin	Mild Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Enterococcus species	Azithromycin;Cefoperazone;cefuroxime;Clindamycin;Cloxacillin;Erythromicin;Linezolid;Penicillin;Tetracyclin	Moderate Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Streptococci pneumoniae	Cefaperazone;Cefuroxime;Cotrimoxazxole;Erythromycin;Linezolid;	Moderate Obstructive	Emphysema	P Pulmonale	AECOPD;HTN	Discharged
Negative	Pseudomonas aerruginosa	Amikacin;Carbenicillin;Cefaperazone;Ciprofloxacin;Gentamicin;Levofloxacin;netilmycin;Norfloxacin;sensitive	Severe Obstructive	Emphysema	P pulmonale	AECOPD;IHD	Discharged
Negative	Escherichia coli	Amikacin;Cotrimoxazole;Gentamicin;Netilmicin;tobramicin	Not Done	Emphysema	P pulmonale	AECOPD;ALD;HTN;OLD PTB	Discharged
Negative	Streptococci pneumoniae	Azithromycin;Cefaperzone;cefuroxime;Ciprofloxacin;Clindamycin;Cloxacillin;Erythromycin;linezolid	Moderate Obstructive	Emphysema	P Pulmonale	AECOPD;HTN;T2DM	Discharged
Negative	Citrobacter species	Cefoperazone;Ceftriaxone	Mild Obstructive	Emphysema	P Pulmonale	AECOPD;T2DM	Discharged
Negative	Coagulase negative staphylococcus	Ciprofloxacin;Linezolid	Severe Obstructive	Emphysema	P Pulmonale	AECOPD;IHD;HTN	Death
Negative	Escherichia coli	Amikacin;Netilmicin	Moderate Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Klebsiella pneumoniae	Amikacin;Cephalexin;Ciprofloxacin;Cotrimoxazole;Gentamicin;Lomefloxacin;Netilmicin;Tobramycin	Mild Obstructive	Emphysema	RAD;RVH;P Pulmonale	AECOPD;Vestibular Neuritis	Discharged
Negative	Streptococci pneumoniae	Amoxyclav;Cefoperazone;Cefuroxime;Piperacllin;Tetracycline	Mild Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Streptococci pneumoniae	Azithromycin;Cefapertazone;Cefuroxime;Cephalexin;Ciprofloxacin;Cotrimoxazole;Piperacillin;Tetracycline	Moderate Obstructive	Emphysema	P Pulmonale	AECOPD;HTN;AKI	Discharged
Negative	Streptococci pneumoniae	Amoxyclav;Cefoperazone;Linezolid;Penicillin;Piperacillin	Severe Restrictive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Pseudomonas aerruginosa	Amikacin;Carbeicillin;Cefoperazone;Ceftazidine;Ciprofloxacin;Gentamicin;Levofloxacin;Netilmicin;Norfloxacin;Piperacillin	Mild Obstructive	Emphysema	P Pulmonale	AECOPD;CKD;Anemia	Discharged
Negative	Acinetobacter species	Amikacin;Ciprofloxacin;Cotrimoxazole;Gentamicin;Lomefloxacin;Piperacillin;Tetracycline	Mild Obstructive	Emphysema	P Pulmonale	AECOPD;HTN	Discharged
Negative	Staphylococcus aureus	Cefuroxime;Clindamycin;Cloxacillin;Erythromycin;Linezolid	Moderate Obstructive	Emphysema	P Pulmonale	AECOPD;T2DM	Discharged
Negative	Aspergillus Niger	NOT DONE	Mild Obstructive	Emphysema	P Pulmonale	AECOPD;T2DM	Discharged
Negative	Staphylococcus aureus	Azithromycin;Cefoperazone;Cefuroxime;Cephalexin;Ciprofloxacin;Clindamycin;Cloxacillin;Erythromicin;Gentamicin;Linezolid	Severe Obstructive	Emphysema	P Pulmonale	AECOPD;T2DM	Discharged
Negative	Streptococcus sp;Acinetobacter sp	Cefuroxime;Piperacillin	Very severe Obstructive	Emphysema	P Pulmonale	AECOPD;HTN	Discharged
Negative	Pseudomonas aerruginosa	Amikacin;Amoxyclav;Cefoperazone;Ceftazidine;Ciprofloxacin;Gentamicin;Levofloxacin;Netilmicin;Piperacillin;Tobramycin	Severe Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Pseudomonas aerruginosa	Amikacin;Carbenicillin;Cefoperazone;Ceftazidine;Ciprofloxacin;Gentamicin;Levofloxacin;Netlimicin;Piperacillin;Tobramycin	Severe Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Streptococcus sp; Klebsiella pneumoniae	Cefoperazone;Clindamycin;Erythromycin;Gentamicin;Linezolid;Penicillin;Piperacillin;Tetracycline	Severe Obstructive	Emphysema	RAD;P Pulmonale	AECOPD;T2DM	Discharged
Negative	Citrobacter species	Netilmicin	Moderate Obstructive	Emphysema	RAD	AECOPD;T2DM;HTN	Discharged
Negative	Coagulase negative staphylococcus	Cephalexin;Cloxacillin;Erythromycin;Linezolid;Penicillin;Tetracycline	Severe Restrictive	Emphysema	P Pulmonale	AECOPD;BPH	Discharged
Negative	Staphylococcus aureus	Clindamycin;Gentamicin;Linezolid;Tetracycline	Moderate Obstructive	Emphysema	RAD	AECOPD;IHD;T2M	Discharged
Negative	Klebsiella pneumoniae	Cotrimoxazole;Ciprofloxacin;Netilmicin;Tetracycline;Tobramycin	Not Done	Emphysema	RAD	AECOPD	Discharged
Negative	Enterococcus species	Cotrimoxazole;Linezolid	Severe restrictive	Emphysema	RAD	AECOPD;HTN	Discharged
Negative	Streptococci pneumoniae	Azithromycin;Cefoperazone;Cefuroxime;Ciprofloxacin;Clindamycin;Cotrimoxazole;Erythromycin;LinezolidPenicllin	Moderate Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Streptococci pneumoniae	Cefoperazone;Cefuroxime;Linezolid;Penicillin;Tetracycline	Very severe Obstructive	Emphysema	P Pulmonale	AECOPD;OLD PTB;LEFT SIDED PNEUMOTHORAX	Discharged
Negative	Citrobacter species	Amikacin;Ciprofloxacin;Gentamicin;Lomefloxacin;Netilmicin;Tobramycin	Not Done	Emphysema	P Pulmonale	AECOPD;HTN;ANEMIA	Discharged
Negative	Staphylococcus aureus	Cefoperazone;Ciprofloxacin;Linezolid	Severe Obstructive	Emphysema	P Pulmonale	AECOPD;OLD PTB	Discharged
Negative	Streptococci pneumoniae	Amoxyclav;Azithromycin;Cefaperazone;Ciprofloxacin;Clindamycin;gentamicin;Linezolid;Piperacillin	Severe Restrictive	Emphysema	RAD	AECOPD;HTN	Discharged
Negative	Klebsiella pneumoniae	Amikacin;Ceftrixone;Ciprofloxacillin;Cotrimoxazole;Netilmicin;Tobramycin	Very severe Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Streptococci pneumoniae	Amoxyclav;Cefoperazone;Cefuroxime;Clindamycin;erythromycin;Gentamicin;Linezolid;Penicillin;Piperacillin;Tetracycline	Very severe Obstructive	Emphysema	P Pulmonale	AECOPD;HTN	Discharged
Negative	Coagulase negative staphylococcus	Gentamicin;Pefloxacin;Piperacillin	Very severe Obstructive	Emphysema	P Pulmonale	AECOPD;HTN;OLD PTB	Discharged
Negative	Klebsiella pneumoniae	Amikacin;Ceftriaxone;Cefuroxime;ciprofloxacin;Cotrimoxazole;Levofloxacin;Netilmicin;Tetracycline;Tobramycin	Very severe Obstructive	Emphysema	P Pulmonale	AECOPD;HTN	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Severe Restrictive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Very severe Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Severe restrictive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	Escherichia coli	Imipenem;Meropenem;	Very severe Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Mild Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged
Negative	No Pathogenic bacteria isolated	NOT DONE	Mild Obstructive	Emphysema	P Pulmonale	AECOPD	Discharged