TO STUDY THE PREVALENCE OF ASTHMA COPD OVERLAP IN A TERTIARY CARE HOSPITAL

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

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BONAFIDE CERTIFICATE

This is to certify that the dissertation "**To study the prevalence of asthma COPD overlap in a tertiary care hospital"** is the bonafide work done by **Dr. Prakash.S** during his MD (Tuberculosis and Respiratory Diseases) course from May 2017 to May 2020 at Government Kilpauk Medical College, Chennai.

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This is to certify that the dissertation titled **"To study the prevalence of asthma overlap in a tertiary care hospital"** is the bonafide work done by **Dr. S. PRAKASH** during his **MD (Tuberculosis and Respiratory diseases)** course in the academic year 2017-2020 at Government Kilpauk Medical College under my guidance.

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DECLARATION BY THE SCHOLAR

I, **Dr. S. Prakash**, solemnly declare that the dissertation titled **" To Study the prevalence of Asthma COPD overlap in a tertiary care hospital "** has been prepared by me. This is submitted to " **The Tamil Nadu Dr. M.G.R. Medical University, Chennai** " in partial fulfilment of the requirement for the award of M.D degree examination branch XVII **Tuberculosis and Respiratory Diseases** from May 2017 to May 2020.

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) [1]is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases.

Asthma is a disease with many variations characterized by chronic airway inflammation, with a history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and intensity , variable expiratory airflow limitation.[2]

Asthma usually has an early onset with intermittent symptoms, a good response to inhaled therapy, and is often associated with other allergic diseases. whereas COPD is of late onset, slowly progressive symptoms, poor response to inhaled therapy, and is usually associated with long-term smoking, However, patients can sometimes have features of both diseases, and this condition has been termed asthma-COPD overlap syndrome (ACOS).

Asthma COPD overlap is characterised by persistent airflow limitation with several features usually associated with asthma and COPD, therefore it is identified in clinical practice by features that shares both asthma and COPD.Asthma and COPD are the most prevalent chronic respiratory conditions affecting > 500 million people worldwide resulting in significant morbidity and an increasing health-care expenditure. It is therefore not

surprising that these diseases are frequently encountered in clinical practice and often coexist.

Both are highly prevalent conditions, it is very likely that they overlap in some individuals. In the last decade there has been increasing interest over this entity that is now known as asthma–COPD overlap (ACO). However, this interest is not new which was already addressed by Burrows and colleagues in 1987, describing a group of patients who had a clinical evolution and a prognosis that was between asthma and COPD, at that time labelled as 'asthmatiform bronchitis', supporting the view of a common origin of asthma and COPD, the so-called Dutch hypothesis.

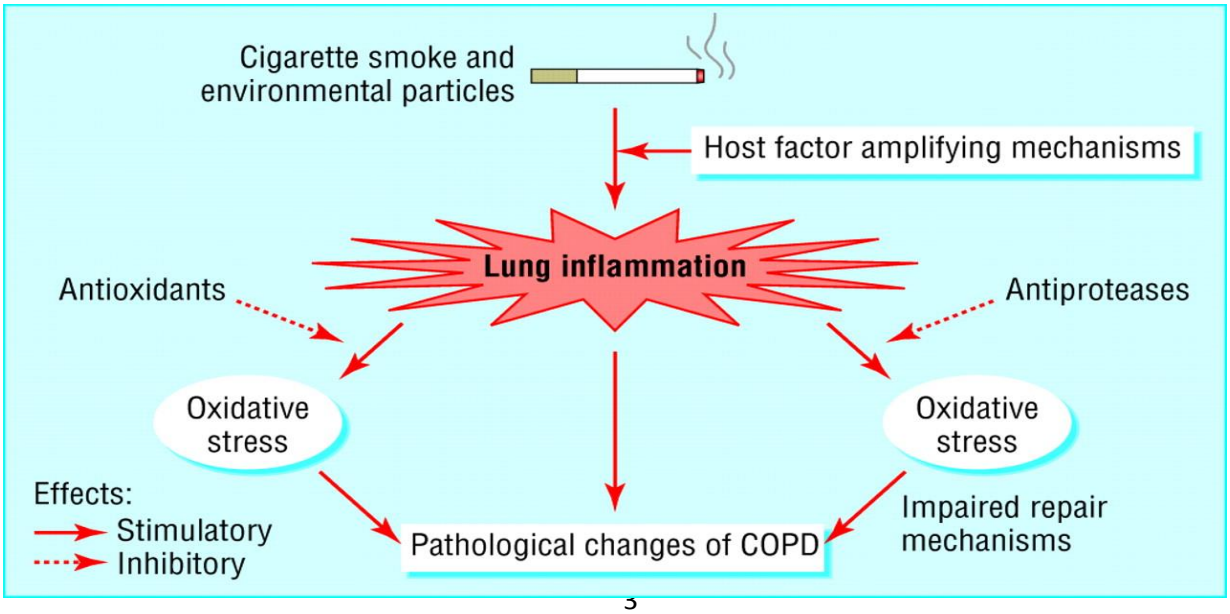
CHRONIC OBSTRUCTIVE PULMONARY DISEASE:

Chronic obstructive pulmonary disease (COPD) is characterised by poorly reversible airflow obstruction and an abnormal inflammatory response in the lungs. The latter represents the innate and adaptive immune responses to long term exposure to noxious particles and gases, particularly cigarette smoke. All cigarette smokers have some inflammation in their lungs, but those who develop COPD have an enhanced or abnormal response to inhaling toxic agents. This amplified response may result in mucous hypersecretion (chronic bronchitis), tissue destruction (emphysema), and disruption of normal repair and defence mechanisms causing small airway inflammation and fibrosis (bronchiolitis).

These pathological changes result in increased resistance to airflow in the small conducting airways, increased compliance of the lungs, air trapping, and progressive airflow obstruction—all characteristic features of COPD. We have good understanding of the cellular and molecular mechanisms underlying the pathological changes found in COPD.

PATHOGENESIS:

Inflammation is present in the lungs, particularly the small airways, of all people who smoke. This normal protective response to the inhaled toxins is amplified in COPD, leading to tissue destruction, impairment of the defence mechanisms that limit such destruction, and disruption of the repair mechanisms. In general, the inflammatory and structural changes in the airways increase with disease severity and persist even after smoking cessation. Besides inflammation, two other processes are involved in the pathogenesis of COPD—an imbalance between proteases and antiproteases and an imbalance between oxidants and antioxidants (oxidative stress) in the lungs.



Inflammatory cells:

COPD is characterised by increased numbers of neutrophils, macrophages, and T lymphocytes (CD8 more than CD4) in the lungs. In general, the extent of the inflammation is related to the degree of the airflow obstruction. These inflammatory cells release a variety of cytokines and mediators that participate in the disease process. This inflammatory pattern is markedly different from that seen in patients with asthma.

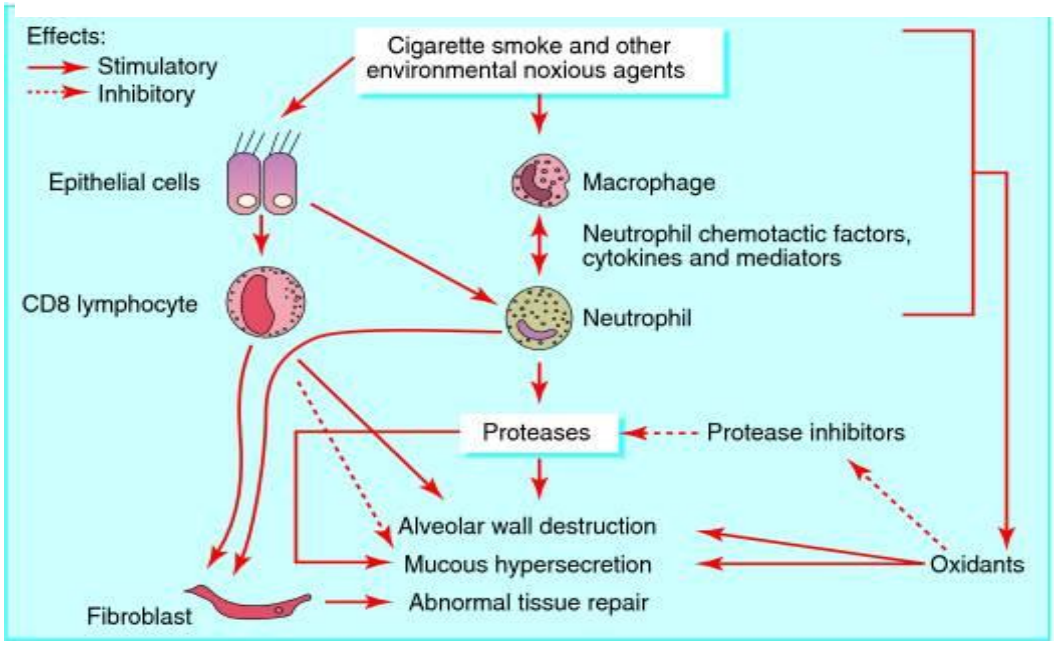
Inflammatory mediators

Many inflammatory mediators are increased in COPD, including

- Leukotriene B_4, a neutrophil, T cell chemoattractant which is produced by macrophages, neutrophils, and epithelial cells.
- Chemotactic factors such as the CXC chemokines interleukin 8, growth related oncogene α, which are produced by macrophages and epithelial cells. These attract cells from the circulation and amplify pro-inflammatory responses
- Pro-inflammatory cytokines such as tumour necrosis factor α and interleukins 1β and 6
- Growth factors such as transforming growth factor β, which may cause fibrosis in the airways either directly or through release of another cytokine, connective tissue growth factor.

Protease and antiprotease imbalance:

Increased production (or activity) of proteases and inactivation (or reduced production) of antiproteases results in imbalance. Cigarette smoke, and inflammation itself, produce oxidative stress, which primes several inflammatory cells to release a combination of proteases and inactivates several antiproteases by oxidation. The main proteases involved are those produced by neutrophils (including the serine proteases elastase, cathepsin G, and protease 3) and macrophages (cysteine proteases and cathepsins E, A, L, and S), and various matrix metalloproteases (MMP-8, MMP-9, and MMP-12). The main antiproteases involved in the pathogenesis of emphysema include α_1 antitrypsin, secretory leucoprotease inhibitor, and tissue inhibitors of metalloproteases.



Inflammatory mechanism in COPD:

Cigarette smoke activates macrophages and epithelial cells to release chemotactic factors that recruit neutrophils and CD8 cells from the circulation. These cells release factors that activate fibroblasts, resulting in abnormal repair processes and bronchiolar fibrosis. An imbalance between proteases released from neutrophils, macrophages and antiprotease leads to alveolar wall destruction, which leads to emphysema.

Oxidative stress:

The oxidative burden is increased in COPD. Sources of oxidants mainly include cigarette smoke, reactive oxygen and nitrogen species released from inflammatory cells. This creates an imbalance in oxidants and antioxidants of oxidative stress. Many markers of oxidative stress are increased in stable COPD and are further increased in exacerbations. Oxidative stress can lead to inactivation of antiproteases or stimulation of mucous production. It can also amplify inflammation by enhancing transcription factor activation (such as nuclear factor κB) and hence gene expression of pro-inflammatory mediators.

RISK FACTORS FOR COPD:

Although cigarette smoking is the best-studied COPD risk factor, it is not the only one and there is consistent evidence from epidemiologic studies that non-smokers may also develop chronic airflow limitation. [3-6]

COPD results from a gene-environment interaction. Among people with the same smoking history, not all will develop COPD due to differences in

genetic predisposition to the disease, or in how long they live. Risk factors for COPD may also be related in more complex ways. For example, gender may influence whether a person takes up smoking or experiences certain occupational or environmental exposures; socioeconomic status may be linked to a child's birth weight (as it impacts on lung growth and development and in turn on susceptibility to develop the disease); and longer life expectancy will allow greater lifetime exposure to risk factors.

Genes:

The genetic risk factor that is best documented is a severe hereditary deficiency of alpha-1 antitrypsin [7], a major circulating inhibitor of serine proteases. Although alpha-1 antitrypsin deficiency is relevant to only a small part of the world's population, it illustrates the interaction between genes and environmental exposures leading to COPD. A significant familial risk of airflow limitation has been observed in smoking siblings of patients with severe COPD [8], suggesting that genetic together with environmental factors could influence this susceptibility. Single genes such as the gene encoding matrix metalloproteinase 12 (MMP12) have been related to decline in lung function [9]. Although several genome wide association studies indicate a role of the gene for the alpha-nicotinic acetylcholine receptor as well as the hedge-hog interacting protein gene and possibly one or two others, there remains a discrepancy between findings from analyses of COPD and lung function as well as between genome-wide association study analyses and candidate gene analyses[10-14]

Age and Gender:

Age is often listed as a risk factor for COPD. It is unclear if healthy aging as such leads to COPD or if age reflects the sum of cumulative exposures throughout life. In the past, most studies showed that COPD prevalence and mortality were greater among men than women but data from developed countries [15], show that the prevalence of the disease is now almost equal in men and women, probably reflecting the changing patterns of tobacco smoking. Some studies have even suggested that women are more susceptible to the effects of tobacco smoke than men. [16-19]

Lung Growth and Development:

Lung growth is related to processes occurring during gestation, birth, and exposures during childhood and adolescence [20],[21]. Reduced maximal attained lung function (as measured by spirometry) may identify individuals who are at increased risk for the development of COPD [22]. Any factor that affects lung growth during gestation and childhood has the potential for increasing an individual's risk of developing COPD.

Exposure to Particles:

Across the world, cigarette smoking is the most commonly encountered risk factor for COPD. Cigarette smokers have a higher prevalence of respiratory symptoms and lung function abnormalities, a greater annual rate of decline in FEV1, and a greater COPD mortality rate than non-smokers [23]. Other types of tobacco (e.g., pipe, cigar, water pipe45) and marijuana [24] are also risk factors for COPD[25],[26]. Passive exposure to cigarette smoke (also

known as environmental tobacco smoke or ETS) may also contribute to respiratory symptoms [27] and COPD [28] by increasing the lung's total burden of inhaled particles and gases [29],[30]. Smoking during pregnancy may also pose a risk for the foetus, by affecting lung growth and development in utero and possibly the priming of the immune system [31],[32].

Occupational exposures, including organic and inorganic dusts and chemical agents and fumes, are an underappreciated risk factor for COPD [33-35]. An analysis of the large U.S. population-based NHANES III survey of almost 10,000 adults aged 30-75 years estimated the fraction of COPD attributable to work was 19.2% overall, and 31.1% among never-smokers [36]. These estimates are consistent with a statement published by the American Thoracic Society that concluded that occupational exposures account for 10-20% of either symptoms or functional impairment consistent with COPD [37]. The risk from occupational exposures in less regulated areas of the world is likely to be much higher than reported in studies from Europe and North America.

Wood, animal dung, crop residues, and coal, typically burned in open fires or poorly functioning stoves, may lead to very high levels of indoor air pollution. Evidence continues to grow that indoor pollution from biomass cooking and heating in poorly ventilated dwellings is an important risk factor for COPD [38-43]. Almost 3 billion people worldwide use biomass and coal as their main source of energy for cooking, heating, and other household needs, so the population at risk worldwide is very large [44].

High levels of urban air pollution are harmful to individuals with existing heart or lung disease. The role of outdoor air pollution in causing COPD is unclear, but appears to be small when compared with that of cigarette smoking. It has also been difficult to assess the effects of single pollutants in long-term exposure to atmospheric pollution. However, air pollution from fossil fuel combustion, primarily from motor vehicle emissions in cities, is associated with decrements of respiratory function [45]. The relative effects of short-term, high-peak exposures and long-term, low-level exposures are yet to be resolved.

Socioeconomic Status:

Poverty is clearly a risk factor for COPD but the components of poverty that contribute to this are unclear. There is strong evidence that the risk of developing COPD is inversely related to socioeconomic status [46]. It is not clear, however, whether this pattern reflects exposures to indoor and outdoor air pollutants, crowding, poor nutrition, infections, or other factors that are related to low socioeconomic status**.**

Asthma/Bronchial Hyperreactivity:

Asthma may be a risk factor for the development of COPD, although the evidence is not conclusive. In a report from a longitudinal cohort of the Tucson Epidemiological Study of Airway Obstructive Disease, adults with asthma were found to have a twelve-fold higher risk of acquiring COPD over time than those without asthma, after adjusting for smoking [47]. Another longitudinal study of people with asthma found that around 20% of subjects

developed irreversible airflow limitation and reduced transfer coefficient [48], and in a longitudinal study self-reported asthma was associated with excess loss of FEV1 in the general population [49]. In the European Community Respiratory Health Survey, bronchial hyperresponsiveness was second only to cigarette smoking as the leading risk factor for COPD, responsible for 15% of the population attributable risk (smoking had a population attributable risk of 39%) [50]. The pathology of chronic airflow limitation in asthmatic non-smokers and non-asthmatic smokers is markedly different, suggesting that the two disease entities may remain different even when presenting with similarly reduced lung function [51]. However, clinically separating asthma from COPD may not be easy.

Bronchial hyperreactivity can exist without a clinical diagnosis of asthma and has been shown to be an independent predictor of COPD in population studies [52] as well as an indicator of risk of excess decline in lung function in patients with mild COPD [53].

Chronic Bronchitis

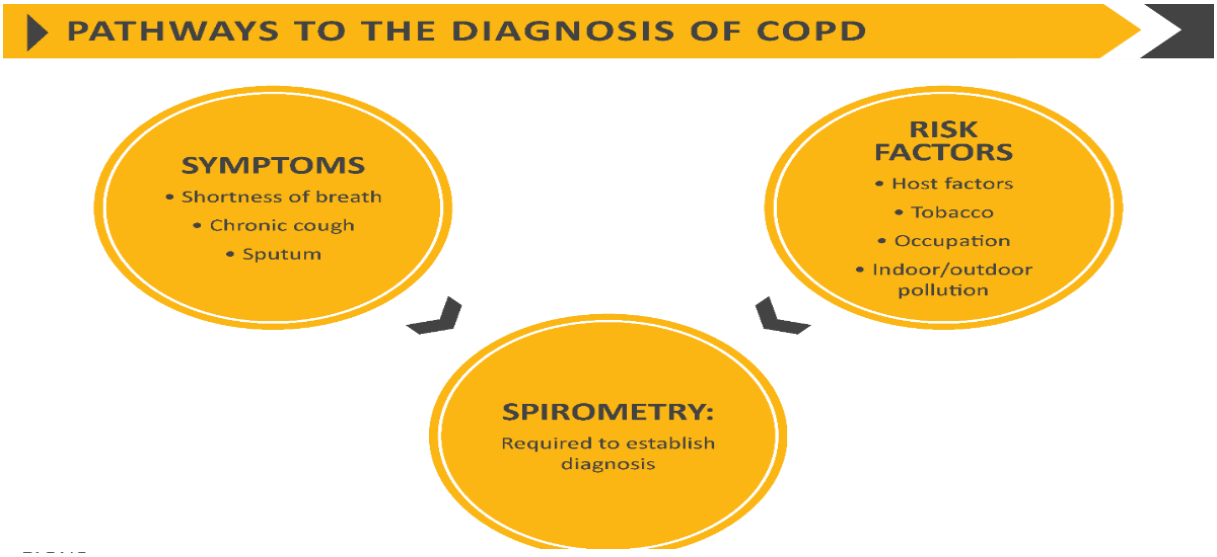
In the seminal study by Fletcher and coworkers, chronic bronchitis was not associated with decline in lung function [54]. However, subsequent studies have found an association between mucus hypersecretion and FEV1 decline [55], and in younger adults who smoke the presence of chronic bronchitis is associated with an increased likelihood of developing COPD [56],[57].

Infections

A history of severe childhood respiratory infection has been associated with reduced lung function and increased respiratory symptoms in adulthood. Susceptibility to infections plays a role in exacerbations of COPD but the effect on the development of the disease is less clear. HIV infection has been shown to accelerate the onset of smoking-related emphysema [58]. Tuberculosis has been found to be a risk factor for COPD [59],[60]. In addition, tuberculosis is both a differential diagnosis to COPD and a potential comorbidity [61],[62].

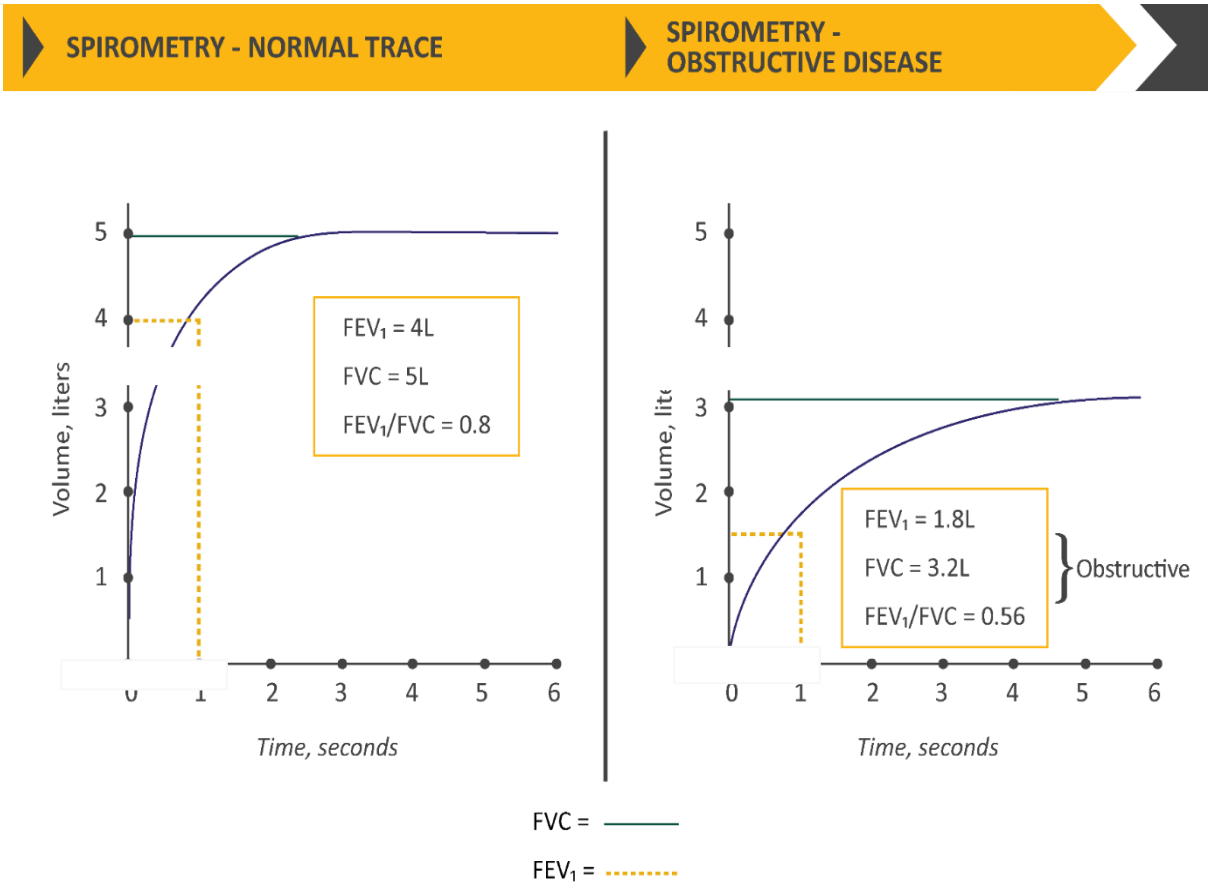
DIAGNOSIS OF COPD:

A clinical diagnosis of COPD should be considered in any patient who has dyspnoea, chronic cough or sputum production, and a history of exposure to risk factors for the disease. Spirometry is required to make the diagnosis in this clinical context, the presence of a postbronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation and thus of COPD.



SPIROMETRY:

Spirometry is required to make the diagnosis, that the presence of post bronchodilator FEV1/FVC < 0.70 confirms the presence of persistent airflow limitation and thus of COPD in patients with appropriate symptoms and exposure to noxious stimuli. Spirometry is the most reproducible, and objective measurement of airflow limitation .



POST BRONCHODILATOR FEV1:

CLASSIFICATION OF AIRFLOW LIMITATION SEVERITY IN COPD (BASED ON POST-BRONCHODILATOR FEV_1)		
In patients with FEV1/FVC < 0.70:		
GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

TABLE 2.4

ASTHMA COPD OVERLAP

Asthma-COPD overlap captures the subset of patients with airways disease who have features of both asthma and chronic obstructive pulmonary disease (COPD). Although definitions of ACO vary, it is generally thought to encompass persistent airflow limitation in a patient older than 40 years of age with either a history of asthma or large bronchodilator reversibility.

ACO affects about a quarter of patients with COPD and almost a third of patients who previously had asthma. Compared with their counterparts with asthma or COPD alone, patients with ACO have significantly worse respiratory symptoms, poorer quality of life, and increased risk of exacerbations and hospital admissions.

PREVALENCE OF ASTHMA COPD OVERLAP

On the basis of the literature review, the prevalence of Asthma COPD overlap among patients with COPD is estimated to range from 12.1% to 55.2% and the prevalence of ACOS among patients with asthma is estimated to range from 13.3% to 61.0%. The wide variations in prevalence are most likely due to the method by which ACOS cases were classified, but differences in population inclusion criteria, in the data source, and in the definitions of asthma and COPD including airflow reversibility criteria and spirometry versus clinical diagnoses can also influence the prevalence of ACOS.

Study population:

The prevalence of ACO varies widely due to the difference of definition, population characteristics and study design. Of course, among the same population, the prevalence of ACO was different due to the definition.[63][64][65]. In the general population, the prevalence of ACO ranged from 0.9% to 11.1%.

Menezes *et al.* defined ACO as a combination of features of both asthma and COPD, and the criteria for asthma were a positive answer to the question about wheezing in the 12 months plus post-bronchodilator airflow reversibility and the criterion for COPD was post-bronchodilator irreversible airflow obstruction in their cross sectional study. Their prevalence of ACO was 1.8% among participants who were over 40 years old.[66] Diaz-Guzman *et al.* defined ACO as a self-reported physician

diagnosis of both asthma and COPD in their cohort study. Their prevalence of ACO was 2.7% among participants who were over 25 years old.[67]

In a cross sectional cohort study in Hisayama, Japan, Matsumoto *et al.* described ACO as combination of not fully reversible airflow with variable airflow limitation, post-bronchodilator irreversibility and without a clinical history suggestive of asthma. Their prevalence of ACO was 0.9% among the participants who were over 40 years old.[68] Among the population who had airway obstruction, the prevalence of ACO was between 3.1% and 55.5%. In Japan, that ranged from 15.4% to 20.7%.[69],[70]

In the patients with asthma, the prevalence of ACO was between 11.1% and 61.0%.54 In Japan, few studies of population with asthma have yet been published. Harada *et al.* found that the prevalence of ACO was 27.1% among patients who were previously diagnosed with asthma.[71]

In patients with COPD, the prevalence of ACO ranged from 4.2% to 66.0%.12. Cosio *et al.* showed that the prevalence of ACO was 15.0% according to their definition above.[72] In a meta-analysis, Alshabanat *et al.* defined ACO as a combination of post-bronchodilator airflow irreversibility and a diagnosis of asthma, airflow reversibility, peak expiratory flow variability or airflow hyperresponsiveness. Their prevalence of ACO was 27% and 28% in the population- and hospital-based studies, respectively.

Among COPD patients in Japan, the prevalence of ACO was between 4.2% and 49.7%.[73].Suzuki *et al.* describe ACO as the combination of bronchodilator reversibility,blood eosinophilia (peripheral

blood eosinophil count of ≥300 cells uL^{-1}), and/or atopy (the presence of specific serum IgE to at least 1 of the 14 common inhaled allergens) in Hokkaido cohort study. Their prevalence of ACO was 49.7% in patients who were over 40 years old and had a smoking habit.

In Japan, the prevalence of ACO remains uncertain among any population because of the lack of data from multiple large-scale cohort studies. Furthermore, it is important to minimize potential selection bias for the estimation of prevalence, and it might be valuable to perform consecutive recruitment of eligible patients at each study site or to use less-biased community surveys. One study, using the protocol regulating consecutive recruitment, reported that the proportion of patients identified as having ACO based on the stepwise approach stated in the GINA/GOLD report was 9.2% or 4.2%, depending on the FEV_1 variability cut-off used, among the 1008 outpatients medically treated for COPD in a real-life clinical setting.[74].

Age and gender:

The patients with ACO were older than those with asthma in many studies.[75]. In comparison with COPD patients, it was reported both that ACO patients were younger than COPD patients [76], and that the age of ACO patients was not different from that of COPD patients. The prevalence of ACO increases as age rises, and this result is the same as that for COPD [77]

In Japan, all studies showed that the gender of ACO patients was predominantly male. Outside Japan, there were different gender distributions in ACO patients; some reports showed a predominantly male distribution [78] and

others shows a predominantly female one.[79] Because biomass exposure is one of the causes of COPD, there is a large population of female patients with COPD in some regions.

PATHOGENESIS:

Two explanations of the mechanism by which a disease with the characteristics of both asthma and COPD forms have been proposed: The Dutch Hypothesis and the British Hypothesis.

1) The Dutch Hypothesis

The Dutch Hypothesis was first proposed by Dutch researcher Dick Orie in 1961. He hypothesized that "asthma, chronic bronchitis, and pulmonary emphysema (COPD) is a single disease that occurs as a result of the same genetic factors (atopic status, promotion of airway hyperreactivity), and only presents different clinical phenotypes due to different environmental factors (allergens, smoking, and infections)." This hypothesis was referred to as the Dutch Hypothesis by Fletcher, who laid the basis for the disease concept of chronic non-specific lung disease (CNLD). According to this hypothesis, an individual with certain genetic factors presents the clinical phenotype of COPD when exposed to smoking and the clinical phenotype of asthma when exposed to allergens. Additionally, there is ACO, which is characterized by the fact that the patient has features of both COPD and asthma as a result of having been exposed to both environmental factors and therefore the two cannot be separated.[80]

2) The British Hypothesis

The British Hypothesis was first proposed in 1965 by Charles Fletcher, who described it as “A disease in which asthma and COPD occur as a result of different mechanisms triggered by different pathogens” [81]. Unlike the Dutch Hypothesis in which asthma and COPD are described as being impossible to separate, the British Hypothesis proposes that ACO is a pathophysiology that has features of both asthma and COPD in cases in which factors such as smoking contribute to asthma and in cases in which factors related to asthma, including antigen sensitization, contribute to COPD.

The major cause of COPD onset is smoking. However, only approximately 10%–15% of smokers develop COPD. This is thought to be due to whether or not the individual has disease susceptibility genes for smoking and other factors in addition to smoking. Genetic and other factors identified in smokers who experience major decreases in respiratory function over time include airway hyperreactivity, peripheral eosinophilia, and elevated IgE. In addition, it has been indicated that, in addition to smoking, COPD onset requires genetic factors such as atopy and promotion of airway hyperreactivity. In other words, individuals who have these genetic factors will develop COPD as a result of smoking. In contrast, those who are exposed to allergens or allergen stimulation will develop bronchial asthma.

RISK FACTORS:

Factors that tend to increase the probability of asthma and COPD overlap – include atopy and airway hyperreactivity. Promotion of airway hyperreactivity, which is a feature of the pathophysiology of asthma, is a risk factor for COPD. Pulmonary hypoplasia, which is greatly affected by the intrauterine environment and the external environment up to the age of 5 years, is a risk factor for both asthma and COPD. Thus, in the presence of these risk factors, the probability of asthma and COPD overlap onset tend to increase. [82] [83].

AIRWAY HYPERREACTIVITY:

Airway hyperreactivity is regulated by both reversible and irreversible factors. The reversible factors include mediators that accompany inflammation of airway and changes in the autonomic nervous system. Irreversible factors include changes in airway diameter. The reversible factors are associated with airway hyperreactivity caused by inflammation of airway in cases of asthma. The irreversible factors are associated with constricted airway diameter caused by airway remodelling in cases of asthma or constricted airway diameter caused by histopathological changes in cases of COPD. It has been reported that in cases of COPD neutrophilic inflammation is also related to hyperreactivity of airway. In general, airway diameter is a regulatory factor for COPD-related airway hyperreactivity, but since airway hyperreactivity is related to accelerated pulmonary function decrease, the acceleration may might

result in obstructive ventilatory defect. Moreover, atopy has been alternately reported to be a risk factor for COPD onset.[84]

GENETIC BACKGROUND:

Genetic analysis associated with asthma and COPD onset has identified several disease susceptibility genes that are common to both asthma as well as COPD. In recent years, comprehensive genetic analysis had led to the identification of disease susceptibility genes associated with COPD, asthma, and the functions of these genes are currently in the process of being elucidated[85] Orie sought a common genetic factor for both atopy and promotion of airway hyperreactivity, and Orie's hypothesis was confirmed by molecular functions elucidated by comprehensive analysis of disease susceptibility genes and molecular biological techniques. The following ones are description of some of those molecules.

1, **ADAM33** (**A Disintegrin and Metalloprotease Domain**)

The ADAM gene is a gene that encodes the ADAM (A Disintegrin and Metalloprotease Domain) family of genes. It suppresses cell–cell and cell–matrix interactions and is related to variety of biological process, including fertilization, muscle development, and neurogenesis. In recent years, the ADAM gene has been identified as related to asthma susceptibility and airway hyperreactivity.[86] ADAM33is expressed in tracheal smooth muscle and epithelial cells and is involved in airway remodelling. The

ADAM33 genotype is related to pulmonary function in infancy, the course of pulmonary function in cases of bronchial asthma, COPD.[87] [88].

2) **Orosomucoid like 3(ORMDL3):**

ORMDL3 is present in endoplasmic reticulum (ER) membranes. It is a membrane protein that contributes to the accumulation of proteins with folding anomalies or structural anomalies (unfolded protein) in the ER as a result of intra-and extracellular stimuli that inhibit protein modification, i.e. a membrane protein involved in ER stress response. When under ER stress, GRP78/BiP separates, ATF6, IRE, and PERK are activated, and metalloproteases (MMP-9, ADAM-8), CC chemokines (CCL-20), CXC chemokines (IL-8, CXCL-10, CXCL-11), oligoadenylate synthetases (OAS) genes, and SERCA2b are expressed. Genome-wide association (GWA) analysis has identified *ORMDL3* as a gene that is related to paediatric asthma.[89] ORMDL3 expression is promoted by smoking, antigen stimulus, and IL-4/IL-13 stimulus.[90]

(3) IL-17

IL-17 is produced by Th17 cells that were differentiated and induced from Th0 by TGFβ. IL-17 plays an important role in the onset of neutrophilic inflammation in cases of bronchial asthma and is involved in matrix metalloproteases (MMP) from macrophages in cases of COPD. MMP are

related to the formation of COPD lesions, and the MMP-12 polymorphism is related to the onset of COPD.[91]

3) Viral infection:

Viral infections during early childhood are risk factors for the occurrence of asthma and COPD. As mentioned before, ORMDL3 is a factor that increases the likelihood of viral infections during early childhood. ORMDL3 is also a risk factor for bronchiolitis caused by rhinovirus infection and for the onset of asthma.[92]

4) Pulmonary hypoplasia:

Genetic factors and growth promoting factors influence the growth of the airway and lungs from the time, a child is still in the uterus until the age of five years, with bronchus and lung growth continuing until it reaches its maximum level of development at around the age of 22 [93]. Dysfunctional bronchus and lung growth particularly during the period of time from the foetal period until the age of five years has an effect on airway, lung growth during childhood and youth, and this may lead to the so-called “reduced lung growth” that occurs when the lungs are smaller as compared to the maximum under normal growth at around the age of 22. Respiratory function is also reduced as compared to normal FEV_1. Thereafter (i.e. after the age of 22), respiratory function continues to gradually decline year by year. Impeded growth of the airway and lungs caused by a variety of factors associated with an early life event – that is, from the foetal stage to early childhood – of asthma and COPD

is related to subsequent onset of asthma and COPD. For example, smoking by the mother during the child's foetal stage is a risk factor for onset of paediatric asthma, and paediatric asthma is a risk factor for onset of COPD.

COURSE OF OVERLAP:

In general, there are cases of asthma in which COPD overlaps – e.g. " currently diagnosed with asthma that have a history of smoking or currently smoke and present chronic, gradual progressive shortness of breath during exertion as well as chronic coughing and phlegm" – and cases of COPD in which asthma overlaps – e.g." current smokers that become sensitized to an inhalation antigen and develop asthma." Early childhood asthma is a cause of reduced lung growth and function due to its effect on lung growth, and in such cases, there is a likelihood that the individual will develop a pathophysiology that has features of both asthma and COPD. These are issues that require careful attention in cases that develop the pathophysiology of ACO.

REVIEW OF LITERATURE

Asthma and chronic obstructive pulmonary disease (COPD) are common and are associated with substantial morbidity. Both diseases are characterized by airflow limitation and chronic airway inflammation. In asthma, the airflow limitation is, similar to the symptoms, variable and in most cases reversible either spontaneously or following treatment, e.g. in response to a bronchodilator.

In contrast, the airflow limitation in COPD is, by definition, persistent and often progressive and may be associated with chronic cough and sputum production, and, with increasing severity, also exacerbations and comorbidities. However, when examining an individual patient with symptoms of OLD, it may be difficult to reach a final diagnosis, especially in the elderly, because patients may present features characteristic for both asthma and COPD.[94][95]. So far, the important question remains largely unanswered whether the overlap between asthma and COPD represent patients with coexisting asthma and COPD or a unique disease entity. Some publications [96][97] emphasize that the asthma– COPD overlap (ACO) should be regarded as an independent disease entity, although no agreement on definition has been reached so far.[98]

The outcome of a very recent collaboration between the Global Initiative for Asthma (GINA) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) are dealing with a clinical description of ACO. The document describes the syndrome as having shared features with both asthma and COPD

together with non-reversible airflow limitation, although at the same time emphasizing that the document is intended only for clinical work and not to be used as a definition of ACO.

The proportion of patients suffering from obstructive lung disease that may be classified as having ACO varies between studies, depending on the definition, but in recent publications, it has been estimated to be 15%–25%.[99][100] Further knowledge, not least with regard to clinical characteristics and risk factors of ACO is, therefore, clearly needed and might lead to a generally accepted definition.

Asthma chronic obstructive pulmonary disease (COPD) overlap syndrome (ACOS) seems an important clinical phenotype, but multiple definitions have been proposed.

- American Thoracic Society (ATS), in their guidelines of 1995[101] defined asthma, chronic bronchitis, emphysema, COPD, airflow obstruction and identified 11 distinct syndromes. There was an overlap at 6 of these 11 syndromes.
- The Spanish COPD guidelines propose four COPD phenotypes that determine treatment: non exacerbator with emphysema or chronic bronchitis, mixed COPD asthma, exacerbator with emphysema and exacerbator with chronic bronchitis. The mixed COPD—asthma phenotype was defined as an airflow obstruction that is not completely reversible accompanied by symptoms or signs of an increased reversibility of the obstruction.[102]

- In another study from Spain, Soler-Cataluña *et al*. defined the clinical phenotype known as "overlap phenotype COPD-asthma". For this diagnosis were established two major and two minor criteria. Major criteria include very positive bronchodilator test (increase in FEV_1 ≥15% and ≥400 mL), eosinophilia in sputum and personal history of asthma. Minor criteria include high total IgE, personal history of atopy and positive bronchodilator test (increase in FEV_1 ≥12% and ≥200 ml) on 2 or more occasions . Airway eosinophilia is not exclusive to asthma and is present in COPD patients.[103] Furthermore, a clinically significant bronchodilator response (≥15%) can be elicited in the majority of COPD patients.
- Zeki *et al*.,[104] defined the ACOS as one of two clinical phenotypes: (I) asthma with partially reversible airflow obstruction, with or without emphysema or reduced carbon monoxide diffusing capacity (Dlco) to <80% predicted; and (2) COPD with emphysema accompanied by reversible or partially reversible airflow obstruction, with or without environmental allergies or reduced Dlco.
- Louie *et al*.,[105] in another review prefer the following major criteria for ACOS: a physician diagnosis of asthma and COPD in the same patient, history or evidence of atopy, for example, hay fever, elevated total IgE, age 40 years or more, smoking >10 pack-years, postbronchodilator FEV_1 <80% predicted and FEV_1/FVC <70%. Minor criteria were a

≥15% increase in FEV_1 or ≥12% and ≥200 ml increase in postbronchodilator treatment with albuterol.

- Brzostek and Kokot[106]defined ACOS as a mixed phenotype with a combination of features of both asthma and COPD.
- Chung et al[107]defined it as an FEV_1/FVC ratio <0.7 plus a history of self-reported wheeze, whereas de Marco et al[108] defined it as having a self-reported physician diagnosis of both asthma and COPD (defined as a diagnosis of COPD, emphysema, or chronic bronchitis).
- Apart from having respiratory symptoms, patients classified as having ACOS in the study by Fu et al[109] were required to have increased airflow variability, defined as airway hyperresponsiveness or bronchodilator reversibility, and not fully reversible airflow obstruction (ie, postbronchodilator [post-BD] FEV_1/FVC <0.7 and post-BD FEV_1 <80% of predicted).
- Hardin et al[110] overlap subjects were defined as COPD patients with self-reported physician diagnosed asthma before the age of 40 years.
- In the study by Kauppi et al[111] they were defined as patients having both a diagnosis of asthma and COPD, where asthma was defined according to the GINA guidelines and COPD according to the GOLD strategy document.
- Lee et al[112]defined ACOS patients as having asthma (defined as a bronchodilator reversibility test with an increase in FEV_1 of >200ml and 12%, and/or positive methacholine/mannitol challenge test) together with a post-BD

FEV_1/FVC <0.70 at the initial assessment, and continuing airflow obstruction after at least 3 months follow-up, irrespective of treatment.

- Menezes et al[113]classified patients as having ACOS if they fulfilled the criteria for both asthma, i.e. wheezing in the last 12 months plus post-BD increase in FEV_1 (200 ml and 12%) or a self-reported doctor diagnosis of asthma and COPD, ie, post-BD FEV_1/FVC <0.7.
- Milanese et al[114] classified overlap patients as subjects ≥65 years with physician diagnosis of asthma (defined according to the GINA guidelines 2012) plus chronic bronchitis, ie, chronic mucus hypersecretion or/and impaired diffusion capacity, ie, total diffusion capacity <80% of the predicted value.
- Miravitlles et al [115] classified ACOS patients on the basis of a post-BD FEV_1/FVC <0.7 together with physician diagnosis of asthma before the age of 40 years.
- Pleasants et al [116] defined ACOS as answering affirmatively to questions about a physician diagnosis of both COPD and asthma.

AIMS AND OBJECTIVES

OBJECTIVE:

- ✓ To study the phenotypes in COPD
- ✓ To study epidemiological profile in asthma COPD overlap
- ✓ To study the occurrence of ASTHMA COPD OVERLAP among COPD patients.

SAMPLE SIZE:

- ✓ Prevalence of asthma overlap among COPD patients is 17 %.
- ✓ Allowable alpha error is 7% with a confidence level of 95%.
- ✓ Sample size calculated using open epi software
- ✓ Sample size is 124

INCLUSION CRITERIA:

- ✓ Male Patients over the age of 40 and above.
- ✓ Patient who were known cases of COPD

EXCLUSION CRITERIA:

- ✓ Patients who were sputum positive for AFB.
- ✓ Patient with other comorbidities.
- ✓ Those who are not willing to participate.

SAMPLE SELECTION:

Patient attending Government Thiruvotteeswarar Hospital for thoracic medicine outpatient clinic who were previously diagnosed as COPD through spirometry are selected.

METHODS AND MATERIALS:

Study group : Patients with COPD

Study design : Cross sectional study

Place of Study : Govt Thiruvotteeswarar Hospital of Thoracic medicine Chennai.

Duration of study : 1 year

Sample size : 124

Sampling method : simple random sampling

Conflict of interest : Nil

Hazards of study : Nil

DATA COLLECTION:

- **Demographic data**
- **BMI**
- **Symptomatology:**
    - Cough with expectoration
    - Shortness of breath
    - Wheeze
    - Chest tightness
- **Past history**
    - Prior TB treatment
    - Prior treatment for COPD/ asthma
    - Any comorbid illness
    - Family h/o asthma

- **Personal history**
    - Addictions
    - Biomass exposure
    - Marital status
    - Children
- **PFT**
- **X RAY CHEST**
- **ABSOLUTE EOSINOPHIL ACCOUNT**

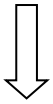
Allowable alpha error is 7% with a confidence level of 95%.

Patients who were diagnosed as COPD

Questionnaires regarding asthma/COPD (e.g. h/o atopy, h/o allergic rhinitis smoking history, biomass exposure)

chest X ray to exclude other causes

PFT to rule out airflow limitation <0.70 (reversibility with BDR > 400 ml in FEV1



Peripheral eosinophilia (> or equal to 300 eosinophils/micro litre)

According to international journal of pulmonary and respiratory medicine, there are major and minor criteria.

MAJOR CRITERIA:

1. Persistent airflow limitation <0.70 in patients over 40 years of age,
2. Exposure to smoking of at least 10 packs-year or the equivalent in biomass smoke exposure,
3. A documented history of asthma before age 40 or BDR>400ml in FEV1.

MINOR CRITERIA:

1. Documented history of atopy or allergic rhinitis,
2. BDR≥200ml and 12%on at least 2 occasions,
3. Peripheral eosinophilia ≥300eosinophils/μL.

For a diagnosis of ACO, 3 out of 4 major criteria and at least one of minor criteria proposed had to be met.

STATISTICAL ANALYSIS:

Statistical analysis were done with Microsoft excel and SPSS software, with the help of statistician P value is used to assess the significance of correlation between variables.

A statistically significant correlation is one in which Pearson correlation is used to assess the strength of correlation between variables.

Pearson correlation:

> 0.5 – strong correlation

0.3 to 0.5 – Moderate correlation

0.3 – weak correlation

Chi- square test:

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

Chi square test of independence is used to test for a statistically significant relationship between two categorical variables.

The term “degrees of freedom” is used to refer to the size of the contingency table on which the value of the chi square statistic has been computed.

RESULTS AND ANALYSIS

Table 1: Age Distribution

Age (In years)	**Cases**	
	No	**%**
41-50 years	47	37.9
51-60 years	55	44.4
61-70 years	17	13.7
>70	5	4.0
Total	124	100.0
Range	40-75 years	
Mean	54.15	
S. D	8.2 years	

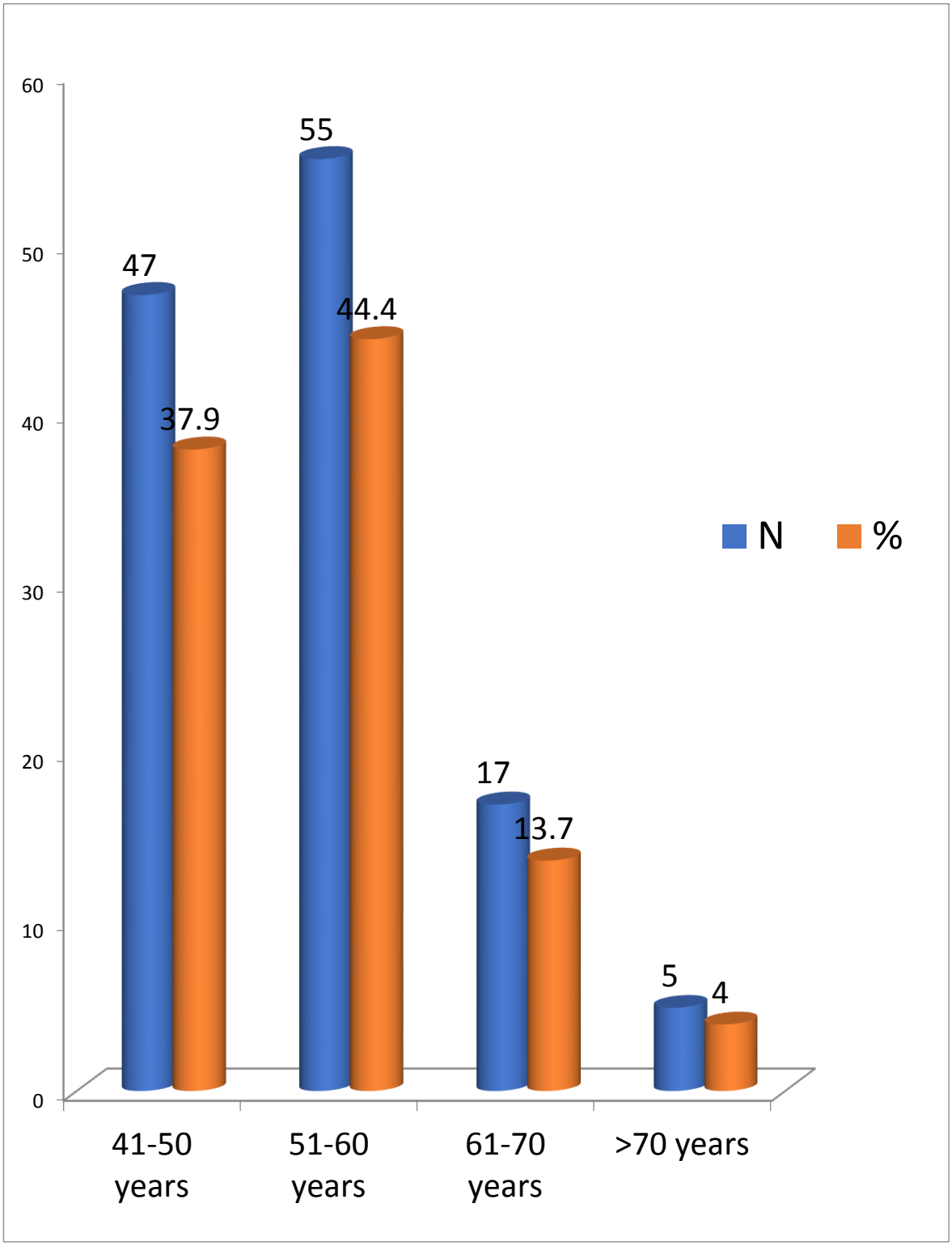


Fig 1: Distribution of age in my study population

Table 2: Distribution of COPD types according to symptoms and Chest x ray findings

COPD	Cases	
	No	**%**
Chronic Bronchitis	60	48.4
Emphysema	64	51.6
Total	124	100.0

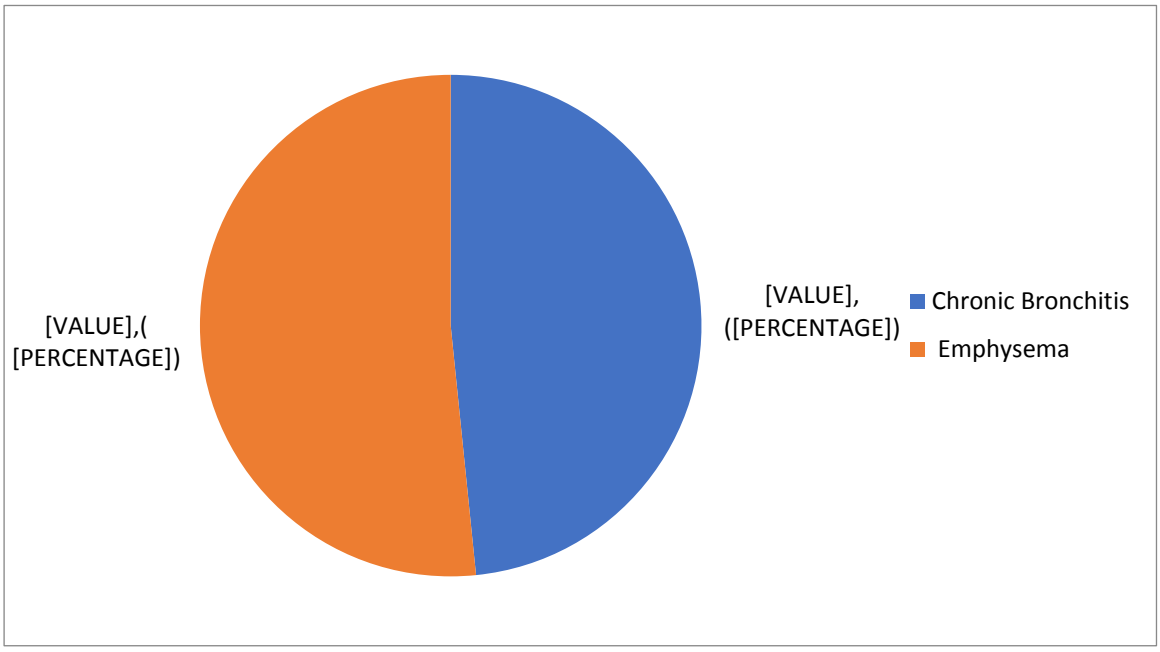


Fig 2: Pie chart showing distribution of COPD types.

COPD phenotypes:

- COPD phenotype generally refers to a single or combination of disease attributes that describe differences between COPD patients based on clinically significant parameters, such as exacerbation, symptoms, response to treatment, rate of progression of disease, and mortality.[116]

- In 2012, the Spanish Society of Pulmonology and Thoracic Surgery published the Spanish COPD guideline (GesEPOC), which was the first clinical guideline that phenotypes COPD patients are classified based on their exacerbation frequency and dominant clinical manifestations, such as bronchitis, emphysema, and asthma COPD overlap.

- The COPD clinical phenotypes were defined according to the GesEPOC guideline.[117]
    - ✓ Non-exacerbator phenotype (NON-AE) was defined by the presence of <2 episodes of moderate exacerbation and without severe exacerbation in the past 1 year.

    - ✓ Exacerbator phenotype (AE) was defined by the presence of 2 or more episodes of moderate exacerbation or an episode of severe exacerbation in the past 1 year. This phenotype was further divided into AE with chronic bronchitis phenotype (AE CB) and

AE with emphysema phenotype (AE NON-CB).

- ✓ The former phenotype was defined by the presence of CB, while the latter phenotype was defined by the presence of air-trapping on examination or investigations. Asthma-COPD overlap syndrome phenotype (ACOS) was defined by the presence of COPD definite PB-FEV_1 improvement of >400 mL and 15%, or blood eosinophil of >300 cells/mm.[118][119].

Table 3: Distribution of COPD phenotypes

COPD Phenotypes	Cases	
	No	**%**
No exacerbator	31	25
Asthma COPD overlap	25	20
Exacerbator with chronic bronchitis	30	24
Exacerbator with emphysema	38	31
Total	124	100.0

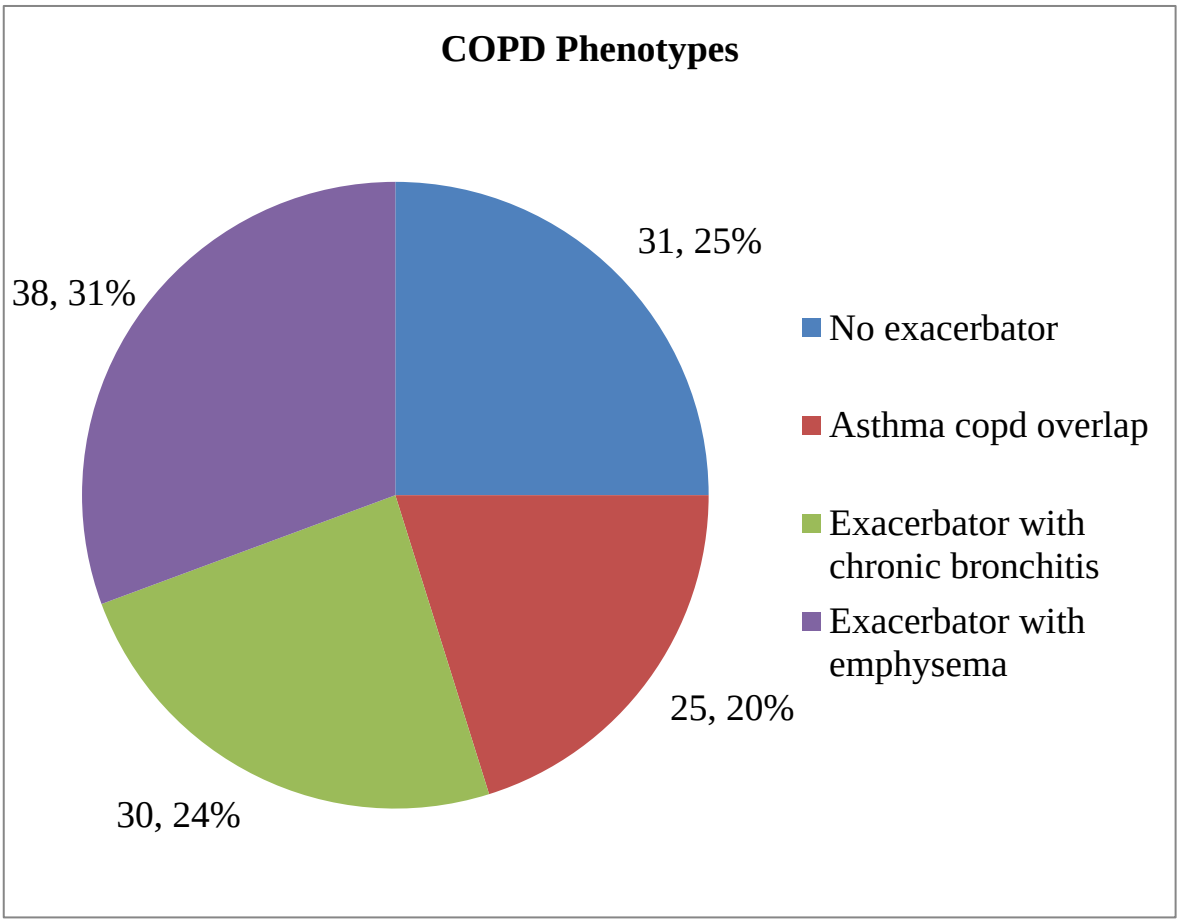


Fig 3 : Pie chart representing COPD phenotypes

Table 4: Distribution of H/o atopy

Atopy	Cases	
	No	**%**
Yes	59	47.6
No	65	52.4
Total	124	100.0

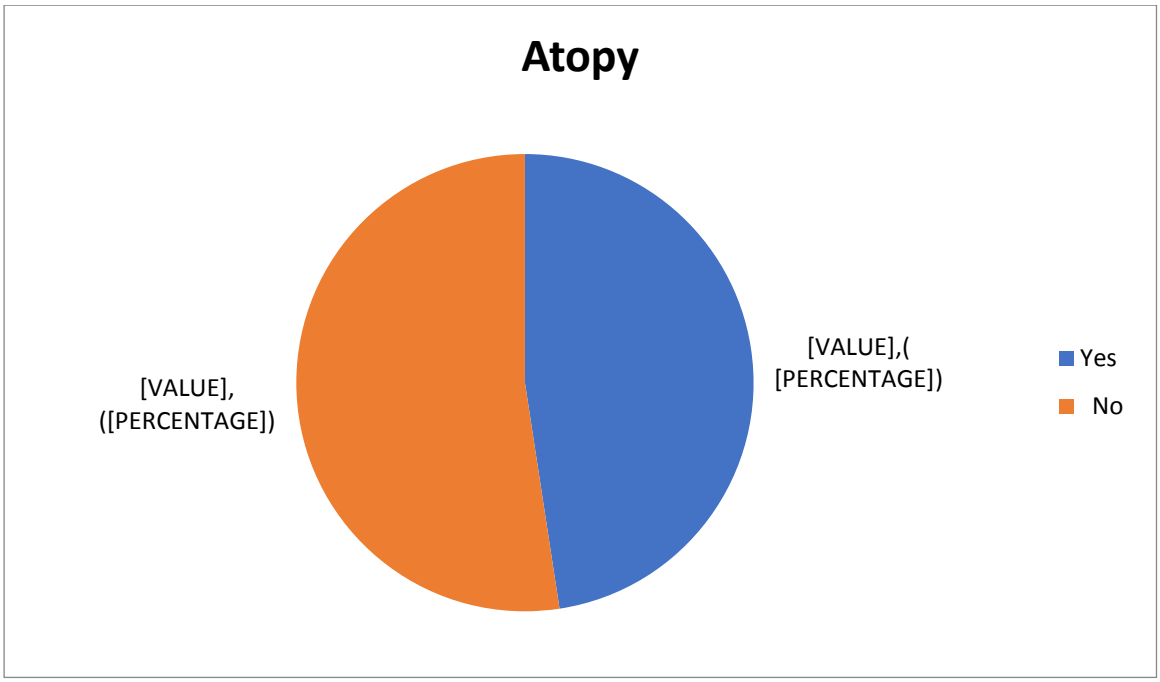


Fig 4: Pie chart showing Distribution of History of Atopy

Table 5: Distribution of H/O smoking

Smoking	Cases	
	No	%
>10-- <20	54	43.5
≥20--<30	52	41.9
≥30 yrs	18	14.5
Total	124	100.0

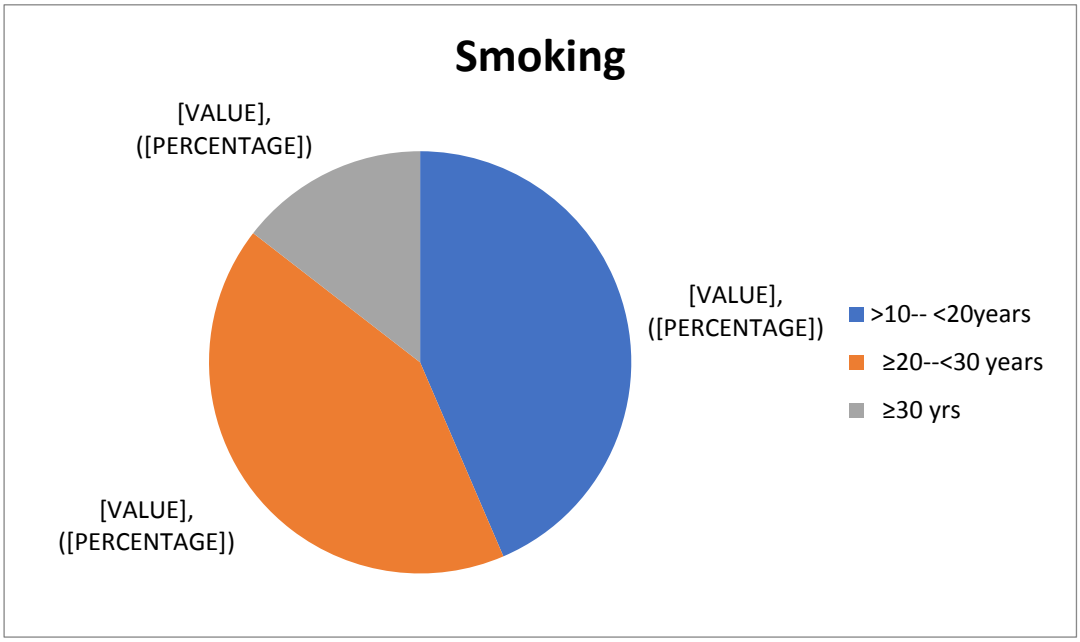


Fig 5: Pie chart showing Distribution of smoking history in my study population

Table 6: Distribution of absolute eosinophil count value

AEC	Cases	
	No	**%**
<300	36	29.0
>300	88	71.0
Total	124	100.0

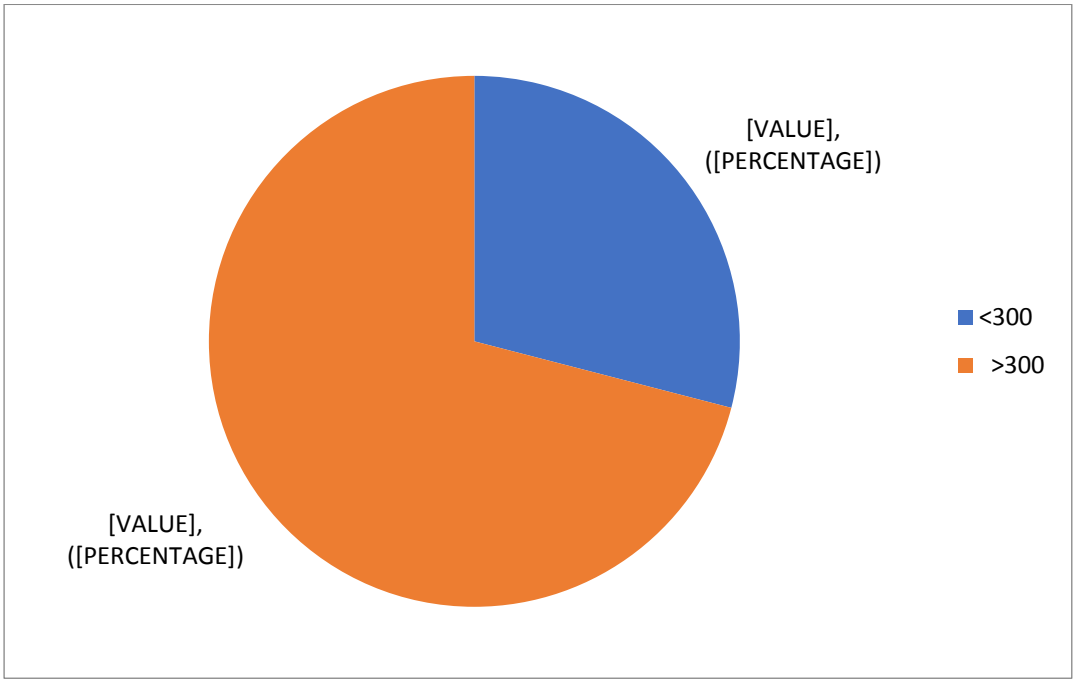


Fig 6: Pie chart showing Distribution of absolute eosinophil value

Table 7: Distribution of reversibility values in pulmonary function test

PFT	Cases	
	No	**%**
No reversibility (0%)	37	29.8
No significant reversibility (1-14%)	62	50.0
Significant Reversibility (>15%)	25	20.2
Total	124	100.0

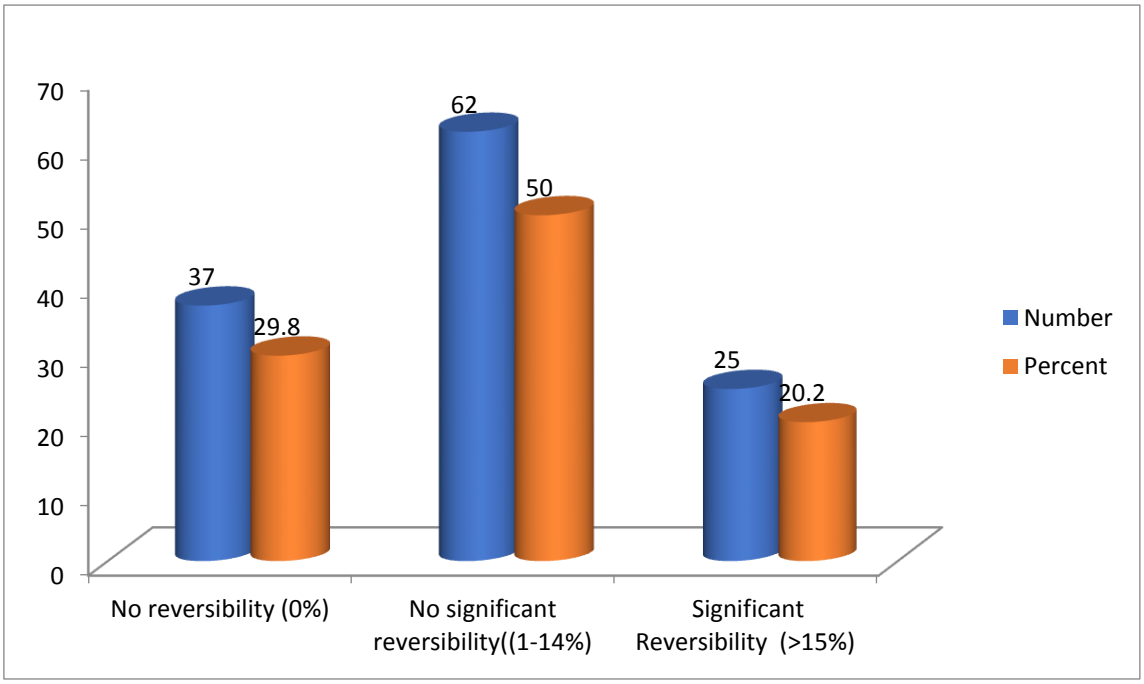


Fig 7: Pie chart showing Distribution of reversibility in Pulmonary function

Table 8 : Asthma COPD overlap among my study population

Study subjects	Cases	
	No	**%**
Asthma COPD overlap	25	20
COPD	99	80
Total	124	100.0

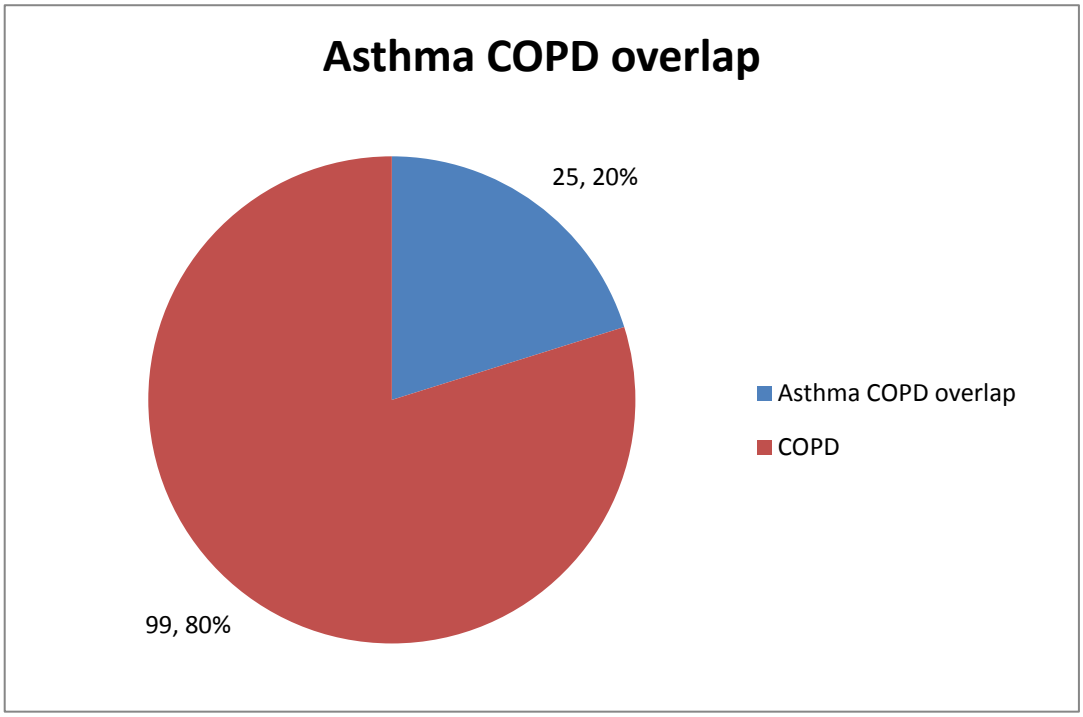


Fig 8 : Pie chart showing distribution of Asthma COPD overlap

Table 9: Comparison of asthma COPD overlap with age category

AGE in yrs	Asthma COPD Overlap		Total	P value Df=2
	YES	NO		
41-50	6	41	47	>0.05 (NS)
51-60	13	42	55	
61-70	4	13	17	
>70	2	3	5	
Total	25	99	124	

Data are expressed as N (%).Chi Square test & Fischer exacts tests was applied to find statistically significant association between groups based on asthma COPD overlap and age category. It was found to be not statistically significant p value >0.05

Table 10: Comparison of asthma COPD overlap with H/O atopy

H/O Atopy	Asthma COPD overlap		Total	P value Df=1
	Yes	No		
Yes	18 (72)	41(41.4)	59	<0.05* (S)
No	7 (18)	58 (58.6)	65	
Total	25	99	124	

Data are expressed as N (%).

Chi Square test was applied to find statistically significant association between groups based on asthma COPD overlap and history of atopy .

The prevalence of asthma COPD overlap is higher in patient who have history of atopy than who don't have history of atopy. It was found to be statistically significant p value <0.05

Table 11: Comparison of Asthma COPD overlap with history of smoking category

H/O smoking	Asthma COPD overlap		Total	P value Df=2
	Yes	No		
10-19 yrs	6 (24)	48 (48.4)	54	<0.05* (S)
20-29 yrs	14 (56)	38 (38.4)	52	
>30	5 (20)	13 (13.1)	18	
Total	25	99	124	

Data are expressed as N (%). Chi Square test was applied to find statistically significant association between groups based on asthma COPD overlap and duration of smoking in years. The prevalence of Asthma COPD overlap is higher in patients who have more number of years exposed to smoking. It was found to be statistically significant p value <0.05

Table 12: Comparison of Asthma COPD overlap with absolute eosinophil count

AEC	Asthma COPD overlap		Total	P value Df=1
	Yes	No		
<300	0	36(36.3)	36	<0.05* (S)
>300	25 (100)	63 (63.7)	88	
Total	25	99	124	

Data are expressed as N (%).Chi Square test & Fischer exacts tests was applied to find statistically significant association between groups based on Asthma COPD overlap and absolute eosinophil count. The absolute eosinophil count is higher in patient who have Asthma COPD overlap among my patients. It was found to be statistically significant p value <0.05.

AGE DISTRIBUTION OF STUDY POPULATION:

- The age in our patients range from 40 to 75yrs of age. The number of patients in the age category 40-50, 51-60, 61-70, more than 70 are 47 (37.6%), 55(44.4%), 17 (13.7%), 5 (4.0%) respectively. The mean age is 54.15
- The minimum age of subject is 40 yrs and maximum age 75.
- Out of 124 in this study most of the asthma COPD overlap fall under the age group 40 to 60 yrs of age, which is about 76% (19).
- In literature ACO occurred in the age group more than 40

DISTRIBUTION OF STUDY SUBJECTS ACCORDING TO HISTORY OF ASTHMA OR ATOPY BEFORE 40 YRS OF AGE:

- A history of childhood or adult-onset asthma should be a major criterion for ACO. As the prevalence of COPD increases after age 40 years, an age cutoff of 40 years is reasonable to improve the accuracy of the diagnosis. However, the committee also recognised that asthma can develop in individuals 40 years of age and older. Although COPD patients can demonstrate a significant BDR, it is generally less than 400 mL. Thus, in those without a documented history of asthma before 40 years of age, this criterion may be met by demonstrating a BDR of >400 mL [46]. While many patients with asthma have a history of atopy

and/or rhinitis, a substantial proportion of adults with atopy and rhinitis do not have or develop asthma. Thus, a history of atopy and rhinitis should not be a major criterion for ACOS.

- Among 124 study subjects 59 had given positive history of atopy which is about 47.5%, and in ACO 18 had history of atopy, which is about 72%. History of atopy was found to be significant with the diagnosis of ACO.

DISTRIBUTION OF STUDY SUBJECTS ACCORDING TO YEARS OF EXPOSURE TO SMOKING:

- Current or past cigarette smoking is a major criterion for ACO. However, there is uncertainty on the exact pack–year cut-off that is appropriate for ACO. Until more data are available, a reasonable cut-off is ⩾10 pack–years for smokers in countries where biomass exposure is not a major contributor to airflow limitation.

- It should also be noted that in some parts of the world (e.g. Africa, Southeast Asia and China), indoor and outdoor pollution play a key pathogenic role in asthma and COPD in non-smokers or intermittent (light) smokers. However, there is no universally accepted method to quantitate these exposures.

- In our study years of exposure to smoking were categorised into 10-19, 20-29, >30 and number of patients with years of exposure are 6(24%), 14(56%), 5(20%) respectively. In our study prevalence of Asthma COPD overlap is higher in patients who have more number of years exposed to smoking.

DISTRIBUTION OF STUDY SUBJECTS ACCORDING TO ABSOLUTE EOSINOPHIL COUNT:

- Measurement of blood eosinophils, unlike sputum eosinophil counts, is a well-standardised and reproducible test in most clinical laboratories. Although, on average, COPD patients with asthmatic features have elevated peripheral eosinophils, there is little agreement on what constitutes the most appropriate cut-off values. Some have suggested a cut-off of 5%, while others have advocated a 2% cut-off and still others have suggested using an absolute cell count cut-off (e.g. 300 cells·uL−1)

- Among 124 study subjects 88 had eosinophil count more than 300, and also in all asthma COPD overlap patients.

DISTRIBUTION OF STUDY SUBJECTS ACCORDING TO SPIROMETRY:

- Persistent airflow limitation should be a major criterion for ACOS. Thus, it is imperative to perform pre and post-bronchodilator spirometry

according to ATS/European Respiratory Society (ERS) recommendations in all patients. An age-adjusted cut-off value for FEV1/FVC is preferred; however, in some jurisdictions where normative values are not widely available, fixed ratio cutoffs can be used.

- In our study spirometry is one among the criteria for diagnosing ACO. Out of 124 study subjects 25 (20%) had bronchodilator response > 15%, less than 15% in 62 (50%), and no reversibility in 37 (29.8%). While significant BDRs have been traditionally linked with asthma, it is now well known that some patients with COPD demonstrate significant improvements in FEV1 following bronchodilators. However, in general, the BDRs tend to be small in magnitude and quite variable in patients with COPD [45], unlike in asthma where BDRs are generally larger and more robust.
- In individuals who do not have a physician diagnosis of asthma before the age of 40 years, BDR may be used as a major diagnostic criterion of ACO if the subject demonstrates a very large BDR, defined as >400 mL increase in baseline FEV1 following 400 ug of albuterol/salbutamol (or equivalent). This exception is being permitted as some individuals may manifest their first symptoms of asthma at age 40 years or older.

DISTRIBUTION OF COPD PHENOTYPES AMONG STUDY POPULATION:

- COPD phenotypes were classified into no exacerbator, asthma COPD overlap, exacerbator with chronic bronchitis, exacerbator with emphysema and number of patients with these types are 31 (25%), 25 (20%), 30 (24%), 38 (31%) respectively.

DISTRIBUTION OF ASTHMA COPD OVERLAP AMONG STUDY POPULATION:

- In literature the prevalence of asthma COPD overlap among COPD patients is 12.1% to 55.2%. In our study Out of 124 study population, 25 (20%) had Asthma COPD overlap.
- Most of ACO patients were between the age group of 40-60.
- A study in US, ACO was defined as the presence of all of the following *1*) age ≥40 years, *2*) current or former smoking, 3) post-bronchodilator airflow limitation (forced expiratory volume in 1 second/forced vital capacity <0.7), and *4*) ≥12% and ≥200 ml reversibility in post-bronchodilator forced expiratory volume in 1 second.
- The prevalence of ACO in the total population ranges from 1.6 to 4.5% in different studies around the world The prevalence of ACO among patients with COPD ranges from 12.1 to 55.2%, and among patients with asthma from 13.3 to 61.0% The wide variation in prevalence is

related to the diagnostic criteria applied while defining asthma (self-reported physician diagnosis vs. clinical and/or spirometry-based diagnosis) and COPD (self-reported physician diagnosis vs. spirometric criteria: forced expiratory volume in 1 second/forced vital capacity [FEV_1/FVC] <0.70), together with the population being studied.

- A study in UK, 2165 Patients were taken into study, among that individuals (1,015 COPD only, 395 with asthma COPD overlap, and 755 asthma only), the overall prevalence of ACO was 20%. In this Patients with ACO had a mean age of 70 years (standard deviation, 11 yr), 60% were men, 73% were former smokers (the rest were current smokers), and 66% were overweight or obese.

CONCLUSION:

- The prevalence of ACO in asthma and in COPD cohorts is highly variable, these divergences might be explained by the diversity of study designs. Using the GINA GOLD stepwise approach in literature have identified an identical ACO prevalence of 11% from asthma and COPD cohorts, both sampled from respiratory clinics.
- In the literature, the overlap rate of doctor-diagnosed asthma-COPD was reported to be 1.6% at age 20–44 years, 2.1% at age 45–64 years, and 4.5% at age 65–84 years.
- The number of hospital admissions for any reason or for exacerbation of the disease were observed to be higher in ACO than in asthma and COPD alone

- In most cross sectional studies of ACO, the frequency of exacerbations in ACO were higher than that in COPD patients.
- In the prognosis of patients with ACO, no generally accepted definitive outcome has been reached yet.
- The basis for diagnosing ACO is that when compared to asthma and COPD, ACO is also associated with more rapid decline in lung function, more frequent exacerbations, increase health care resource utilization, worsening quality of life and higher mortality rates.
- There by diagnosing ACO at the earliest one can prevent exacerbation, morbidity by altering the line of management.

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LIST OF ABBREVIATIONS USED

NHANES	-	National Health and Nutrition Examination Survey
FVC	-	Forced Vital Capacity
FEV1	-	Forced Expiratory Volume in one second
HIV	-	Human Immunodeficiency Virus
GINA	-	Global Initiative for Asthma
GOLD	-	Global initiative for Obstructive Lung Disease
IgE	-	Immunoglobulin E
IL	-	Interleukin
BMI	-	Body Mass Index
PFT	-	Pulmonary Function Test
COPD	-	Chronic Obstructive Pulmonary Disease
ACO	-	Asthma COPD overlap
AEC	-	Absolute Eosinophil Count

PROFORMA

PATIENT'S DEMOGRAPHY

Id No:

Date:

Name:

Age:

Gender:

Address:

Phone:

Occupation: _____

SYMPTOMATOLOGY:

Cough with expectoration Yes/No

Shortness of breath Yes/No

Wheeze Yes/No

Chest tightness Yes/No

PAST HISTORY:

Prior TB treatment: Yes/No

Prior treatment for COPD/asthma Yes/No

Any comorbid illness: Yes/No

Family h/o asthma: Yes/No

(DM/SHT/epilepsy/HIV/CAD) Yes/No

PERSONAL HISTORY:

Addictions: Smoking/ alcohol/ tobacco/ substance abuse

Biomass exposure: yes/No

Marital status: married/ unmarried

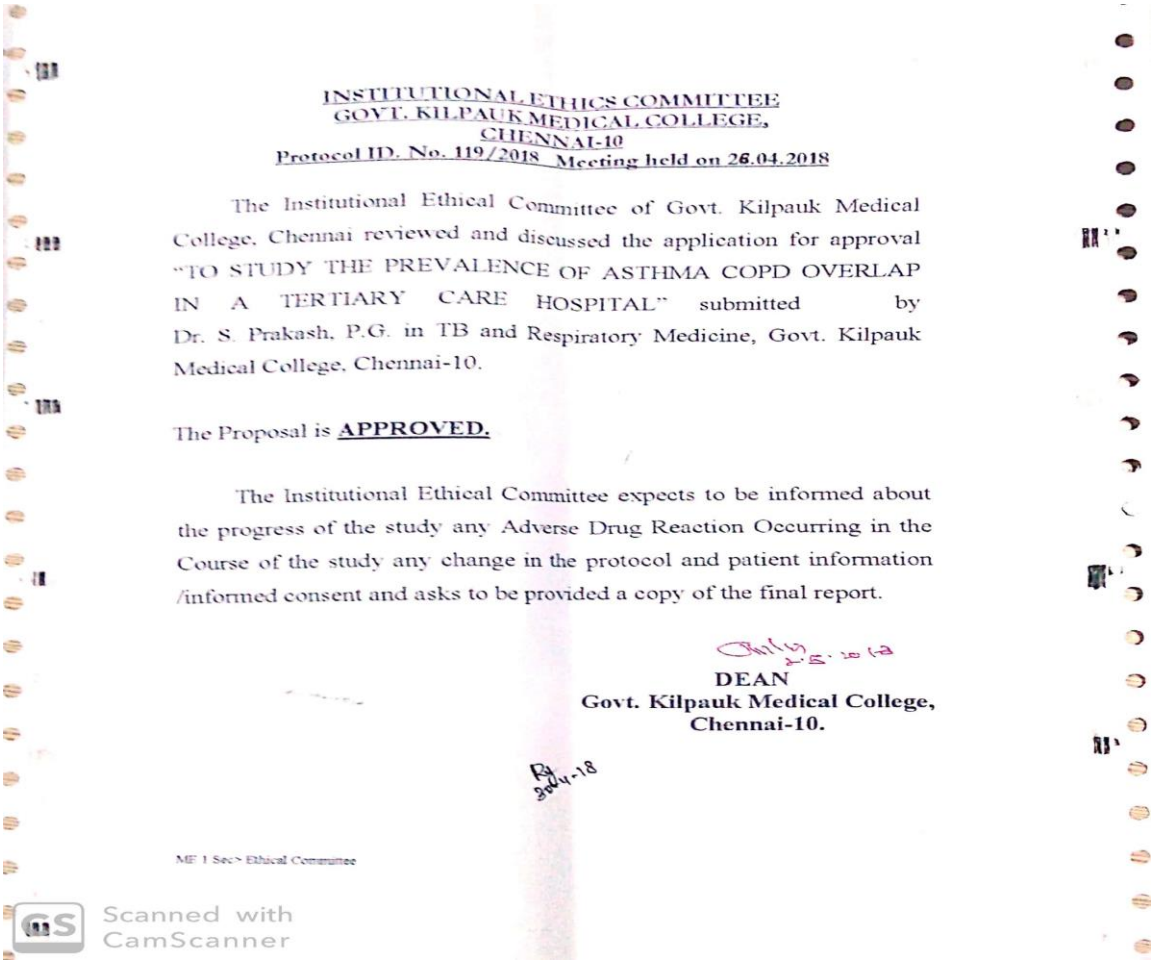
Children: Yes/no

PFT:

X RAY CHEST:

ABSOLUTE EOSINOPHIL ACCOUNT:

ETHICAL APPROVAL CERTIFICATE



INSTITUTIONAL ETHICS COMMITTEE
GOVT. KILPAUK MEDICAL COLLEGE,
CHENNAI-10
Protocol ID. No. 119/2018 Meeting held on 26.04.2018

The Institutional Ethical Committee of Govt. Kilpauk Medical College, Chennai reviewed and discussed the application for approval "TO STUDY THE PREVALENCE OF ASTHMA COPD OVERLAP IN A TERTIARY CARE HOSPITAL" submitted by Dr. S. Prakash, P.G. in TB and Respiratory Medicine, Govt. Kilpauk Medical College, Chennai-10.

The Proposal is **APPROVED.**

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

DEAN
Govt. Kilpauk Medical College,
Chennai-10.

MF 1 Sec> Ethical Committee

CERTIFICATE II

This is to certify that this dissertation work titled "**To Study the Prevalence of Asthma COPD Overlap in a Tertiary care Hospital"** of the candidate Dr.S.PRAKASH with registration number **201727252** for the award of M.D. Degree in the branch of Tuberculosis and Respiratory Diseases. I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from the introduction to conclusion pages and result shows _9%_ percentage of plagiarism in the dissertation.

GUIDE AND SUPERVISOR

Prof. Dr. P.M. Ramesh, MD (TB& RD)
Head of Department, Tuberculosis and Respiratory Diseases,
Government Kilpauk Medical College

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Instances where selected sources appear:

30

PATIENT CONSENT FORM

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

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

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

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

I hereby consent to participate in this study.

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

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

Place: Date:

Name of the investigator: Signature of the investigator:

Place: Date:

<u>சுயஒப்புதல் படிவம்</u>

<u>ஆய்வு செய்யப்படும் தலைப்பு:</u>"TO STUDY THE PREVALENCE OF ASTHMA COPD OVERLAP SYNDROME IN A TERTIARY CARE HOSPITAL"

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

பங்கு பெறுபவரின் பெயர்:

உறவு முறை:

பங்கு பெறுபவரின் எண்:

பங்கு பெறுபவர் இதனை ( ) குறிக்கவும்

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

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

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

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும், அதைப் பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ( )

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

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

பங்கேற்பவரின் கையொப்பம் / கட்டைவிரல் ரேகை:_____

இடம்: _____

தேதி: _____

பங்கேற்பவரின் பெயர் மற்றும் விலாசம்::

ஆய்வாளரின் கையொப்பம் _____

இடம் _____

தேதி _____

ஆய்வாளரின் பெயர் _____

S.No	NAME	AGE	SEX	H/O ATOPY	YEARS OF SMOKING EXPOSURE	(SPIROMETRY)%FEVI/FVC	BDR	AEC	CHEST XRAY	COPD PHENOTYPES
1	RAM	43	M	NO	10	<0.70	12%	285	BVM	EXACERBATOR WITH CB
2	KATHIRAVAN	44	M	NO	10	<0.70	2%	342	BVM	EXACERBATOR WITH CB
3	RAMESH	45	M	YES	17	<0.70	13%	1150	BVM	EXACERBATOR WITH CB
4	LOGANATHAN	40	M	YES	10	<0.70	15%	890	BHI LUNG FIELDS	ACO
5	GANESHAN	41	M	YES	15	<0.70	10%	1330	BVM	EXACERBATOR WITH CB
6	ALI	59	M	NO	30	<0.70	NO REVERSIBILITY	267	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
7	DHANDABANI	49	M	YES	20	<0.70	7%	1300	BVM	NO EXACERBATOR
8	AMITH	68	M	YES	30	<0.70	10%	720	BVM	EXACERBATOR WITH CB
9	BALASUBRAMANI	40	M	YES	15	<0.70	10%	304	BVM	EXACERBATOR WITH CB
10	VEERARAGHAVAN	59	M	NO	15	<0.70	NO REVERSIBILITY	820	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
11	RAMAKRISHNAN	51	M	YES	15	<0.70	11%	420	BVM	EXACERBATOR WITH CB
12	MOHAMMAD GHOUSE	56	M	YES	15	<0.70	NO REVERSIBILITY	560	BVM	EXACERBATOR WITH CB
13	VIJAYAN	55	M	NO	15	<0.70	8%	800	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
14	ILAYAVANAN	40	M	YES	15	<0.70	NO REVERSIBILITY	274	BHI LUNG FIELDS	NO EXACERBATOR
15	MOHAMMAD	65	M	YES	25	<0.70	NO REVERSIBILITY	251	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
16	MUTHIAH	67	M	NO	20	<0.70	20%	480	BHI LUNG FIELDS	ACO
17	MOHAN	55	M	NO	20	<0.70	8%	354	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
18	SUBRAMANI	55	M	YES	20	<0.70	20%	520	BVM	ACO
19	MANI	56	M	YES	20	<0.70	20%	480	BVM	ACO
20	RAYAR	60	M	YES	25	<0.70	20%	550	BHI LUNG FIELDS	ACO
21	BALU	72	M	NO	20	<0.70	5%	330	BVM	EXACERBATOR WITH CB
22	AYADBASHA	60	M	YES	20	<0.70	NO REVERSIBILITY	267	BHI LUNG FIELDS	EACERBATOR WITH EMPHYSEMA
23	SUGUKUMAR	55	M	YES	20	<0.70	7%	350	BVM	EXACERBATOR WITH CB
24	BABU	52	M	NO	15	<0.70	20%	550	BVM	ACO
25	PALANI	58	M	NO	20	<0.70	18%	640	BHI LUNG FIELDS	ACO
26	VISWANATHAN	56	M	YES	15	<0.70	22%	720	BHI LUNG FIELDS	ACO
27	BALASUBRAMANI	40	M	YES	15	<0.70	22%	650	BVM	ACO
28	CHINNA	73	M	YES	30	<0.70	6%	272	BVM	NO EXACERBATOR
29	SRINIVASAN	42	M	NO	15	<0.70	7%	242	BVM	EXACERBATOR WITH CB
30	KUMAR	63	M	NO	20	<0.70	8%	440	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
31	NATARAJAN	75	M	NO	15	<0.70	20%	840	BVM	ACO
32	RAJENDIRAN	57	M	YES	20	<0.70	5%	1000	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
33	MURALI	58	M	NO	30	<0.70	NO REVERSIBILITY	293	BVM	NO EXACERBATOR

34	NAGAMUTHU	68	M	NO	10	<0.70	NO REVERSIBILITY	246	BHI LUNG FIELDS	EACERBATOR WITH EMPHYSEMA
35	NATARAJAN	62	M	NO	30	<0.70	NO REVERSIBILITY	251	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
36	RAJA	43	M	NO	10	<0.70	3%	714	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
37	PANEERSELVAM	64	M	NO	30	<0.70	20%	938	BHI LUNG FIELDS	ACO
38	PRAKASH	65	M	NO	20	<0.70	NO REVERSIBILITY	264	BVM	NO EXACERBATOR
39	THANGABABU	70	M	YES	25	<0.70	16%	618	BVM	NO EXACERBATOR
40	SUBRAMANI	69	M	YES	30	<0.70	15%	510	BHI LUNG FIELDS	ACO
41	SHANMUGAM	70	M	NO	10	<0.70	NO REVERSIBILITY	234	BVM	NO EXACERBATOR
42	GAJENDIRAN	72	M	NO	25	<0.70	NO REVERSIBILITY	220	BVM	NO EXACERBATOR
43	RANGANATHAN	56	M	YES	10	<0.70	NO REVERSIBILITY	258	BHI LUNG FIELDS	NO EXACERBATOR
44	RANGARAJAN	58	M	YES	15	<0.70	1%	278	BVM	EXACERBATOR WITH CB
45	KANAGAVEL	47	M	NO	20	<0.70	12%	450	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
46	RAJU	44	M	NO	15	<0.70	NO REVERSIBILITY	298	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
47	MANIVEL	48	M	YES	15	<0.70	4%	272	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
48	DANIEL	54	M	YES	20	<0.70	6%	283	BVM	NO EXACERBATOR
49	ANTHONY	58	M	YES	25	<0.70	15%	560	BHI LUNG FIELDS	ACO
50	BALA	50	M	YES	20	<0.70	10%	436	BVM	EXACERBATOR WITH CB
51	PALANIAPPAN	60	M	NO	30	<0.70	15%	570	BHI LUNG FIELDS	ACO
52	RAJU	57	M	YES	25	<0.70	NO REVERSIBILITY	295	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
53	MOHIDEEN	59	M	NO	15	<0.70	NO REVERSIBILITY	296	BVM	EXACERBATOR WITH CB
54	KANIAPPAN	46	M	YES	20	<0.70	12%	435	BVM	EXACERBATOR WITH CB
55	BASHA	65	M	NO	30	<0.70	NO REVERSIBILITY	280	BHI LUNG FIELDS	NO EXACERBATOR
56	CHINAKARUPPAN	53	M	YES	20	<O.70	5%	355	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
57	JOTHEESWARAN	49	M	YES	15	<0.70	NO REVERSIBILITY	278	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
58	VASU	56	M	YES	20	<0.70	4%	325	BVM	NO EXACERBATOR
59	LINGESHWARAN	51	M	NO	15	<0.70	NO REVERSIBILITY	297	BVM	NO EXACERBATOR
60	MOHAMMAD	55	M	NO	25	<0.70	NO REVERSIBILITY	231	BVM	NO EXACERBATOR
61	MANIYAN	49	M	YES	15	<0.70	8%	379	BVM	EXACERBATOR WITH CB
62	KASINATHAN	44	M	NO	15	<0.70	NO REVERSIBILITY	277	BVM	EXACERBATOR WITH CB
63	KANTHAN	47	M	NO	15	<0.70	11%	234	BVM	EXACERBATOR WITH CB
64	NAGAPPAN	55	M	NO	20	<0.70		275	BVM	NO EXACERBATOR
65	RATHINAVEL	48	M	NO	15	<0.70	NO REVERSIBILITY	224	BVM	EXACERBATOR WITH CB
66	WILSON	42	M	YES	25	<0.70	15%	658	BHI LUNG FIELDS	ACO
67	VAITHIYANATHAN	60	M	NO	30	<0.70	NO REVERSIBILITY	276	BHI LUNG FIELDS	NO EXACERBATOR
68	ABDUL JAFFAR	59	M	NO	20	<0.70	NO REVERSIBILITY	255	BHI LUNG FIELDS	NO EXACERBATOR

69	KATHERESAN	48	M	NO	10	<0.70	NO REVERSIBILITY	298	BHI LUNG FIELDS	NO EXACERBATOR
70	VEERAMUTHU	58	M	YES	25	<0.70	10%	478	BVM	EXACERBATOR WITH CB
71	GANAPATHY	60	M	NO	30	<0.70	5%	315	BVM	EXACERBATOR WITH CB
72	ESWARAN	58	M	YES	25	<0.70	NO REVERSIBILITY	251	BVM	EXACERBATOR WITH CB
73	SARAVANAN	48	M	YES	15	<0.70	NO REVERSIBILITY	276	BVM	NO EXACERBATOR
74	SIVARAJA	50	M	YES	25	<0.70	15%	467	BVM	ACO
75	THIRUPATNI	61	M	NO	30	<0.70	7%	378	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
76	NAGESH	54	M	NO	20	<0.70	NO REVERSIBILITY	279	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
77	SUBURAYYAN	49	M	YES	15	<0.70	2%	456	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
78	RAJARAJAN	56	M	NO	20	<0.70	NO REVERSIBILITY	287	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
79	MUTHUPANDI	50	M	NO	20	<0.70	NO REVERSIBILITY	266	BVM	NO EXACERBATOR
80	RAMAMOORTHY	57	M	YES	25	<0.70	20%	868	BHI LUNG FIELDS	ACO
81	PANDIYAN	48	M	YES	15	<0.70	7%	324	BVM	NO EXACERBATOR
82	GANDIYAPPAN	45	M	YES	15	<0.70	NO REVERSIBILITY	346	BVM	NO EXACERBATOR
83	MANIKANDAN	49	M	YES	15	<0.70	NO REVERSIBILITY	436	BVM	EXACERBATOR WITH CB
84	KRISHNASAMY	57	M	NO	15	<0.70	5%	365	BVM	EXACERBATOR WITH CB
85	THILAGARAJAN	54	M	NO	20	<0.70	6%	545	BVM	EXACERBATOR WITH CB
86	PRAKASAM	48	M	NO	15	<0.70	4%	378	BVM	EXACERBATOR WITH CB
87	SAMPATH	59	M	YES	25	<0.70	8%	557	BVM	NO EXACERBATOR
88	KARUPPAN	65	M	NO	30	<0.70	15%	795	BHI LUNG FIELDS	ACO
89	BASKAR	45	M	NO	15	<0.70	5%	467	BHI LUNG FIELDS	NO EXACERBATOR
90	NEELAKANDAN	56	M	YES	25	<0.70	7%	344	BHI LUNG FIELDS	EACERBATOR WITH EMPHYSEMA
91	KUPPUSAMY	65	M	NO	30	<0.70	9%	324	BHI LUNG FIELDS	EACERBATOR WITH EMPHYSEMA
92	VEERASAMY	57	M	NO	20	<0.70	9%	456	BHI LUNG FIELDS	EACERBATOR WITH EMPHYSEMA
93	MURUGAN	47	M	NO	10	<0.70	8%	463	BVM	NO EXACERBATOR
94	VELRAJ	49	M	NO	15	<0.70	6%	354	BVM	EXACERBATOR WITH CB
95	AZHAGAPPAN	60	M	YES	25	<0.70	1%	678	BVM	EXACERBATOR WITH CB
96	SENTHIL	45	M	YES	15	<0.70	NO REVERSIBILITY	655	BVM	NO EXACERBATOR
97	MURUGESAN	47	M	NO	20	<0.70	4%	567	BVM	NO EXACERBATOR
98	KALAIARASAN	48	M	YES	20	<0.70	20%	957	BHI LUNG FIELDS	ACO
99	PALANIVEL	50	M	NO	15	<0.70	3%	457	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
100	THANIKACHALAM	57	M	NO	20	<0.70	5%	654	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
101	JANAKIRAMAN	53	M	NO	15	<0.70	11%	788	BHI LUNG FIELDS	EACERBATOR WITH EMPHYSEMA
102	KNAGAIAH	55	M	YES	25	<0.70	8%	465	BHI LUNG FIELDS	EACERBATOR WITH EMPHYSEMA
103	JAYARAJ	43	M	NO	10	<0.70	NO REVERSIBILITY	343	BVM	NO EXACERBATOR

104	SELVARAJ	46	M	YES	10	<0.70	NO REVERSIBILITY	255	BVM	EXACERBATOR WITH CB
105	CHELLAMUTHU	57	M	YES	20	<0.70	15%	876	BHI LUNG FIELDS	ACO
106	VINCENT	50	M	YES	15	<0.70	6%	346	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
107	HARI	47	M	NO	15	<0.70	NO REVERSIBILITY	245	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
108	MOHAN	45	M	NO	15	<0.70	7%	452	BVM	EXACERBATOR WITH CB
109	CHINNARAJ	42	M	YES	15	<0.70	20%	1124	BHI LUNG FIELDS	ACO
110	JOTHILINGAM	48	M	YES	20	<0.70	4%	768	BHI LUNG FIELDS	EACERBATOR WITH EMPHYSEMA
111	THANGARAJ	41	M	YES	15	<0.70	6%	346	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
112	GIRI	50	M	NO	30	<0.70	9%	355	BHI LUNG FIELDS	EACERBATOR WITH EMPHYSEMA
113	GURULINGAM	57	M	NO	30	<0.70	2%	422	BVM	NO EXACERBATOR
114	VINAGAYAM	52	M	YES	20	<0.70	15%	754	BHI LUNG FIELDS	ACO
115	THANIGARAJ	59	M	NO	15	<0.70	3%	566	BVM	NO EXACERBATOR
116	AHMED BASHA	60	M	NO	25	<0.70	8%	325	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
117	BALAIAH	62	M	NO	30	<0.70	9%	436	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
118	NAGESHWARAN	51	M	NO	15	<0.70	1%	314	BVM	NO EXACERBATOR
119	ILAIYARAJA	56	M	NO	20	<0.70	7%	435	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
120	NAGARAJ	61	M	NO	25	<0.70	10%	334	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
121	ABDUL MAJEED	57	M	YES	25	<0.70	15%	875	BHI LUNG FIELDS	ACO
122	KANAGARAJ	51	M	YES	15	,0.70	9%	365	BHI LUNG FIELDS	EXACERBATOR WITH EMPHYSEMA
123	ETHIRAJ	55	M	YES	20	<0.70	20%	985	BHI LUNG FIELDS	ACO
124	KATHIRAVAN	71	M	NO	30	<0.70	15%	450	BHI LUNG FIELDS	ACO