A brief survey on the effect of smoke of different sources on COPD patients

By

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A thesis submitted to the Department of Pharmacy in partial fulfillment of the requirements for the degree of
Bachelor of Pharmacy (Hons.)

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Brac University
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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The project titled “A Brief Survey on effect of smoke of different sources among COPD patients” submitted by Nusrat Nawal (16146014) of Spring, 2016 has been accepted in partial fulfillment of the requirement for the degree of Bachelor of Pharmacy (Hons.) on, 23rd January, 2020.

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Ethics Statement

This study does not involve any human or animal trial.

Abstract

The study was performed on patients diagnosed with COPD (Chronic Obstructive Pulmonary Disease) in different age and stages of life. It was done with a view to looking up to the types & sources of smokes they are exposed in their regular life as in number of hours per day. Sources of smoke created from different stoves systems, use of biomass fuels, mosquito repellants (coil or aerosol), industrial smoke, room fresheners & perfumes were considered. A questionnaire was prepared based on which data from participants were gathered and analyzed. All the patients had significant levels of airflow limitation according to the Spirometry and other tests. The conditions ranged from initial stages of the disease to acute exacerbations, partial lung failure to lung cancer. COPD being irreversible in nature, management of the disease was done with suitable therapeutic agents. Patients seem to face significant, pronounced & frequent symptoms of the disease as they were found unaware due to lack of counseling. They were ignorant about the factors and actions to be taken to avoid daily exposure to smoke of various sources.

Keyword: COPD, PAH, biomass fuel, Spirometry test, FEV_1 / FVC ratio.

Dedication

Dedicated to the Almighty and my parents

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On the completion of this project with success, a couple of people have shown a continuous support thus I am taking some time to thank those ones who have been involved with this project.

Firstly, I would whole heartedly thank the Almighty Allah as the project is completed on time. I present my heartiest gratitude to the most helpful supervisor **Dr. Md. Abu Bakar** (Associate Professor, Department of Pharmacy, Brac University) whose constant guidance and motivation has enlightened the path towards the completion of this project. I could not have given the project a proper shape without his support and encouragement. I am really thankful to our respected chairperson, **Dr. Eva Rahman Kabir** (Professor and Chairperson, Department of Pharmacy, Brac University) for her massive support throughout. Then I would like to show my gratefulness towards my parents, family and friends who helped me out with their utmost capabilities throughout the completion of this project. I would surely show appreciation to the hospitals I visited for the procedure. Lastly, I would like to thank the participants for sharing their experience and enriching my span of knowledge.

Table of Content

List of Tables

List of Figures

List of Acronyms

COPD	Chronic Obstructive Pulmonary Disease
ACOS	Asthma COPD Overlap Syndrome
AE	Acute Exacerbation
FEV_1	Forced Expiratory Volume in 1second
FVC	Forced Vital Capacity

Chapter 1

Introduction

1.1 Clinical definition of COPD

According to the GOLD (Global Initiatives for Lung Diseases) guidelines COPD is defined as a preventable and treatable disease having several major extra pulmonary effects often contributing to the severity in every individual patient having a progressive limitation of airflow with anomalous inflammatory responses in lung towards toxic particles or gases (Global Initiative For Chronic Obstructive Lung Disease Global Strategy For The Diagnosis, Management, And Prevention Of Chronic Obstructive Pulmonary Disease (2018 Report), 2018).

According to the GOLD Guidelines of 2018, COPD is currently the fourth leading cause for death as it has caused 6% of deaths over the world in the year 2012.COPD standing for Chronic Obstructive Pulmonary Disease, is a well-known, preventable & curable disease that presents airflow limitations caused by alveolar or airway abnormalities through obnoxious gases and particles. Limitation of airflow are often seeming to be caused by diseases like emphysema & obstructive bronchiolitis. Factors affecting the origin of disease vary among the patient population and can also vary with the different lifecycle stages & practices of an individual. In an inflamed lung the destruction of parenchymal cells & narrowed airways terminates the linkage of alveoli and small airways resulting in altered elasticity of lung, mucociliary dysfunction & the expiration disability of small airways. Prevalence of COPD widely differs among countries, which is the summation of factors like long-term exposure to noxious gases & particles, hyper-responsiveness of airways, inadequate growth of lung in the early years of life, genetics etc. Here, smoking tobacco or being exposed to smoke

secondarily, household smoke like from burning wood, paper or other biomass fuels, PAHs and other air pollutants are some prominent threat to the susceptible people.

In a study performed from 1990 to 2004 among 28 countries it was found that COPD is more prevalent in men who are smoker or former smoker aging 40years or above in comparison to nonsmoker, other age ranges and women respectively. The morbidity related to COPD increases with increasing age for the additional diseases like diabetes, musculoskeletal diseases, cardiovascular diseases being associated to COPD and aging. Association of COPD in economy is noticeable as cost for respiratory diseases being approximately 6% of the whole healthcare budget in the European Union where 56% of that accounted by COPD. Also, exacerbation holds the major proportion of it with disease progression. Furthermore, COPD hampers the economy of a developing country as COPD makes the patient leave their job in addition to 1 of their family members as a helping body leading to a threatened economy by hampering the nation capital as human resource.

Smokers are more susceptible to development of COPD over their lifetime although some additional factors like sex, occupational exposure, and economic conditions may contribute as well. Socioeconomic status affecting a child's weight during birth which may refer to the impaired lung development or higher life expectancy seems to exhibit increased risk towards getting exposed to various risk factors. Deficiency of alpha 1-antitrypsin (AAT) which is a circulating serine protease inhibitor is a genetic factor effecting COPD being relevant to a very small population in the world. Siblings who smoke of a COPD patient are at a risk of getting the disease due to correlation of genetic & environmental factors. Airways & parenchyma getting aged & extent of exposure to risk factors have effects in development of the disease. Previously, men were found to be more at risk of the disease due to exposure to smoke but in recent times the exposure to tobacco smoke of both the genders are equivalent which shows the changing smoking habits (Global Initiative For Chronic Obstructive Lung

Disease Global Strategy For The Diagnosis, Management, And Prevention Of Chronic Obstructive Pulmonary Disease (2018 Report), 2018).

1.2. Mechanism

Activation of structural cells including alveolar cells (endothelial, epithelial, fibroblasts) and involvement of both adaptive and innate immunity systems are supposed important in case of the inflammation found in COPD patients. Smoke of all kinds and other pollutants activates the epithelial cells with the production of interleukin (IL)-1 beta, (TNF) alpha, granulocyte-macrophage colony–stimulating factor (GM-CSF), IL-6 and CXCL8 (IL-8). Local fibrosis takes place in small airways induced by TGF (Transforming Growth Factor). Production of mucus from goblet cells along with secretion of defensins, antioxidants and antiproteases work in the defense mechanism of epithelial cells present in airways. This may get hampered by exposure to smoke & other harmful particle. Pronounced expression of EGFR (Epithelial Growth Factor Receptors) impact the proliferation of basal cells causing squamous metaplasia in airway as well as higher susceptibility to bronchial carcinoma in COPD patients (Chung & Adcock, 2008)(Barnes et al., 2003).

1.2.1 Neutrophils

Raise in neutrophil numbers is found in BAL fluid and sputum of people with COPD representing the rigorousness of the disease. The wall of airways and lung parenchyma shows less number of them due to their reflection of rapid transit system through the tissues. The production, release and survival gets assisted by factors namely GMF and G-CSF (Granulocyte Colony Stimulating Factor). Neutrophils get adhered to the parenchyma and airways initially through endothelial cells followed by migration of themselves inside the respiratory tract with the direction of chemotactic factors like E-selectin showing pronounced response in airways of COPD patients. In the sputum supernatant of COPD patients,

increased proportion of granule proteins e.g. Human Neutrophil Lipocalin and MPO (Myeloperoxidase) is found causing the activation of neutrophils. Alveolar destruction gets accelerated by several secretion of neotrophils for instance proteinase-3, elastase, cathepsin G and some of the Matrix Metalloproteinase. Rise in neutrophil number in the airways result in excess mucus secretion mediated by goblet cells & submucosal gland.

1.2.2 Eosinophils

Excess number of eosinophil in BAL fluid and airways may represent a stable kind of COPD whereas there is a predicted response towards corticosteroids as in case of asthma neutrophils are supposed to be the dominant leukocyte. Also, eosinohils can be degranulated due to higher level of neutrophil elastase in COPD patients.

1.2.3 Macrophages

Macrophages give the idea about the disease progression showing an increased number in broncho-alveolar fluid (BAL), airways, sputum and lung parenchyma which reaches about 5 to 10 folds than in people with COPD in comparison to others. If emphysema patients are compared to normal smokers, an increment of macrophages in parenchyma specifically tissue & alveolar space, up to about 25 folds is seen. Macrophages having direct effect on the severity of COPD have properties of getting activated by smoke or its extracts resulting in the release of tumor necrosis factor (TNF-a), leukotriene B4 (LTB4), Interleukin -8, Monocyte Chemotactic Peptide (MCP)-1, reactive species of oxygen as well as CXC chemokines. All these substances assist in describing the relation of smoke & the inflammation in COPD. Several elastolytic enzymes are also found to be secreted by the alveolar macrophages namely Matrix Metalloproteinases(MMPs), neutrophil elastase extracted from neutrophils etc and it was found that these macrophages release a greater extent of inflammatory proteins showing a more pronounced ability to lyse the elastic area in COPD patients with the exposure of smoke. Of all this substances MMP-9 is found to dominate in elastolytic enzyme

releasing activity from macrophages of COPD patients. Even in cultured media for duration of 3 days, there are noticeable difference in the macrophages of COPD patients, normal smokers and nonsmoker control subjects.

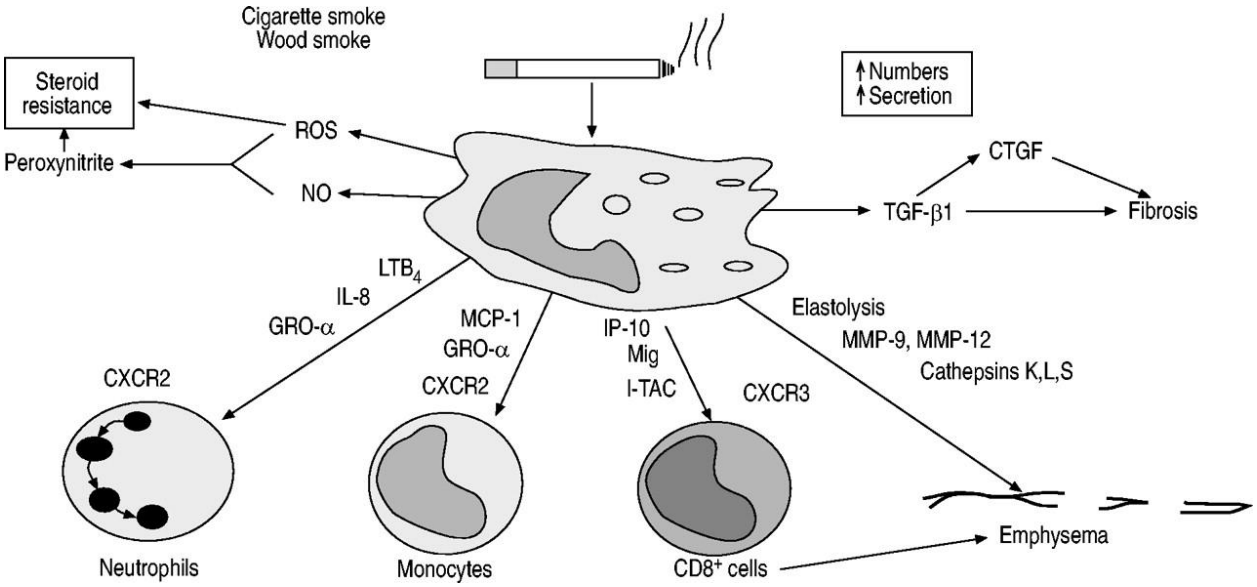

Figure 1: Molecular & Cellular mechanism of COPD (Barnes et al., 2003)

Response derived from monocyte-selective chemokines are the reason behind the increment of macrophage numbers in smoker COPD patients where increased MCP-1 in BAL & sputum of COPD patients in addition to an amplified expression of macrophages. Presence of COPD also makes increased CXC chemokines that are chemo-attractant and act by CXCR2 in BAL fluid and sputum. Despite the expression of CCR2 by all the monocytes, 30% of monocytes are seen expressing CXCR2 instead which may behave in a different way due to their transformation into monocytes. In general, macrophages are known to be survive for a long period in lung with a low proliferating ability, but if monitored with PCNA (Proliferative Cell Nuclear Antigen) an increase in proliferation are found. Presence of Bcl-XL an anti-apoptotic protein & p21CIP/WAF1 are noticed in macrophages of smokers referring to the long

survival of macrophages in COPD patients who are smokers as well. In macrophages from normal smokers, corticosteroids diminish the release of TNF-a, IL-8 and MMP-9. In case of COPD patients, cytokines, proteases and chemokines are ineffectual in stopping the inflammation just like corticosteroids. A diminished action of HDAC (Histone deacetylase) may cause the resistance towards corticosteroids whereas the gene functions by activating the glucocorticoid induced inflammatory genes resulting in deactivation of those genes and thus show a connection with an increased cytokine (TNF-a and IL-8) secretion. Some other drugs instead of corticosteroid be proven more useful as it does not inhibit the protease and cytokines secretion. In spite of macrophages having the ability to run phagocytosis in bacterial cells, a spiked load of bacteria may impair the ability in COPD patients (Barnes et al., 2003).

Recognition of apoptotic cell by macrophages are done through expressed PS (phosphatidylserine) resulting in interaction with specific receptors present on surface of macrophages. Macrophages ingest the apoptotic granulocytes and TGF-b1 secretion is induced resulting in the cleavage of the receptors by neutrophil elastase impairing the apoptotic neutrophil up taking property with their raise in the airways.(Barnes et al., 2003)

1.2.4 T-lymphocytes

In lung parenchyma and airways (both peripheral & central), more specifically CD8 in comparison to CD4 achieve a raised number of T-lymphocytes are seemed in COPD patients. Extent of airflow obstruction, alveolar destruction and T-cell number are interrelated factors. The ratio of CD4 and CD8 cell differs from that in COPD patients than in smokers who may not have airway limitations. Homing of T-cells in lungs needs some steps to be taken place namely activation, adhesion & chemotaxis occurring selectively, whereas the mechanism through which CD4 and CD8 cell get gathered in lungs and airways of COPD patients (Barnes et al., 2003).

1.3. Symptoms

Symptoms of COPD varies depending on the age, extent of exposure to risk factors of individual patients, severity of disease, lifestyle behaviors etc. Particular symptoms vary day to day in intensity and pave the way for the airflow limitation to the lungs over a time period. Also, similar symptoms faced by different patient vary and thus symptoms are studied with great importance before & after diagnosis as it gives indications about steps to be taken in disease management.

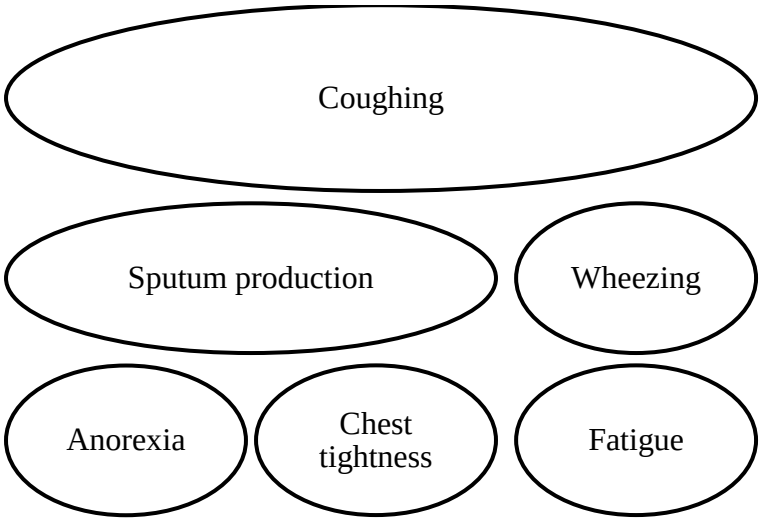

Figure 2: List of symptoms

1.3.1 Coughing

The primitive symptom found is chronic coughing which might be both unproductive and productive in nature. At the primary stages this symptom seems to be intermittent while in later stages its noticed regularly often whole day every day. Also there might be cases where cough is not present but limitation of airflow is significant. According to GOLD guidelines, more than 30% of patients undergo regular coughing with sputum production. Coughing might be misunderstood as a predicted symptom for smokers and those who are highly exposed to environmental pollutants. Prolonged and powerful events of coughing may result in rib fractures (Global Initiative For Chronic Obstructive Lung Disease Global Strategy For

The Diagnosis, Management, And Prevention Of Chronic Obstructive Pulmonary Disease (2018 Report), 2018).

1.3.2 Sputum production

Commonly COPD patients are found to produce tenacious sputum with coughing. The production of sputum may vary in intermittent stages with sudden outbreak and sudden remission. Sputum being produced which is purulent in nature indicates increased number of inflammatory mediators resulting in bacterial exacerbation. Here, sputum production is not enough for evaluation of presence of COPD as sputum being produced for 2-3months regularly for 2 or more consecutive years indicates the presence of bronchitis. Also, patients seem to engulf the sputum produced rather than expectorating it out due to cultural behaviors.

1.3.3 Chest tightness & wheezing

Although the presence of chest tightness & wheezing neither does confirm the presence of the disease nor the absence of these symptoms exclude a patient from being identified with COPD. Chest tightness being not localized fully might be arising from intercostal muscles contracting isometrically. The symptom being muscular in nature often seems to follow exertion.

Wheezing might vary as in some cases audible wheezes are heard during auscultation without any abnormalities being present whereas in other cases wheezes are heard during inhalation and exhalation.

1.3.4 Dyspnea

The symptom is typically described as a feeling of heaviness in chest, increased breathing effort, hunger for air, gasping etc. This symptom majorly causes the anxiety associated to the disease.

1.3.5 Other symptoms

Apart from the aforementioned symptoms a couple of additional ones could be felt by patient undergoing through severe disease conditions such as fatigue, weight loss and anorexia which might indicate some other related diseases like lung cancer, tuberculosis etc. Syncope along with coughing results from increased intra-thoracic pressure.

1.4 Comparison between asthma and COPD

Often, COPD is confused with other lung disease like asthma, bronchitis, emphysema but they are not similar. Each of them different & specific pathophysiology involved but those diseases do add to the risk of a person's susceptibility to COPD.

In consideration of asthma & COPD, both similarities and differences exist. The inflammation caused in asthma is held by eosinophils & in COPD it's held by neutrophils. Also, the pharmacological agent used in asthma is corticosteroid whereas for COPD it is not the same. But often times the symptoms of exacerbation turn out to be similar as the respective cell (eosinophil or neutrophils) numbers or proliferation do alter resulting in suggestion of corticosteroids in the exacerbated situation of COPD which otherwise is not the case. Airway obstruction due bronchoconstriction of smooth muscle, increased response of airway towards allergens in addition to increased eosinophils & activated T-cells whereas in COPD, the smooth muscle obstruction & constriction occurs from excess secretion of mucus and infiltration of inflammatory cells in mucosa resulting in denaturation of alveolar structure hampering the pulmonary circulation and oxygenation.

Clinical representation of COPD and asthma patients also differs at some points. In COPD patient's shortness of breath which is progressively deteriorating, hampered physical activities in addition to mucous being produced with cough in people who were former smokers aging 40years or above. On the other hand, asthma patients have frequent and spasmodic coughing and wheezing during exhalation in addition to tightness in their chest & short breaths and can be found in nonsmokers, smokers and children as well.

Both the diseases being obstructive in nature hold some more dissimilarity. The obstruction in COPD is irreversible but in asthma it can be reversed by treatment or spontaneously. In asthma patient's symptoms are not constant and often show normal lung functions without any experience of dysfunctional lungs activity if continuity of medication is ensured. But in COPD symptoms remain latent upto a FEV_1 (Forced Expiratory Volume in one minute) level of 50% of the predicted value and symptoms may keep worsening even if medication is continued as prescribed. Symptoms of asthma can be minimized by inhalation of corticosteroids, short-acting bronchodilators or often long-acting beta 2-agonists if solo steroid therapy turns out ineffective for the patients. In contrast, bronchodilators are the first treatment option for COPD but combination of beta 2-agonists and bronchodilators in exacerbated situations. If corticosteroids are prescribed to COPD patients, it can be titrated depending on the rate or degree of exacerbation and can be withdrawn if intended improvement not found. Moreover, occurrence of COPD and asthma can happen at the same time in an asthma patient who is smoker. Identification of the exact disease is thus needed in addition to adequate patient knowledge. (pharmaceutical-journal.com-Knowing the differences between COPD and asthma is vital to good practice, n.d.)

1.5 Asthma COPD Overlap Syndrome (ACOS)

Differentiating asthma from COPD can be problematic in cases of smokers and elderly patients. ACOS is confused with both asthma & COPD having overlapped symptoms and features related to both partially. Thus approaching the diagnosis in a sequential way is preferred showing the assurance of any chronic disease in airways or lungs being present based on spirometric studies through the syndromic classification of asthma, COPD and the overlap named as the Asthma COPD Overlap Syndrome or ACOS in short. Importance is to be given on the diagnosis based on holistic investigation so that identification of treatment procedure is not ambiguous (Diagnosis of Diseases of Chronic Airflow Limitation: Asthma COPD and Asthma-COPD Overlap Syndrome (ACOS) Based on the Global Strategy for Asthma Management and Prevention and the Global Strategy for the Diagnosis, Management and Prevention of Chronic Obstructive Pulmonary Disease. 2014, 2014).

ACOS is identified in people aging 40 or more years but may be present in children as well. Exertional dyspnea is noticeable with higher possibilities and frequencies than in COPD. The airways are limitation here is not fully reversible, neither fully reversible. In X-ray tests of ACOS patients hyperinflation is found alike in COPD. Neutrophils & eosinophils are found in sputum.

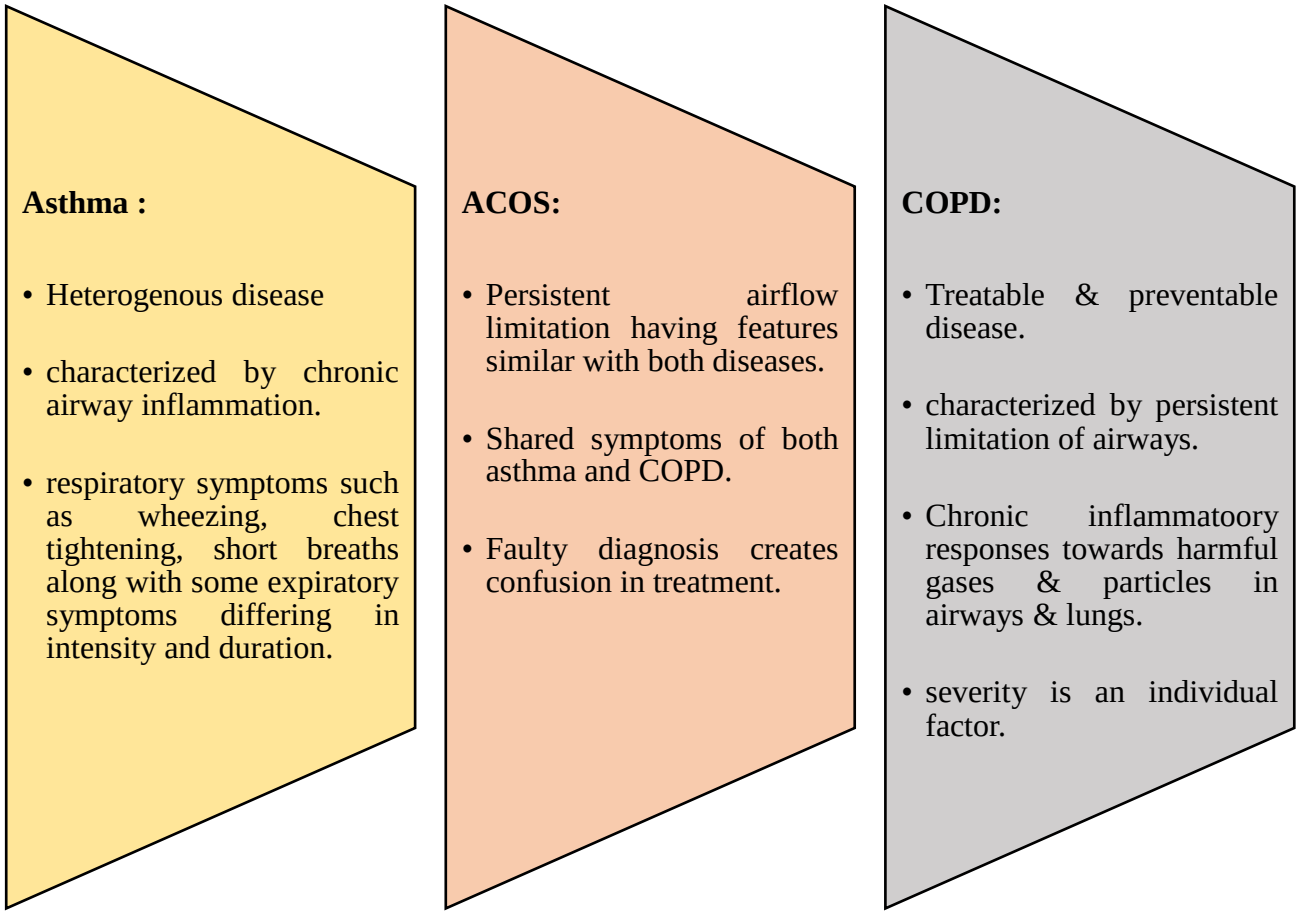

Figure 3: Typical differences in the definition of Asthma, ACOS& COPD

1.6 Pathology of the disease

Significant pathological changes found in COPD includes chronic inflammation occurring due to increased number of inflammatory cells present in lung parenchyma, airways and pulmonary vasculatures or other areas of lung resulting in structural changes after continuous injury & repair (Global Initiative For Chronic Obstructive Lung Disease Global Strategy For The Diagnosis, Management, And Prevention Of Chronic Obstructive Pulmonary Disease (2018 Report), 2018).

1.6.1 Pathogenesis

1.6.1.1 Protease–antiprotease imbalance

Proteases are enzymes destructing the major connective tissue present in parenchyma of lungs named elastin and antiproteases are those who oppose the action of proteases. Proteases

are found to be released from several epithelial & inflammatory cells and their amount in found pronounced in COPD patients.

1.6.1.2 Inflammatory cells & cell mediators

Increased number of inflammatory cells like neutrophils, lymphocytes & macrophages in lung parenchyma, peripheral airways, pulmonary vessels & other areas of lungs are responsible for release of different inflammatory cell mediators. These mediators are released by different structural cells & epithelial cells as well. The released inflammatory cell mediators pull the chemotactic factors from the circulation with a view to catalyzing the inflammatory process causing structural damage in lungs. According to the GOLD guidelines, a deficiency in Immunoglobulin A levels in a localized manner plays a role in inflammation of small airways.

1.6.1.3 Oxidative stress

The mechanism of COPD gets amplified by oxidative stress where different biomarkers of the stress such as hydrogen peroxide and 8-isoprostane are found in a pronounced level in sputum, exhaled condensate during breathing and systemic circulation of patients. Source of oxidants vary from tobacco smoke to other indoor & outdoor particulate materials as they activate the inflammatory cells namely neutrophils & macrophages. Also, reduced levels of transcription factors for antioxidant genes are causing reduced endogenous antioxidants resulting in more pronounced oxidative stress.

1.6.1.4 Peribronchiolar & interstitial fibrosis

Overproduction of growth factors are noticed in COPD patients having airway inflammation which precedes repeated airway injury & fibrosis acting as a contributing factor to small airway limitation.

1.6.2. Pathophysiology

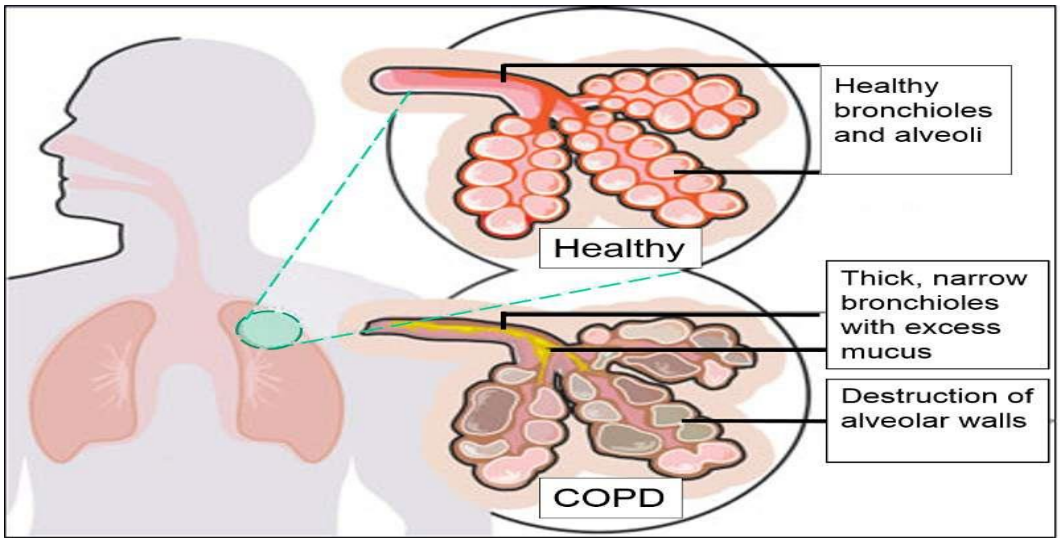

Figure 4: Pathophysiology of COPD

1.6.2.1 Gas trapping & airflow limitation

A declined FEV_1/FVC ratio & FEV_1 value is interrelated to conditions like fibrosis, formation of luminal exudates in the airways in COPD patients. Limitation in the airway results in conditions like hyperinflation due to gas entrapment during exhalation and if the inflation remains stable, may lead to a declined inspiration capacity. Moreover, these factors causes altered contraction properties of lung muscles.

1.6.2.2 Abnormal exchange of gases

Hypercapnea or excess carbon dioxide retention and hypoxemia or declined oxygen level are conditions created by abnormal gas exchange. Reduced ventilation is caused by increment in dead space for ventilation as a result of the abnormality which further causes carbon dioxide retention. Hyperinflation and ventilating muscle impairment amplifies the retention of carbon dioxide and patients face increases effort for breathing.

1.6.2.3 Excessive mucous secretion

Hypersecretion of mucous is caused by enlargement of submucosal glands & increase in goblet cells as they get induced airway irritation created by smokes of different sources and harmful particles**.** Epithelial Growth Factor Receptor (EGFR) get activated by functional activities of different cell mediators and proteases ultimately causing excessive secretion of mucous.

1.6.2.4 Pulmonary hypertension

Constriction in small arteries is caused by hyperplasia or hypertrophy of smooth muscles bringing structural changes and eventually resulting in increased pulmonary pressure in progressed level of the disease. Exacerbation of the disease might lead to severe conditions where partial damage of heart as well.

1.6.2.5 Systemic features

Conditions like abnormal gas exchange, increased number of inflammatory cells hyperinflation and airflow limitation often correlates to diseases like ischemic heart disease, heart failure, osteoporosis, diabetes, skeletal muscle wastage and other metabolic syndromes.

1.6.2.6 Exacerbation

Bacterial & viral infection in respiratory tract induces exacerbation of the disease with increased entrapment of gases, reduced expiratory flow and pronounced limitation in airways. Often conditions namely pneumonia, cardiac failure and thromboembolism might imitate the exacerbated situations in COPD.

1.7 Risk factors assessment

1.7.1 Smoke from burning biomass fuels

Biomass fuel such as wood, animal dung, residues of crops and coal are used in indoor areas for various uses (heating, lighting and cooking). Use of these fuels turn into a source of

household air pollution and mainly affect the children and women in a huge proportion. Biomass smoke consist of majorly carbon monoxide, nitrous oxides, formaldehyde, sulfur oxides etc. with around 200 different compounds. Biomass fuels being a cheaper alternative to electricity and petroleum gas, it is prominently used in developing countries. In today's time use of biomass fuel is increasing in developed countries as well. Basically, the developed countries use biomass fuel in baking wood-fire pizzas, grills, barbeques etc. Countries like China, India, Turkey and sub-urban Africa are found to use these (Holm et al., 2014).

According to estimation around half of the world's population has been found to be users of these fuels. An international workshop held on May, 2011 held by NIH on the topic "Health Burden of Indoor Air Pollution on Women and Children" included detailed discussions on studies done about the correlation of use of biomass fuels and COPD and other respiratory diseases. There were studies done on users of different stove types and their symptoms were noticed along the results of spirometry test. There was a noticeable association of biomass fuels exposure of adult women and COPD but had some confusion with asthma. Data that were found depicted a relation between the exposure and reduction in lung function mostly but no pathophysiological proof was found (Diette et al., 2012).

The population in Low and High Middle Income Countries are mostly exposed to HAPs. Household Air Pollution (HAP) is regarded as the leading environmental cause of death around the world. Use of biomass and coal as fuel in different daily chores contribute hugely to HAP. A prediction says that 65million deaths from COPD can happen as a combined effect of smoking and use of biomass fuel between the year 2003 and 2033 in China.

COPD patients living in rural areas, those who are smokers, less educated, aged, having lower body mass index (BMI) and poor ventilation system in their households and those being exposed to biomass fuels and dust due to their occupation have a higher prevalence.

In the workshop a particular group worked on finding interrelation between HAP and COPD and literature search was performed. It was found that children and women were subjected to the highest exposure to indoor burning of biomass fuels in their daily activities. Pollutant concentrations were measured and found to be high typically as the particles that are released after burning solid biomass fuel is found to be several milligrams present per cubic meter.

A cross-sectional study suggests significant correlation in exposure to smoke from burning biomass fuel and respiratory symptoms and development of COPD. A study done in Brazil has searched for correlation of exposure to particulate matter derived from combustion of biomass fuel and liquefied petroleum gas in two different groups. It was found that exposure to biomass fuel lead to reduced lung function, increased respiratory symptoms towards developing COPD.

A different meta-analysis held in a wide range of countries says that population exposed to biomass smoke showed combined odds ratio (OR) of 2.44 towards development of COPD in both the genders. Tobacco smoking along with exposure to smoke of biomass fuel seems to project a synergistic effect in COPD development with OR value 4.39.

According to a study COPD in rural areas are mostly found to be women who are exposed to open fires for their lifetime. These patients seem to show a worsened disease condition with more pronounced obstruction in airways, less carbon monoxide diffusing capacity if compared to the patients who smoke tobacco. Autopsy results indicate increased thickening of pulmonary arteries and vessels and pulmonary hypertension (Pérez-Padilla et al., 2014).

1.7.2. Smoke from mosquito coil

COPD has a couple of reasons behind progression of the disease in the ones who are nonsmokers and one of them are exposure to smoke created from burning mosquito coils. A cross sectional study done in a clinic over a year (December 2010-December 2011) shows that 82.2% patients showed moderate to severe disease that used biomass fuel along with exposure to smoke from burning of mosquito repellant coils.

Mosquito coil being a prominent source of indoor air may show some effect on the COPD patients, are comprised of some substances where an insecticide is prominent, that burn with the emission of smoke. Pyrethrum marc is supposed to be present up to 25% of the residue which is compulsory for the making of any mosquito coil conventionally with tabu powder, sawdust, ground leaves, barks and coconut shell flour as additional burning agents. Then a better composition of all the dry ingredients which selected by sawdust with mesh sizes 70 & 200, pyrethrum marc, coconut shell flour, potato starch & the insecticide (0.5-3%) etc. Coils made with potato starch as binder showed better sustainability as it lasts for about 7-8hours and structural integrity (US4144318, n.d.).

Composition of mosquito coils according to United States Patent No. 4114318, published on March 13, 1979 is as following:

Table 1: Composition of mosquito coils

Ingredients	**Amount by weight in percentage**
Potato starch	16-26
Mosquito coil carrier agent	72-83
Burning aid	0-2
Insecticidal material	0.5-3

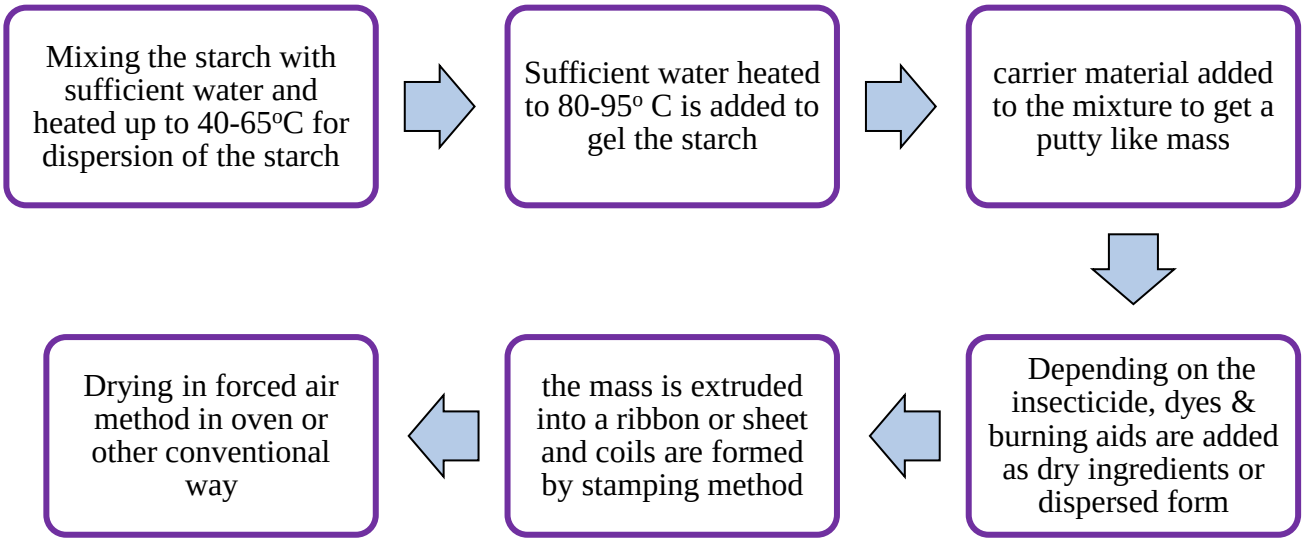

Figure 5: Preparation of mosquito coils

1.7.3. PAH affecting progression of COPD

Chemically, Polycyclic Aromatic Hydrocarbons are organic compounds with two or more benzene rings attached in different arrangements like angular, linear or clustered. Examples include Anthracene, Dibenz-anthracene, Pyrene etc. PAH or Polycyclic Aromatic Hydrocarbons are known to be components generated from incomplete burning of coil, biomass fuel, wood and petrol. Indoor heating and motor vehicle exhaust are considered among the major sources of PAH. As these components remain in gas phase in environmental air, human body can be in easy exposure to these. Also the highly lipid soluble nature of PAHs makes them readily absorbed in the gastrointestinal tracts of human body. This results in a wide spread distribution of these compounds in several body tissues and accumulation in fat tissues specially. Several of these components are found to have mutagenic and carcinogenic properties.

A study was performed by Peking University Health Science Centre(PKUHSC), on 45 stable COPD patients to find out the effect of particulate matter and PAHs on COPD patient by

evaluating the systematic oxidative stress related biomarkers. The participants were called for two follow ups between November 2014-May 2015. The biomarkers that were considered are Malondialdehyde (MDA) and 8-hydroxyl-2'-deoxyguanosine in the urine samples of the participants. The biomarkers were analysed by HPLC and ELISA. The lung function index were measured to have an idea about the severity of the disease of the participants. The result of the study showed a signifcant effect of Ultrafine particles and PAHs on exacerbation of the systemic oxidative stress in COPD patients.

Another study was done to find out the correlation between exposure of particulate matter having a diameter of less than 2.5 micrometer ($PM_{2.5}$) and pathogenesis of COPD. The study was done on Human lung cell line (BEAS-2B) with organic water soluble components of $PM_{2.5}$. The result found showed that the particulate components are involved in creating dysfunction in Pulmonary Epitheial Barrier by depleting proteins from zona occludence. Oxidative stress is induced by the extracts resulting in an increased production of proinflammatory cytokines by the cells in cell line and a decrease in expression of alpha 1-antitrypsin. This mechanism involes in increasing the risk of COPD (Yang et al., 2017).

1.8 Diagnosis methods

A loss of lung function up to 50-60% of predicted value tends to face the symptoms. COPD is strikingly under-diagnosed having recent estimates of between 25 and 50% of patients who are clinically undetected or misdiagnosed instead of raised percentages of consciousness noticed in the past 10 years. However, wrong diagnosis is common in cases of labeling patients with COPD or asthma due to confusion.

There are some main clinical features that represent COPD such as regular or intermittent and productive cough which is chronic, breathing difficulty during exertion found to be either intermittent or persistent, Sputum production showing any pattern of sputum production

along with recurrent exacerbations of bronchitis. Also subjects who age 40years and above having a history of contact to risk factors, particularly tobacco smoke, work-related pollutants and dusts and cooking habits and usage of biomass fuels are considered for performing the test according to the recommendation of the GOLD guidelines.

1.8.1 Spirometry

The term refers to the method where assessment of lung function is done from the measurement of the air volume that is expelled from patients' lungs following a maximal inspiration. In the diagnosis of COPD, the interpretation done from the indices found from this typed of forced exhalation exercise is one of the most accurate ways. The values found from the test done on each patient is compared against the predetermined normal values that are found in a person of a particular gender, age, height and ethnicity and used in the measurement of a degree to which the airways are obstructed. Depending on the results from this test the disease can be divided among degrees of severity from mild, moderate to severe (Johns et al., 2014).

Spirometry is considered as the most useful test for COPD diagnosis as it confirms the presence of airway obstruction with an FEV_1/FVC ratio < 0.7 after bronchodilator. This also provides an index of disease severity at the same time helping in the differentiation between asthma from COPD. The test helps detecting COPD in subjects who are exposed to risk factors with a proper idea of disease progression, measurement of how the subjects are responding to therapy given and prediction of prognosis and long-term survival. Other uses of the test includes the determination of the presence, absence and severity of any lung defects, screening of subjects who are considered to be in different risky occupational environments, screening for certain occupations done in earlier stages before recruitment and also fitness of divers are assessed.

Procedure

The procedure is divided in three steps namely the preparation of patient for the test, the measurement of FEV1, FVC, and Flow–Volume Curves and the differential step for diagnosis (Spirometry For Health Care Providers Global Initiative For Chronic Obstructive Lung Disease (Gold) Contents, n.d.).

A. Preparing the patient for the procedure

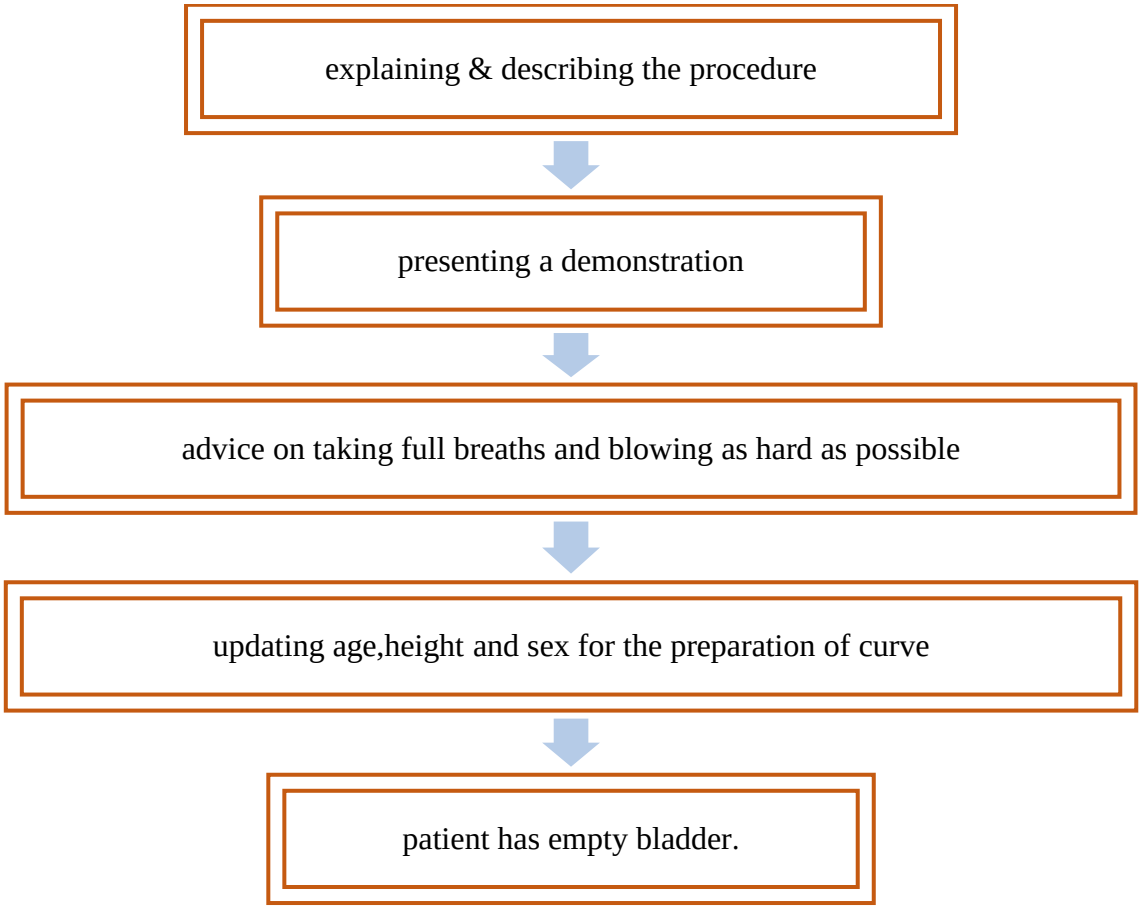

Figure 6: Flowchart showing the steps in preparing a patient for the test

Figure 7: A patient performing spirometry test

B. Measurement of FEV1, FVC, and Flow–Volume Curves:

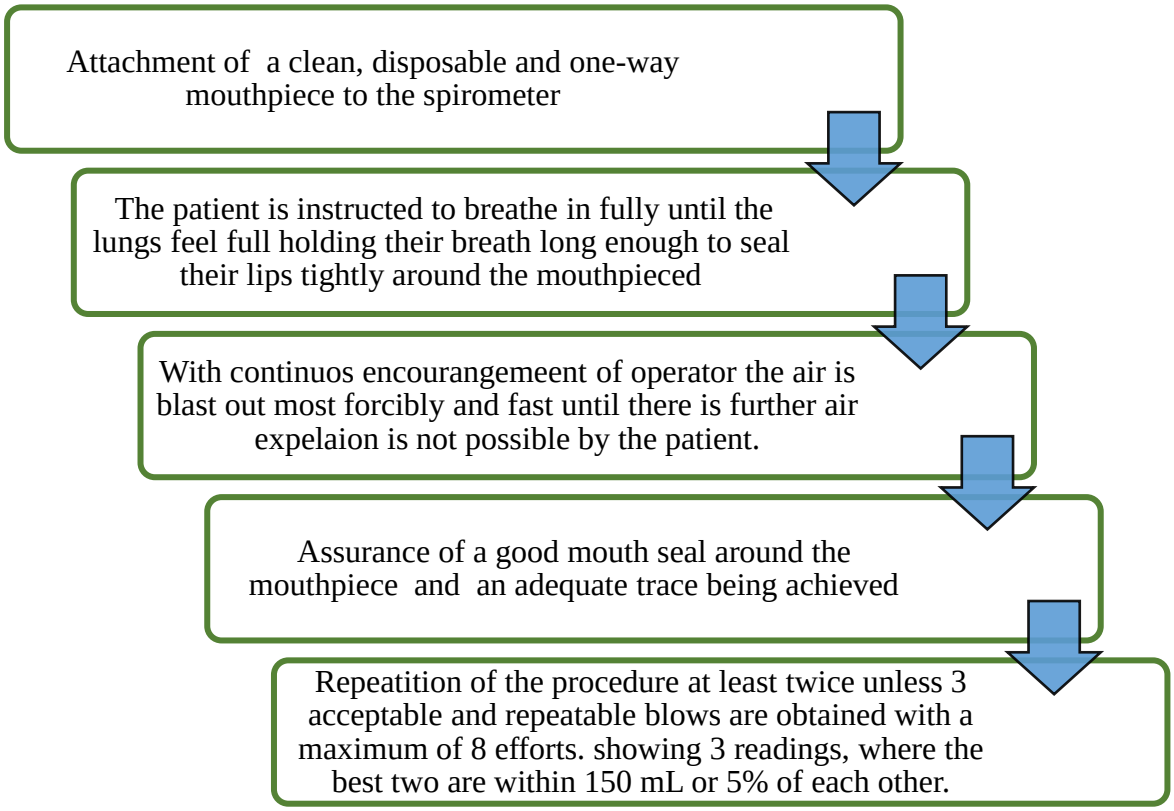

Figure 8: Procedure for measurement of FEV1, FVC & Flow-Volume curve

C. Differential Diagnosis

If the results from spirometer strictly indicate the airway obstruction, the next differential diagnoses are of COPD and asthma noticing the clinical history and smoking and additional exposure patterns. If the value for FEV_1 reversibility comes out more than 12% it represents asthma and higher is found in COPD, even in less frequent cases (Spirometry For Health Care Providers Global Initiative For Chronic Obstructive Lung Disease (Gold) Contents, n.d.).

Common problems occurred during performing this test

Problem is caused by Insufficient or imperfect inhalation, lack of effort in the time of exhalation – resulting in sub-maximal effort. Also, a delay in maximal effort onset causing under-estimation of FEV_1 along with an Incomplete lung emptying which is found common in COPD which often takes about 15 seconds in elderly patients. Often times the lips are not tight around the mouthpiece resulting in an abrupt result. Factors like exhaling in parts by the nose, coughing, Glottic closure, obstruction of mouthpiece due to teeth or tongue, poor posture such as leaning forward along with an improper knowledge and training of the operator and technical issues.

1.8.2 Arterial blood gas exchange test

The COPD patients have damaged airways and lung parenchyma with altered ventilation and metabolic activity. COPD patients show altered oxygen consumption of metabolic tissues as it is not equal to the amount of oxygen taken in the blood from arterial gas. Also, the amount of carbon dioxide produced by the metabolic tissues does not match the amount of carbon dioxide blown off by the alveolus. The arterial blood gas test is done to measure the extent of respiratory failure.

Type I Respiratory failure

Here, the partial pressure of carbon dioxide in arterial blood, Pa(CO_2) is about less than 45mmHg or even low. The partial pressure of oxygen in arterial blood, Pa(O_2) is found low. The alteration of values indicates to an imbalanced ventilation/perfusion.

Type II Respiratory failure

Here, the partial pressure of carbon dioxide in arterial blood, Pa(CO_2) is more than 45mmHg. The partial pressure of oxygen in arterial blood, Pa(O_2) has a value of less than 60mmHg. Both the altered values indicate to a term called 'Ventilatory Failure' according to the Lung Foundation Australia.

Effect of pH on the gas exchange in arterial blood: A balanced pH value helps avoid in any acid-base imbalance in body compartments. The normal range of pH for arterial blood is 7.35-7.45 which has to be maintained in both extracellular and intracellular compartment. If the pH value goes below the lower limit (7.35) acidosis is produced, whereas if the value goes above the highest limit alkalosis is caused. Acidosis is caused by an increase in Pa(CO_2) or a decreased bicarbonate value. Alkalosis is caused by a rise in bicarbonate value or a decreased Pa(CO_2) value. The change in bicarbonate level and carbon dioxide levels indicate to metabolic and respiratory imbalance respectively. A combination of blood buffers help in the improvement of such conditions (Cukic, 2014).

1.8.3 Sputum c/s test

Sputum test is an easy, efficient and noninvasive thus patient friendly diagnostic method of collecting sputum from the participants and store it for analysis. The sputum is then investigated for cellular markers that help in identifying the degree and type of airway inflammation of the patient at that particular time. The collection of data from the study helps predict the treatment and management procedure considering the physiological state as well.

Sputum analysis helps us predict the degree of inflammatory cell activation in airway diseases, being an important indicator for the treatment and management procedures. Sputum induction process is guided by skilled technical support along with consultants so that abrupt bronchoconstrictive episodes can be prevented. Sometimes patients may be unable to generate appropriate amount of sputum for analysis, resulting in altered results after the test.

In cases of COPD, during the sputum analysis, an elevated number of neutrophils and products that are related to the activation of neutrophils such as elastase, myeloperoxidase and proteases are found (Chung 2001; Williams and Jose 2001; Kim and Nadel 2004; O'Donnell RA et al 2004). These markers may indicate the earlier stages of COPD when disease manifestation is taking place. The patients showing eosinophilic COPD have shown improvement when given an inhaled corticosteroid treatment.

1.8.4 Complete Blood Count (CBC) Test

COPD being inflammatory in nature shows increased amount of different inflammatory cells and inflammatory cell mediators in lung areas. Thus a complete blood count (CBC) test gives idea on the extent of increment in those cells that are responsible for the diseases and its progress. In a study, fasting blood samples were obtained for CBC test from participants where White blood cell (WBC) counts were found expressively higher in COPD patients than the control group. No significant difference was found between low and high stages. Absolute and relative count for neutrophils was found to be higher in values than the control group. Also, participants having an exacerbated stage of COPD showed even more increased levels of neutrophils. No significant variances were found in platelets, hemoglobin and mean platelet volume (MPV) between COPD patients, people having different stages of COPD and the control group. Thus it could be said that higher WBC levels along with elevated absolute and relative neutrophils counts in COPD patients indicates the consistent inflammatory nature

of the disease whereas, elevated values of relative neutrophils count indicated the severity of the disease (Xiong et al., 2017)(Malek & Toussy, n.d.).

1.8.5 Chest Ultra sonogram

This is a test where the physical condition of the ventilated lung is depicted as artifacts using ultrasound. But in earlier days it showed a negligible role in respiratory medicine sector. The test is considered as a better and useful way in diagnosing various lung diseases called pneumothorax, interstitial diseases, pleural effusion and pneumonia.

The scanning done in the test procedure was done at the mid-thigh region. Here, the assessment of quadriceps mass was done through the measurement of rectus femoris cross-sectional area and thickness of quadriceps muscle. It was observed that the variations evaluated by ultrasound were greater than the changes in DEXA that stands for (Dual Energy X-ray Absorptiometry), in COPD patients. COPD might get confused as pneumothorax because of the deficient sliding of pleural line. This might occur because of pulmonary excursion being poor. Diagnosis of COPD by this method has the basis of showing the evaluation and extent of dyspnea and pulmonary edema present (Zanforlin et al., 2015).

1.8.6 Serum Creatinine test

Chronic renal failure (CRF) shows an increased prevalence with age being correlated to other chronic diseases namely congestive heart failure and diabetes mellitus often. The association of COPD and CRF is widely unfamiliar. Often a number of patients with COPD are found to have reduced muscular mass showing the serum creatinine level falsely low. This might happen due to a declined release of creatine from the body. CRF may also coexist with normal serum creatinine concentrations which are known as unrecognized or concealed CRF. It is diagnosed by glomerular filtration rate (GFR) being less than 60 mL/min/1.73m^2.

A study was to evaluate the frequency of undiagnosed renal failure in a population of COPD patients. It was performed on 300 COPD patients aging above 60years containing both the genders. They were observed with multiple follow ups during August 2009- August 2012. Spirometry test was performed on the participants to get idea about their severity of disease condition according to the categorization (A, B, C, D) of GOLD. The GFR was estimated and patients were categorized according to their renal function ranging from normal renal function (GFR P 60 mL/min/1.73 m^2), concealed CRF (normal serum creatinine and GFR < 60 mL/min/1.73 m^2), to overt CRF (increased serum creatinine and GFR < 60 mL/min/1.73 m^2). Here the limit considered for serum creatinine was 1.26 mg/dL in men and 1.04 mg/dL in women.

COPD patients are found to have renal arteriolar resistances due to hypercapnia. COPD patients develop CO_2 retention with disease progression with a decreased blood flow in kidney. Excretion of sodium and water is altered. Hypercapnia creates renal vasoconstriction with increased flow of norepinephrine in blood. Mostly prescribed drugs to COPD patients in different stages of exacerbation are water soluble in nature and thus are excreted by kidney. Thus the dosage given to patients having both COPD and CRF must be balanced.

1.9 Aim of study

The survey is supposed to be done among different age groups, gender, sources of secondary smoke, duration of exposure, the treatment plan (counseling or medication), and percentage of people recovering, ways to prevent the intake of smoke. A proper questionnaire survey on the above mentioned variables can give a clear idea about the interest and also will help having a comparison between the rural and urban area over the issue. Breathing smoke secondarily seems to show huge effect on pulmonary diseases which can be from household smoke, wood-burning oven or stoves, biomass fuel, cooking oil, burning candles & mosquito-

repellant coils, burning tobacco products, smoke exhaled by a smoker etc. sometimes found even toxic than the mainstream smoke. Secondhand smoke contains more than 7000 chemicals, 69 carcinogens and also there is no known safe level of exposure to this smoke. Passive smoking may even cause premature death in non-smokers. It even increases the risk of coronary heart disease, by almost the same level as a smoker. Counselling of patient is found to be the treatment plan for these patients. According to a report published (September 9,2017) in the website of The Daily Sun, Dr. Shamim Ahmed, an associate professor of the Pulmonology department of BSMMU, one in five women are suffering from COPDs at different life stages due to household smoke. Also, Biswas & Chowdhury (2017) said that the prevalence of COPDs in rural women aged over 40 was found to be 20.4%, where the risk factor was exposure to biomass smoke. As the issue is significantly alarming these days, the study will help identify the dominance of it in our country in a specific region, age groups, gender etc.

Chapter 2

Methodology

2.1 Research goals

The goal of the study was to find out the correlation between COPD patients and their exposure to household smoke they face per hour, their usage of different type of cooking oils, mosquito repellants, their exposure to other pollutants due to the location of their house etc.

2.2 Designing the method

The flowchart shown following is the outline of the procedure:

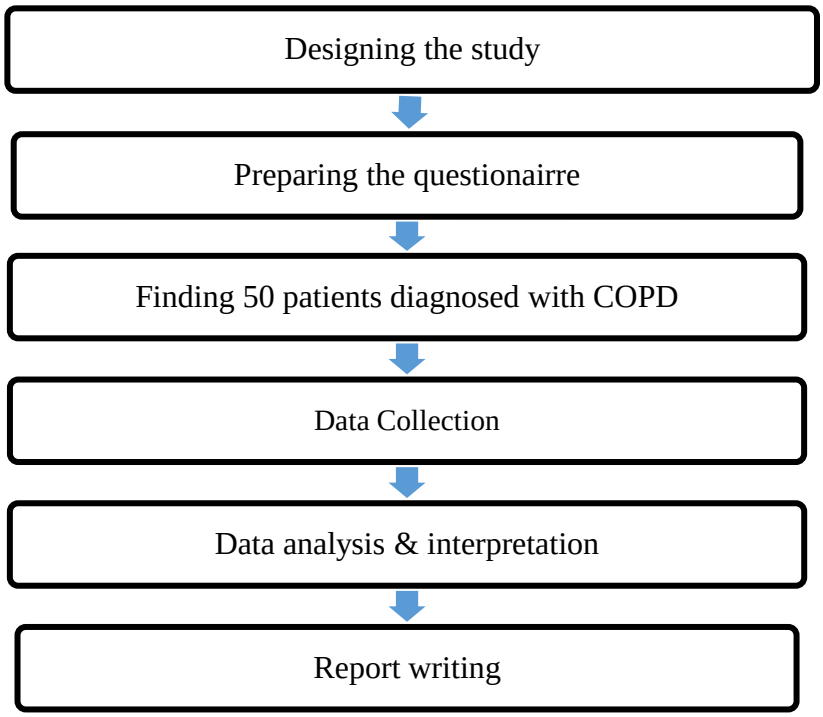

Figure 9: Overview of methodology

2.2.1 Designing the study

The design of the study is a step by step procedure which was determined so that the information needed to culmination the data into the results that are being search in this study.

2.2.2 Preparation of Questionnaire

The questionnaire was prepared keeping on mind that what information are needed to be gathered from the participants. Variables were selected with proper understanding having multiple possible options. A questionnaire of 25 questions was made with suitable options. In the questions the participants were asked about their situation starting from diagnosis, smoking habit, environment they live in, symptoms they feel being in the diseased condition, age, choices they prefer in different lifestyle behaviors to their visit to the doctor.

2.2.3 Questionnaire for Survey

1. How were you diagnosed with COPD?

   i) Chest X-ray ii) CT scan iii) Spirometry

   iv) Arterial blood gas analysis v) Cough/sputum test vi) Others (if any)

2. What kind of stove is used in your house?

   i) Natural gas (methane) stove ii) LP gas cylinder

   iii) Electric heaters iv) Others

3. What kind of cooking oil is used in the kitchen?

   i) Vegetable oils (soybean, rice bran, olive, palm) ii) Butter iii) Ghee

4. Does your kitchen have a chimney or any ventilating system?

   i) Yes ii) No

5. Do you use mosquito-repellant coils?

   i) Yes ii) No iii) Regularly iv) Occasionally

6. Do you use sprays like mosquito repellant aerosols or room freshener?

   i) Yes ii) No iii) Regularly iv) Occasionally

7. How long are you exposed to the smoke in a day?

   i) 1-3 hours ii) 3-5hours iii) 5-7hours iv) More than 7hours

8. Are you exposed to dust (other than smoke) on a daily basis?

   i) Yes ii) No

9. Do you use any biomass fuel or kerosene in the house?

   i) Yes ii) No iii) Regularly iv) Occasionally

10. Do you have any specific lifestyle behavior (deodorant/perfume/antiperspirants)?

    i) Yes ii) No iii) Occasionally

11. Are you exposed to any outdoor air pollutants?

    i) Yes ii) May be unknowingly iii) Not at all

12. What are the symptoms that you face due to the smoke?

    i) Sneezing ii) Burning in eyes iii) Coughing iv) Suffocation v) Others

13. What are the symptoms that you are facing while the smoke is not there? (if any)

    i) Absence of suffocation ii) No burning in eyes iii) No sneezing & coughing

14. Have you tried to alter any of your choices (fuel, stove, ventilator etc.) to improve your condition?

    i) Yes ii) No iii) Not worked

15. Did you find any improvement of your condition after that?

    i) Yes ii) Not sure ii) Not at all

16. Is there any other form of smoke that you are exposed to?

i) Yes ii) No

17. Have safety measures like wearing masks during the exposure helped you?

i) Yes (what is the type) ii) No

18. Is there any place (any industrial plant) near your house from where the smoke comes?

i) Yes ii) No iii) Others

19. Are any other member of your house facing the similar problem or not?

i)Yes (if any-what is the relation?) ii) No

20. When did you consult with a doctor after addressing the problem?

i) Immediately ii) After a while iii) Not at all

21. Did you get any counselling on how to avoid smoke?

i) Yes ii) Insufficient iii) After a long time iv) Not at all

22. Are you on any medication?

a) Yes b) No

i) Brand names?

ii) Dose/dosage form?

iii) Duration?

iv) Route of administration?

23. How often do you visit your consultant?

i) Once a month ii) Once in 3months

iii) Once in 6months iv) Others

24. Patient information :

- Age
- Sex
- Smoker / nonsmoker
- Any previously identified lung disease

25. If nonsmoker, for how long have you withdrawn smoking?

i) 5years and above ii) 7years and above

iii) 9years and above iv) 11years and above

2.2.4 Searching 50 participants diagnosed with COPD

In this study, the questionnaire was performed on 50 participants who are diagnosed with COPD. More number of subjects could be taken in accordance but due to shortage of time to fulfill the overall study procedure, the number of targeted subjects had to be confined.

The participants were found from a hospital specialized for Lung diseases in Dhaka. Moreover, all the participants were in patients admitted in the hospital and thus surely identified as COPD patients.

2.2.5 Data collection

Hospitals were visited a couple of times to fulfill data needed from the expected number of subjects. The questionnaire was taken in printed version and kept one copy for each participant. The patients were asked the questions with the given options and their answers were noted.

2.2.6 Data analysis

The collected data were analyzed using Microsoft excel according to different variables against other variables.

Chapter 3

Result

3.1 Prevalence of COPD among different age groups

Here the subjects on whom the survey was performed had different age groups. 7 of the patients aged 40years and above holding a percentage of 14%. 15 patients were found to be aging 50years and above having a percentage of 30%. Patients aging 60years and above were found to be 11 in number with a percentage of 22%. Also, 34% of the patients were in the age group of 70 years and above with a number of 17 patients.

Table 2: Prevalence of COPD among different age groups

Age groups	No. of patients	Percentage
40 and above	7	14%
50 and above	15	30%
60 and above	11	22%
70 and above	17	34%

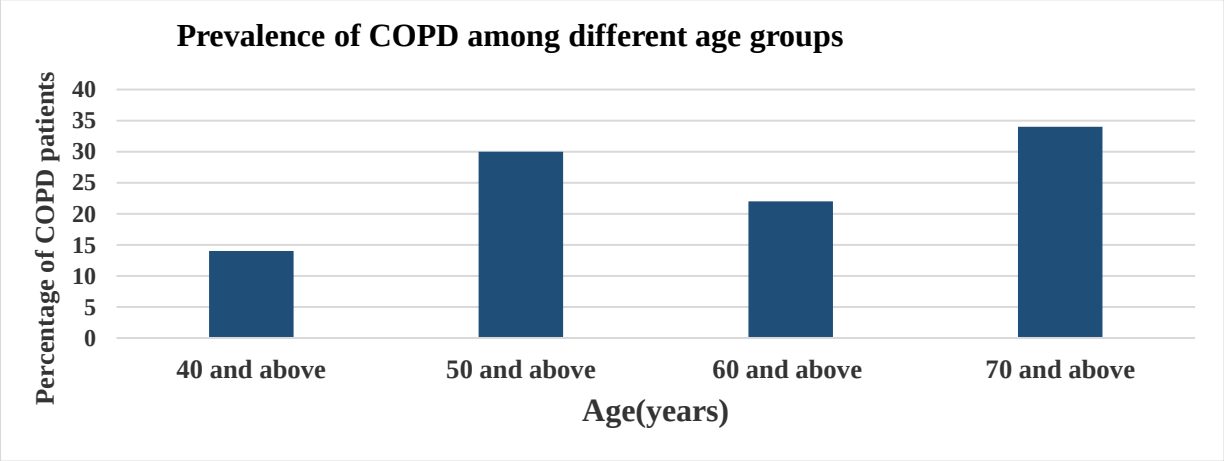

Figure 10: Prevalence of COPD among different age group

3.2 Extent of exposure to smoke

The COPD patients that the survey was performed upon are found to be exposed to smoke for different time limits as seen in the table given below. 85% of patients were exposed to smoke for 1 to 3 hours, where 7.5% of patients were found to be exposed for 3 to 5 hours, 2.5% of patients were exposed to smoke for 5 to 7 hours and 10% of the patients were exposed for more than 7hours.

Table 3: Patients' exposure to smoke per day

Time range	Percentage of patients
1-3hours	85%
3-5hours	7.5%
5-7hours	2.5%
More than 7hours	10%

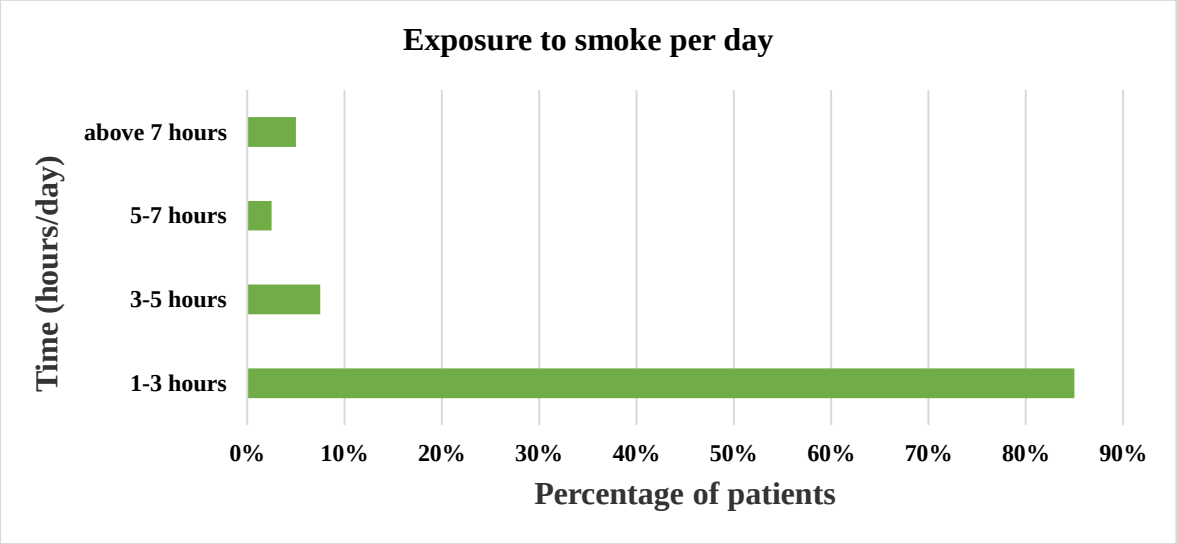

Figure 11: Patients exposure to smoke per day

3.3 Percentage of smokers and nonsmokers among the patients

Here, among the subjects 30% were currently smokers and rest of 70% subjects were found to be nonsmokers as they have quitted smoking more than 5years earlier from the date the survey was performed.

Table 4: Smoking habit of patients &their percentage

Smoking habit	Percentage of each type
Nonsmokers / Former smokers	70%
Smokers	30%

The following pie chart shows the percentage of participants having different smoking habits either smokers or non-smokers.

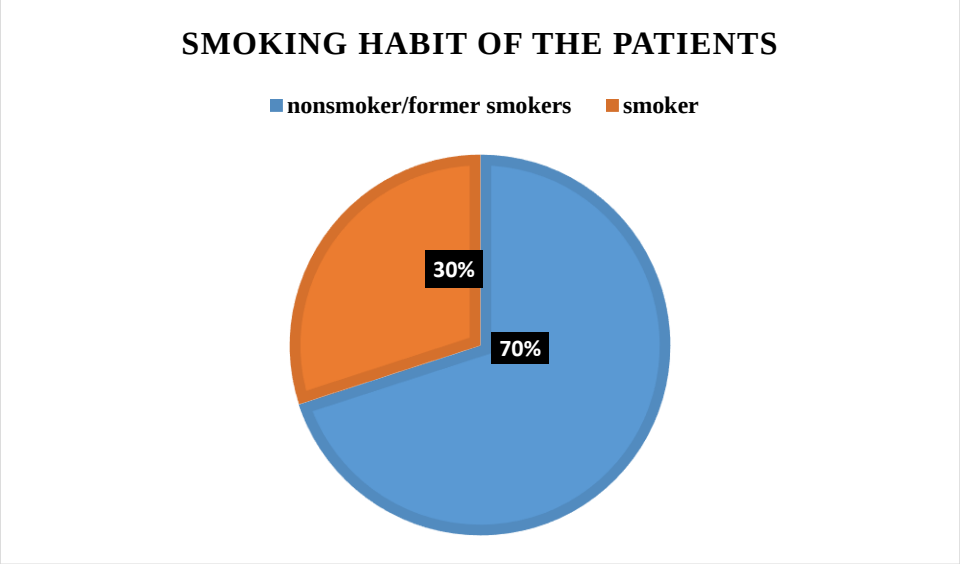

Figure 12: Smoking habit of patients

3.4 Time span of former smokers' withdrawal of smoking

Among the participants 70% of them were found to have quitted smoking for about 5years and above holding the highest percentage among the nonsmokers. Also, 14% of patients had left smoking about 7years and above whereas 9% and 7% are percentages for patients leaving smoking for 9years and above and 11years and above respectively.

Table 5: Time span of former smokers' withdrawal of smoking

Time span	Percentage
5years and above	70%
7years and above	14%
9 years and above	9%
11years and above	7%

Of the participants who were considered nonsmokers, are basically former smokers who have quit smoking in different life stages and the duration of withdrawal varies. Thus, the following chart shows the variance in withdrawal span of time in terms of smoking.

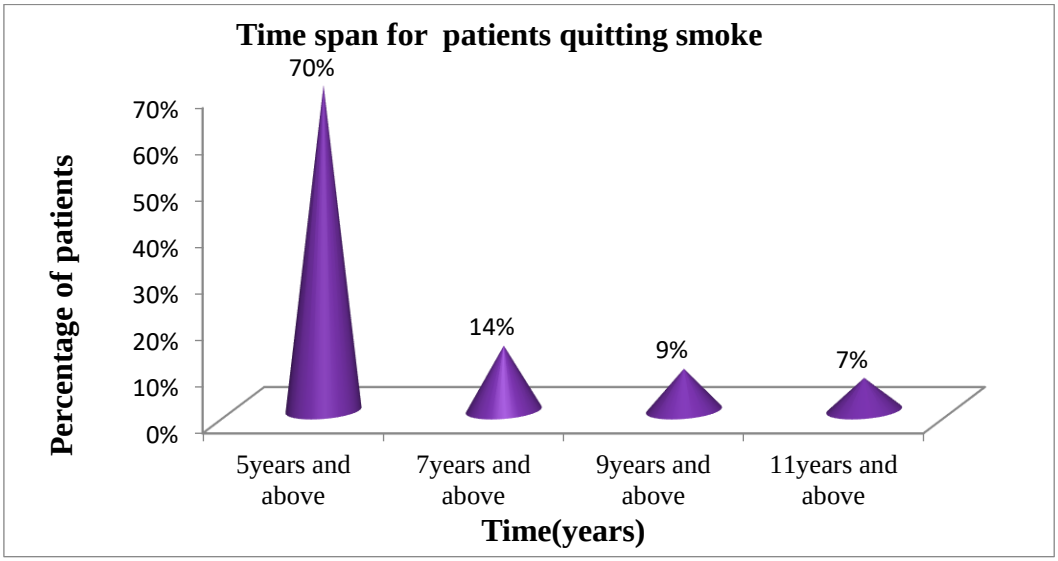

Figure 13: Time span of participants' withdrawal of smoking

3.5 Types of stove used in patients' household

Among the subjects that the survey was performed on were found to use gas stove running by natural gas methane, Liquid Paraffin Cylinders and biomass fuel and in some cases combination of both biomass fuel and gas stove is used. Here, 30% of the patients used gas stove in their household, 10% of the patients used LP gas cylinders, 55% of patients used biomass fuel and 5% of patients used both biomass fuel-run stoves and gas stove in their household.

Table 6: Types of stoves used by participants with percentage

No.	Types of stove	Percentage
(i)	Gas stove	30%
(ii)	LP gas cylinders	10%
(iii)	Biomass fuel	55%
(iv)	Both (i) & (iii)	5%

The pie chart shows percentages of participants using different stove types ranging from natural gas stoves, LP gas cylinders, biomass fuel derived stoves or combinations.

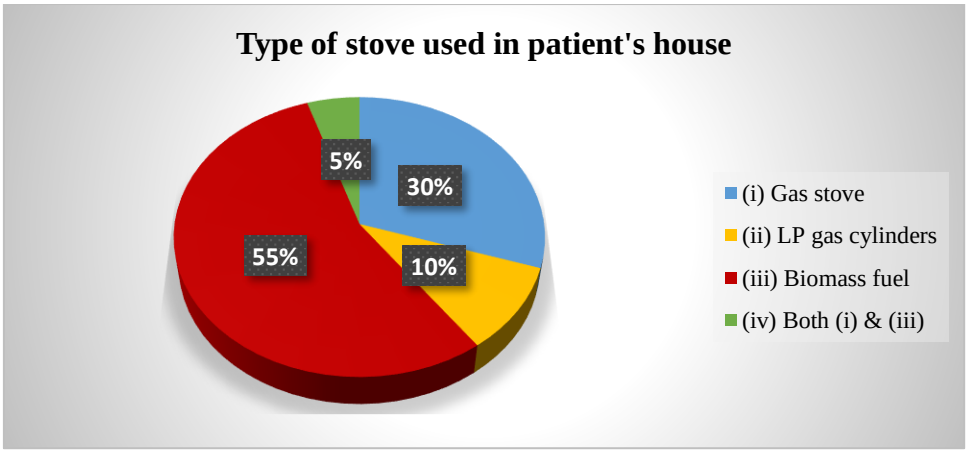

Figure 14: Percentage of patients using different stove types

3.6 Severity of different symptoms among the patients

COPD patients are seem to have symptoms such as suffocation, sneezing, coughing and often burning of eyes and from the survey the percentages were found 63%, 11%, 17% and 9% respectively.

Table 7: Different symptoms faced by patients

Symptoms	Percentage of patients facing them
Suffocation	63%
Sneezing	11%
Coughing	17%
Burning in eyes	9%

A range of symptoms are noticed in COPD patients with variant degree of recurrence and severity of each. Here is the depiction of data found from the participants of the survey.

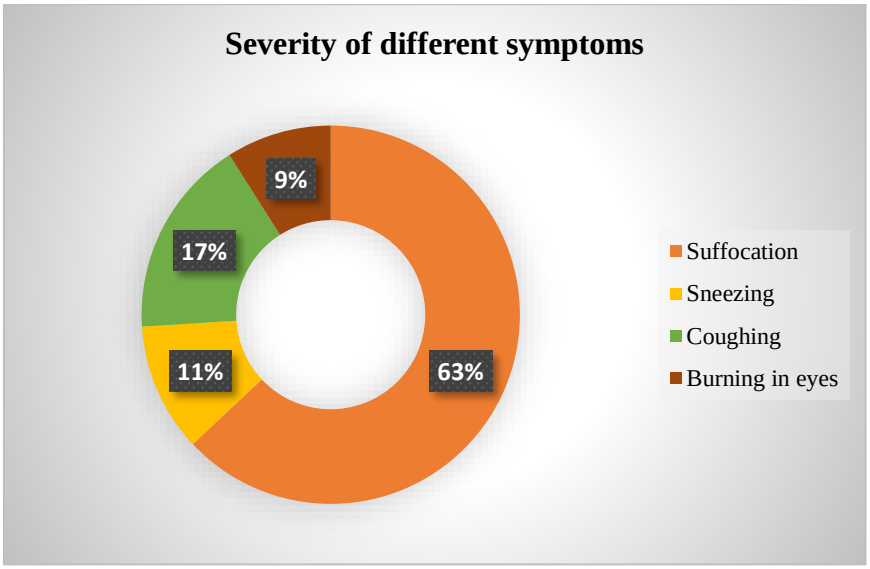

Figure 15: Percentage of patients suffering from different symptoms

3.7 Type of mosquito repellant users among the patients

From the subjects that the survey is performed, there were groups of patients using mosquito repellants of different types like coils, spray or aerosol, some used both whereas some used neither holding percentages of 72%,19%,5% and 4% respectively.

Table 8: Percentage of patients using different mosquito repellants

Type of users	Percentage
Coils	72%
sprays/ aerosol	19%
both	5%
neither	4%

The following chart represents the rate of usage of different mosquito repellants in the household of the COPD patients performing the survey.

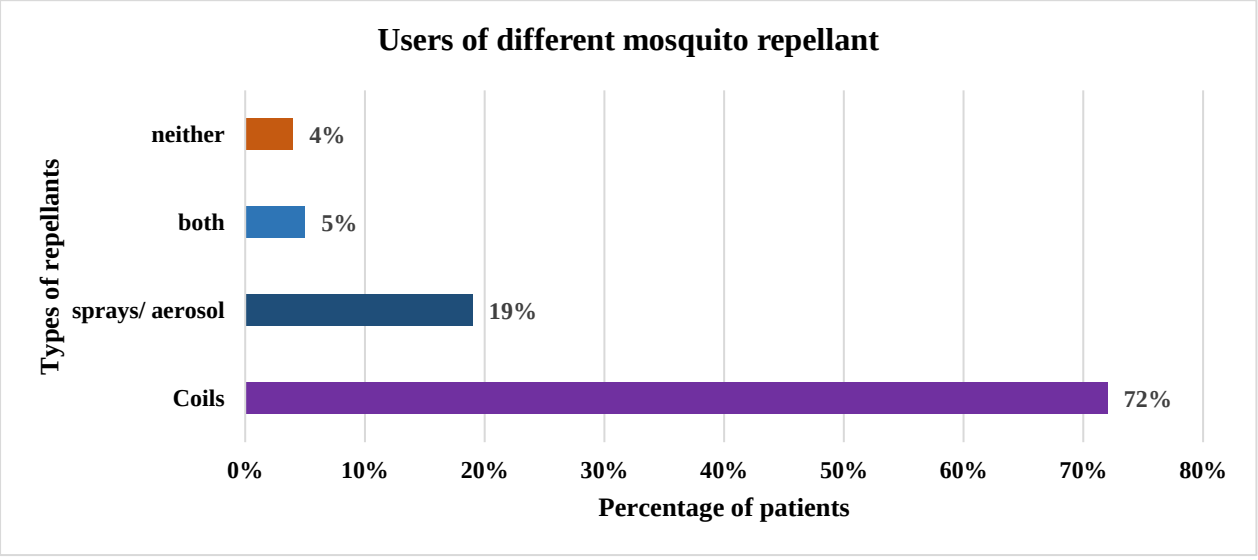

Figure 16: Percentage of patients using different mosquito repellants

3.8 Tests done for Patients

Every participant found to have multiple tests asked by the physician so that the disease progression and current situation of the disease can be interpreted from the test reports.

Percentage of patients given different tests varies. Here, tests namely Spirometry, Sputum c/s, Chest X-ray, USG of chest, CBC, Serum Creatinine, Serum Billirubin holding percentages of 99%, 85%, 82%, 71%, 58%, 67% and 57% respectively.

Table 9: Percentage of patients given different diagnostic tests

Name of tests	**Percentage of Patients asked for them**
Spirometry	99%
Sputum c/s	85%
Chest X-ray	82%
USG of chest	71%
CBC	58%
Serum Creatinine	67%

The participants of the survey were asked to do different diagnostic tests by the physician and the following chart shows the most common ones along with their percentages.

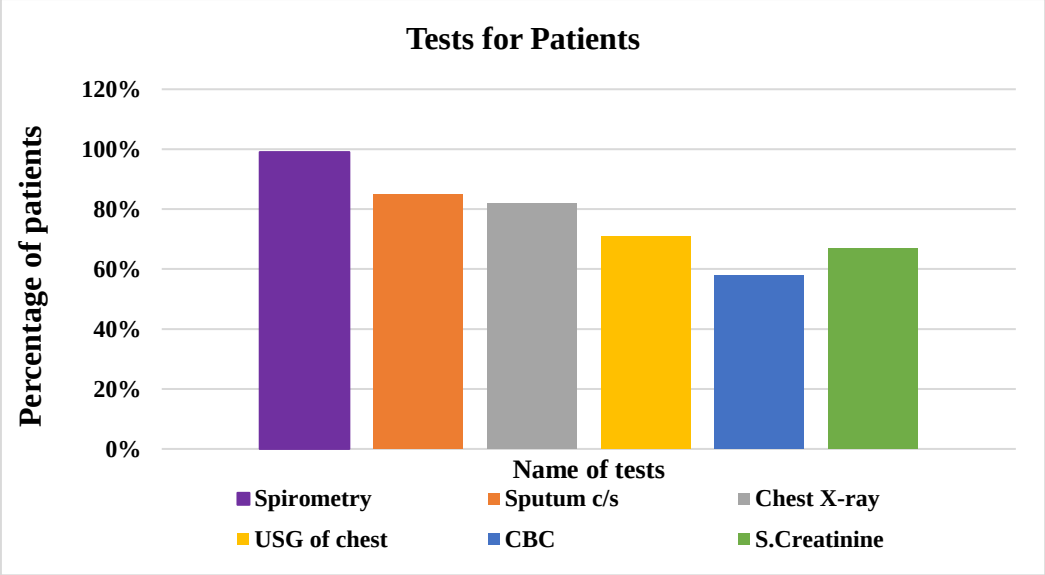

Figure 17: Percentage of patients asked for different diagnostic tests

3.9 Participants' frequency of consulting to a physician

Among the participants different percentage of patients visited or consulted the doctor with differing frequency. 2% of patients only visited the consultant once in a month. However, 14% of patients visited the doctor once in every three months. Patients visiting the doctor once in every 6months and once in every year or more hold percentages of 44% and 50% respectively.

Table 10: Patients' frequency of visit to a doctor

Frequency of visit	Percentage
Once in a month	2%
Once in 3months	14%
Once in 6months	44%
Once in a year or more	50%

The following chart (figure 18) is the representation of the frequency of patients visiting the physician in a particular time period.

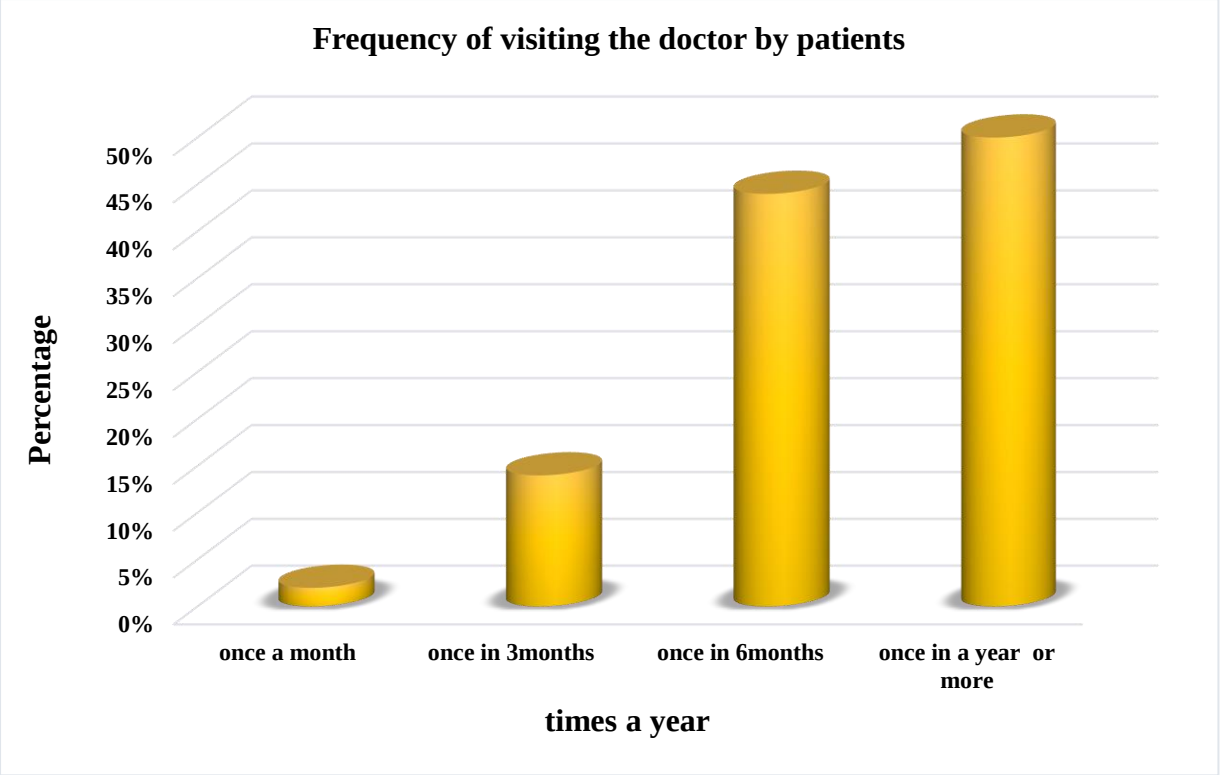

Figure 18: Frequency of patients' visit to a doctor

3.10 Percentage of participants following different lifestyle behaviors

In the survey questionnaire, there were questions about some lifestyle behaviors that are followed by the patients in day to day life. Users of room freshener, perfumes and mask hold percentages of 4%, 2% and 16% respectively.

Table 11: Variety of lifestyle behaviors & percentage of patients using them

Type of behaviors	Percentage of patients following them
Use of room freshener	4%
Use of perfumes	2%
Use of mask	16%

The following chart shows percentages of patients practicing a particular choice to be used in their regular life out of habits.

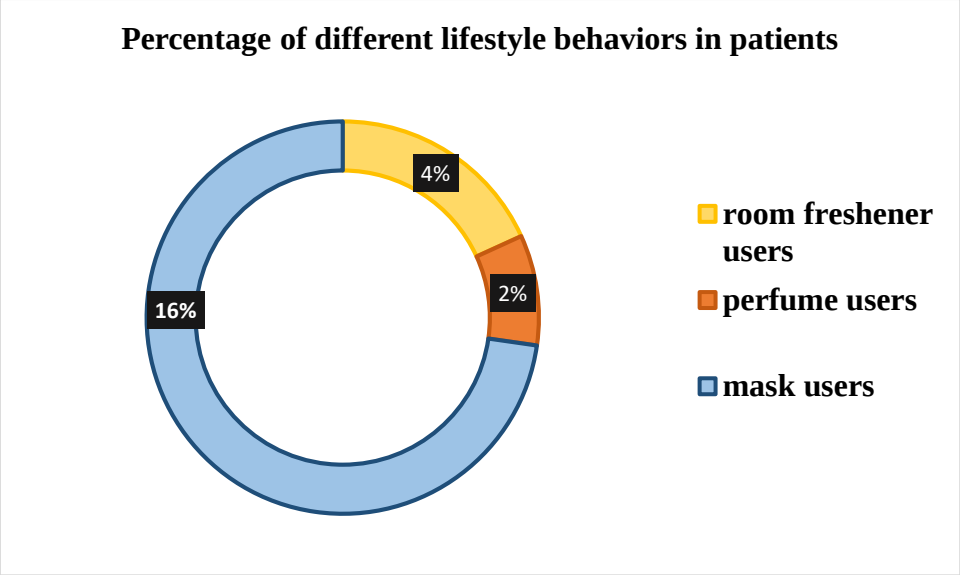

Figure 19: Percentage of different Lifestyle behavior in patients

3.11 Patients having additional lung diseases

72% of the participants were found to have additional lung disorders and other did not have any. Of them severity of conditions varied in person to person where patients having stable COPD was holding a percentage of 8%, and a huge 63% of patients had acute exacerbations of COPD. The other conditions included partial lung failure, lung cancer, pulmonary emphysema, and bronchitis with percentages of 6%, 4%, 10% and 14% respectively.

Table 12: Percentage of patients having additional lung diseases

Name of Conditions	Percentages
Stable COPD	8%
Acute Exacerbation of COPD	63%
Partial lung failure	6%
Lung cancer	4%
Pulmonary Emphysema	10%
Bronchitis	14%

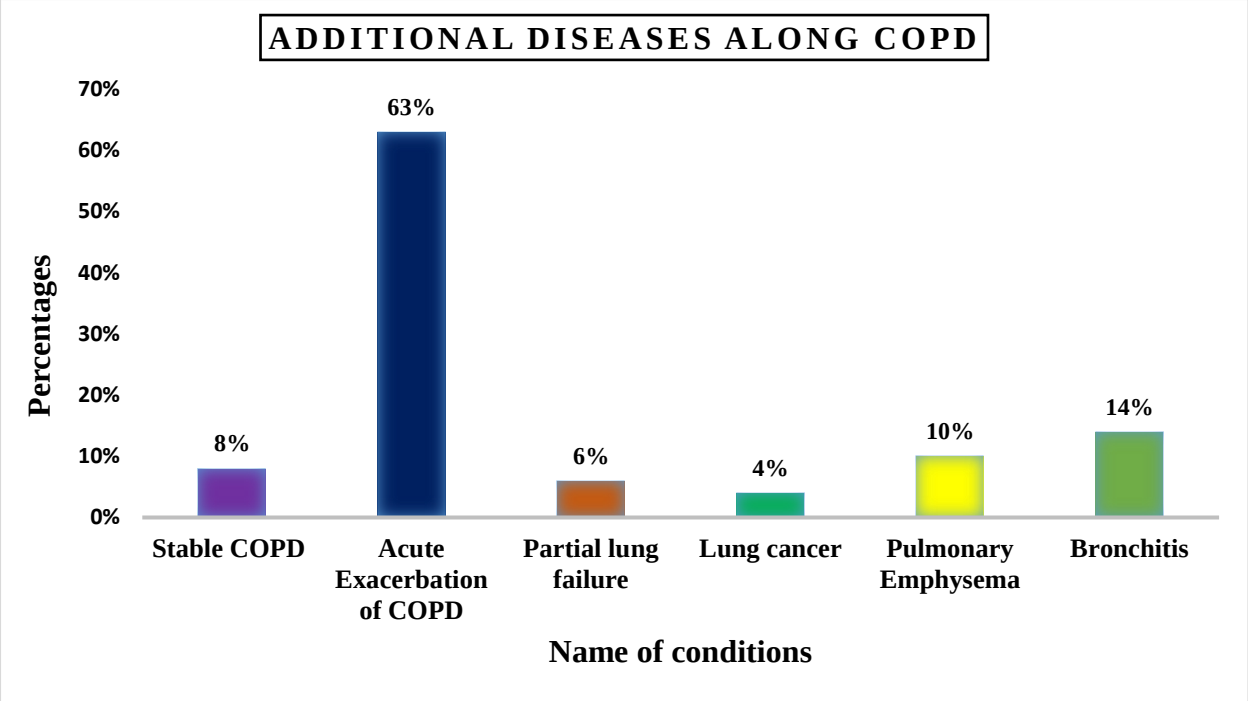

Figure 20: Percentage of patients having additional lung diseases

3.12 Management of COPD

3.12.1 Categorization of the disease

According the Global Guidelines for Lung Diseases, COPD is categorized into four different groups according to the findings of Spirometry test. The patients having FEV_1/FVC ratio of less than 70% are considered to have persistent airflow limitation. The following classification shows severity of COPD in terms of the extent of airflow limitation (Global Initiative For Chronic Obstructive Lung Disease Global Strategy For The Diagnosis, Management, And Prevention Of Chronic Obstructive Pulmonary Disease (2018 Report), 2018).

Table 13: Categorization of COPD

GOLD 1	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2	Moderate	$50\% \leq FEV_1 \leq 80\%$ predicted
GOLD 3	Severe	$30\% \leq FEV_1 \leq 50\%$ predicted
GOLD 4	Very severe	$FEV_1 < 30\%$ predicted

The treatment plan followed for different categories of COPD differs from each other as shown in the figure below.

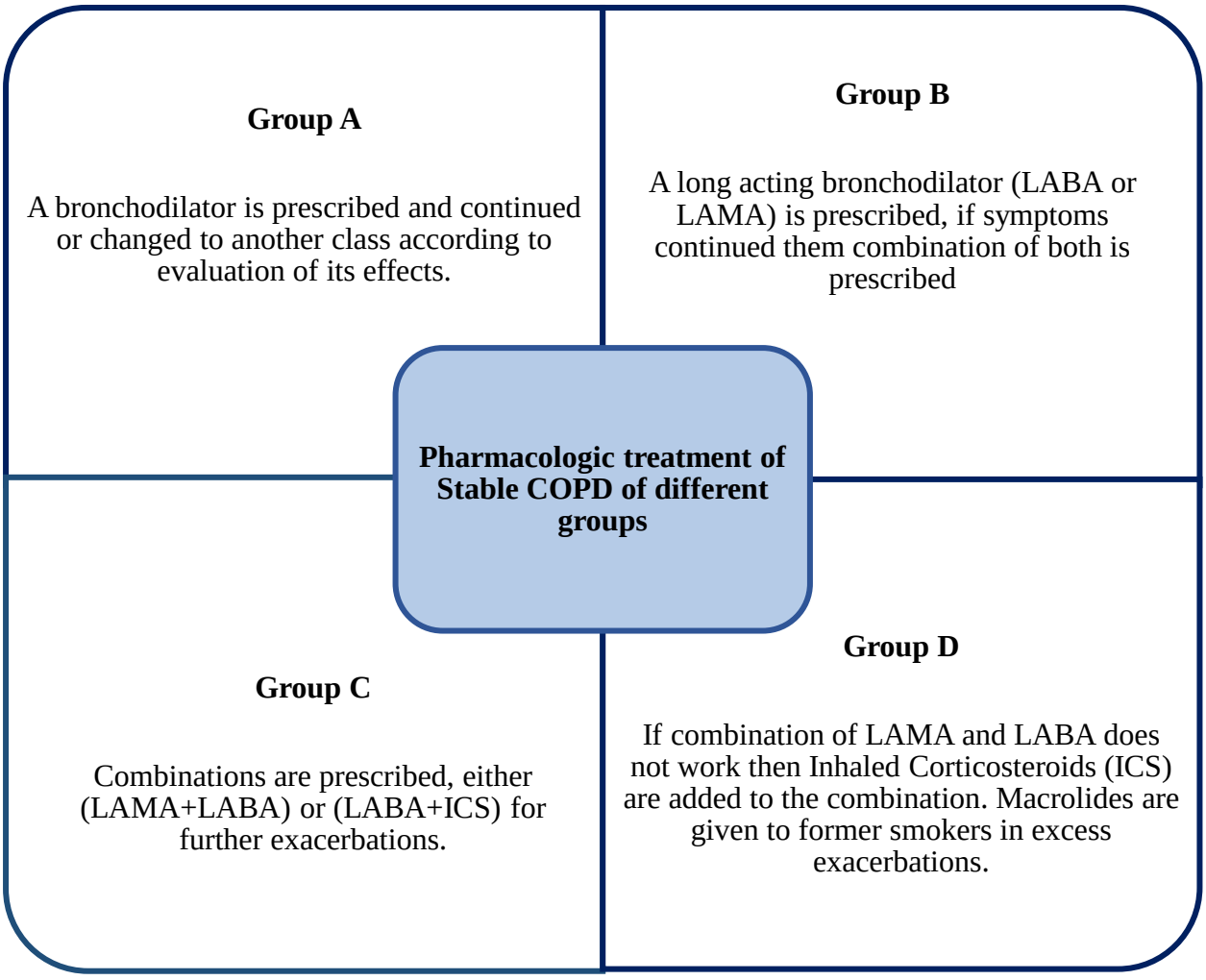

Figure 21: Pharmacologic management of COPD

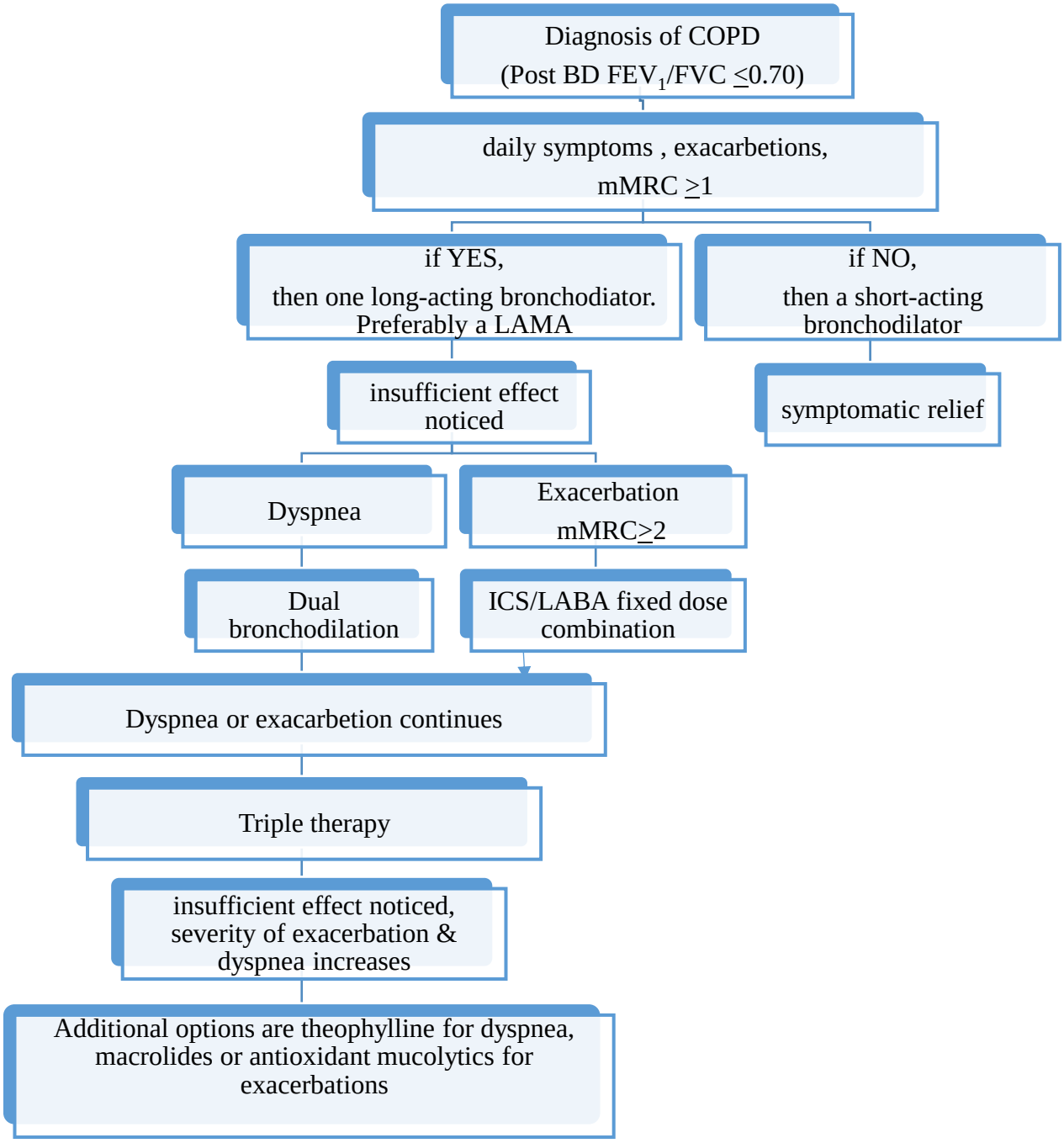

Figure 22: Flowchart of COPD management

The diseases is managed in several steps basing on the severity and frequency of disease symptoms along with the lung function tests specifically showing the extent of airflow limitation to the lungs. At first the spirometry results are taken into consideration where the ratio of Forced Expiratory Volume in 1 second (FEV_1) and Forced Vital Capacity (FVC) if

found lesser or equal 70% in presence of a bronchodilator, is determined as COPD. Initially counselling is done on cessation of smoking with vaccination of pneumococcal & influenza virus.

Also, patients are encouraged for increasing their regular physical activity and rehabilitation of pulmonary activity is suggested, if difficulty is faced. If the Modified Medical Research Council (mMRC) value is not found to be 1 or more for dyspnea with exacerbation then a short acting bronchodilator is prescribed for symptomatic relief. If, the mMRC value is found to be 1 or more indicating low levels of dyspnea with exacerbation then a long acting bronchodilator is suggested.

If, exacerbation remains with further increasing dyspnea (mMRC value being 2 or more) dual bronchodilator is given in combination of a Long-acting beta-2 adrenergic agonist and a Long acting muscarinic antagonist (LABA + LAMA) or the combination of an inhaled corticosteroid and a long acting beta-2 agonist (ICS + LABA). Patient with further exacerbation are suggested Theophylline for dyspnea & mucolytic antioxidants for exacerbation.(Zysman et al., 2017)

3.12.2 Mostly prescribed drugs to patients

Here patients on whom the study was performed had some additional diseases too and thus were prescribed different types of therapeutic agents. With respect to COPD treatment some common medicines were prescribed to each of the patients. Percentage of each medicine prescribed is depicted in the chart below.

Table 14: Percentage of patients prescribed common drugs

Name of agents	Percentage
Montelukast	87%
Salbutamol	75%
Acetylcysteine	91%
Doxophylline	81%
Tiotropium	79%
Budesonide	83%

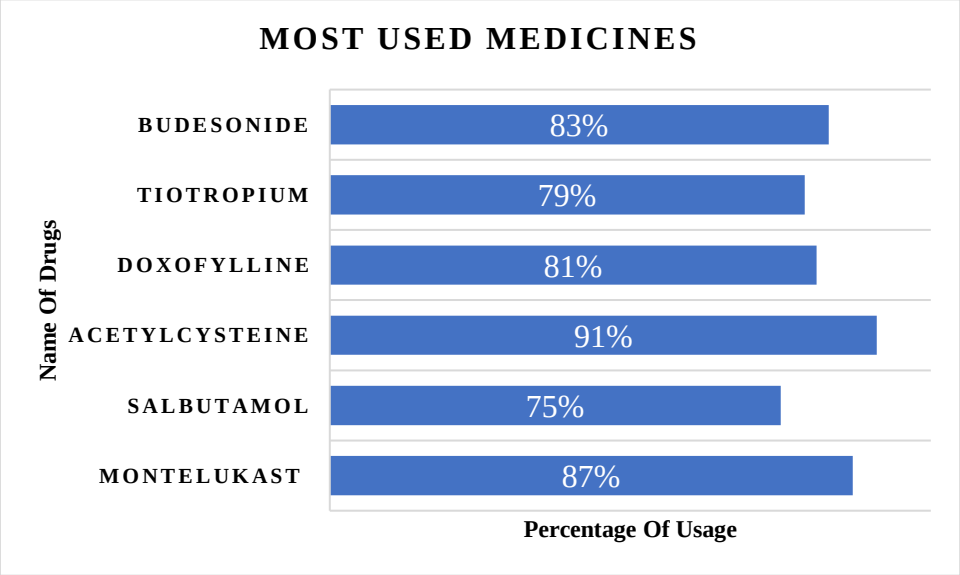

Figure 23: Percentage of commonly prescribed drugs

3.12.3 Mechanism of action of Drugs

3.12.3.1 Doxophylline

Doxophylline is a theophylline derivative showing the similar mechanism of action. The agent being an oxopurine which is a derivative of xanthine, methylated at N-1 and N-3 and carrying a 1,3-dioxolan-2-ylmethyl group at N-7, used in the treatment of asthma. It acts as a bronchodilator along with functioning as an antitussive and an anti-asthmatic drug. It derives from a 7H-xanthine.

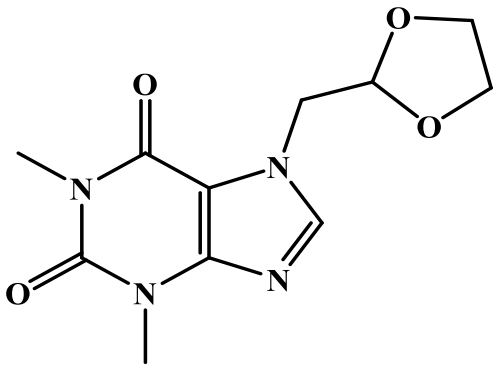

Figure 24: Structure of Doxophylline

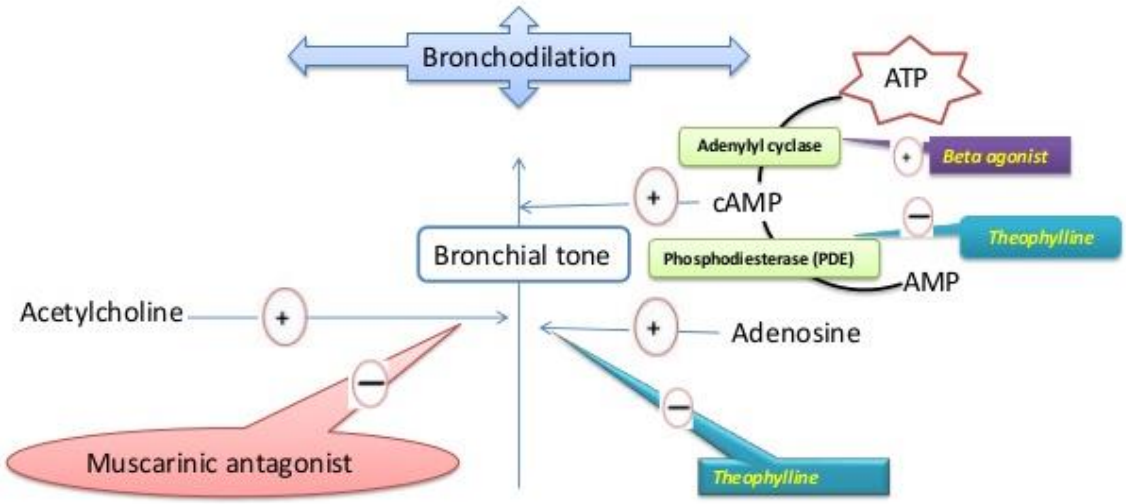

Figure 25: Mechanism of action of Doxophylline

3.12.3.2 Budesonide

Budesonide being a corticosteroid works by undergoing a high first pass elimination by the liver thus systemic levels after oral administration resulting in minimal. Budesonide is used nasal spray or by inhalation for diseases namely allergic rhinitis, asthma and chronic obstructive lung disease.(Toogood et al., 1990)

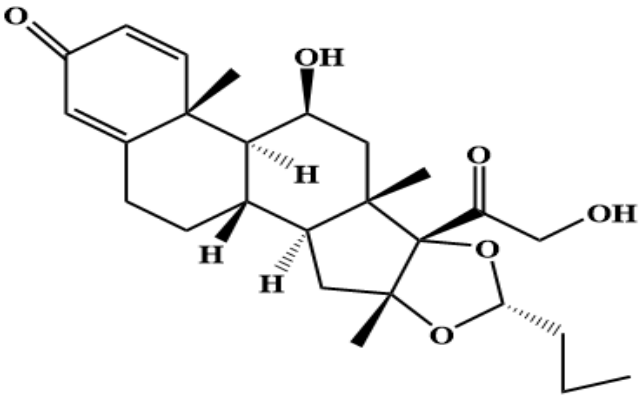

Figure 26: Structure of Budesonide

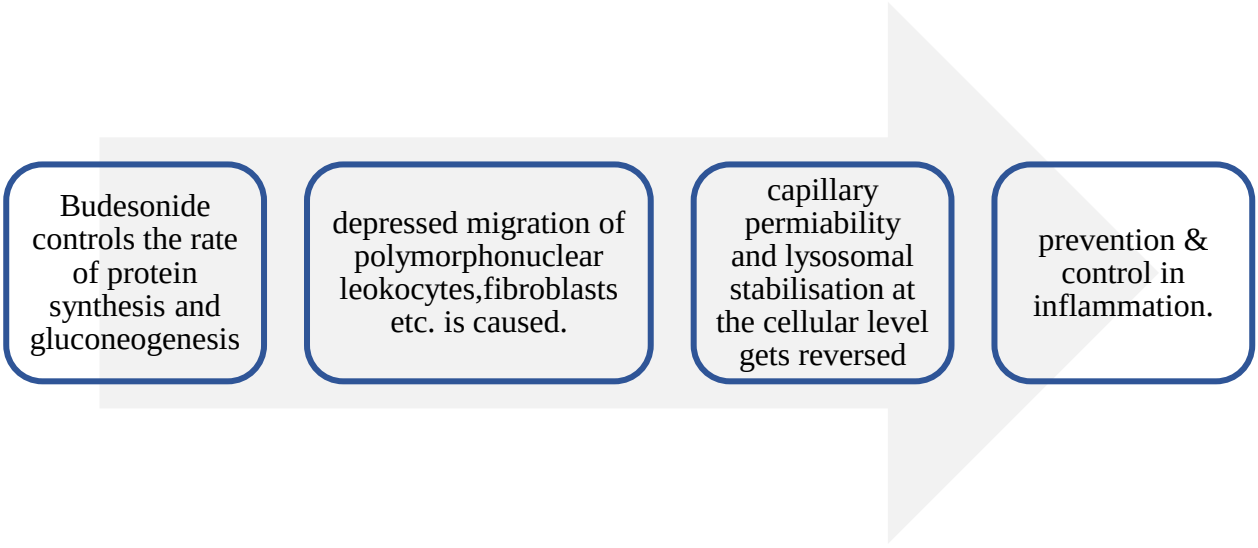

Figure 27: Flowchart showing mechanism of action of Budesonide

3.12.3.3 Tiotropium

Tiotropium is a synthetic anticholinergic agent that is used as an inhalant for treatment of acute bronchospasm due to chronic bronchitis or emphysema. Tiotropium has not been implicated in causing liver enzyme elevations or clinically apparent acute liver injury.(Alvarado-Gonzalez & Arce, 2015)

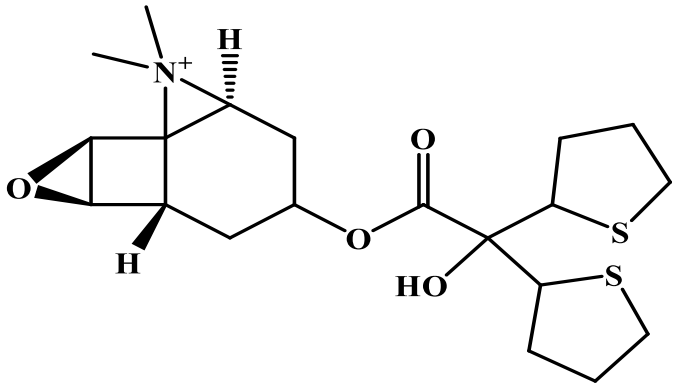

Figure 28: Structure of Tiotropium

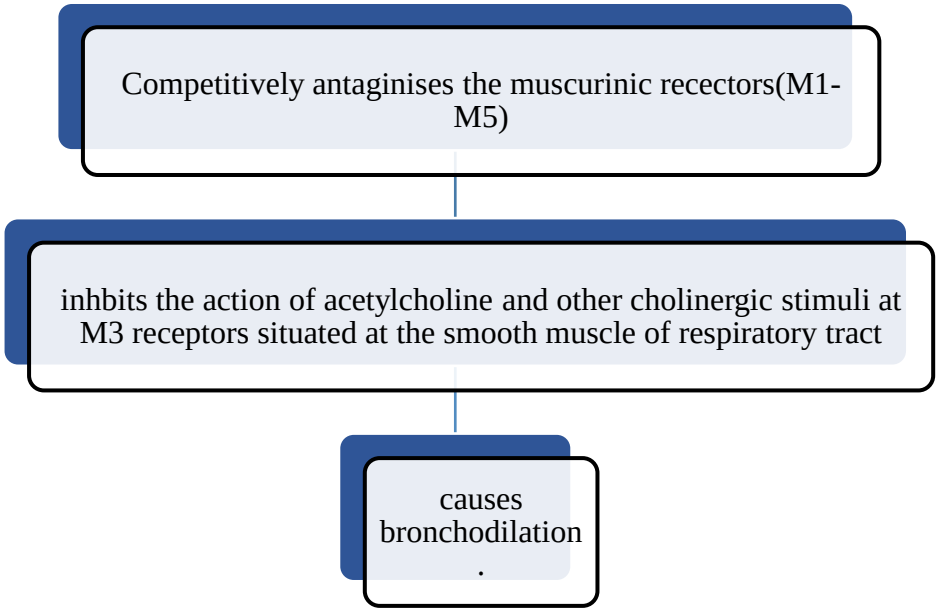

Figure 29: Flowchart showing mechanism of action of Tiotropium

3.12.3.4 Acetylcysteine

Acetylcysteine being a synthetic N-acetyl derivative of the endogenous amino acid L-cysteine which is a precursor of the antioxidant enzyme named glutathione. The agent regenerates glutathione stored in liver. The agent works as a mucolytic agent by liquefying mucus, decreasing the viscosity of secretions by splitting of disulphide bonds in mucoproteins.

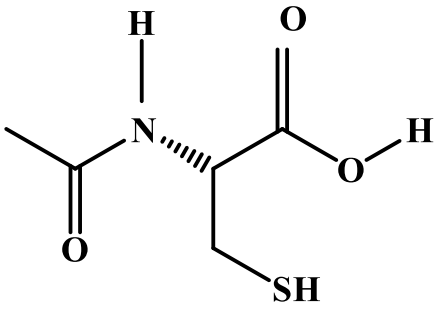

Figure 30: Structure of Acetylcysteine

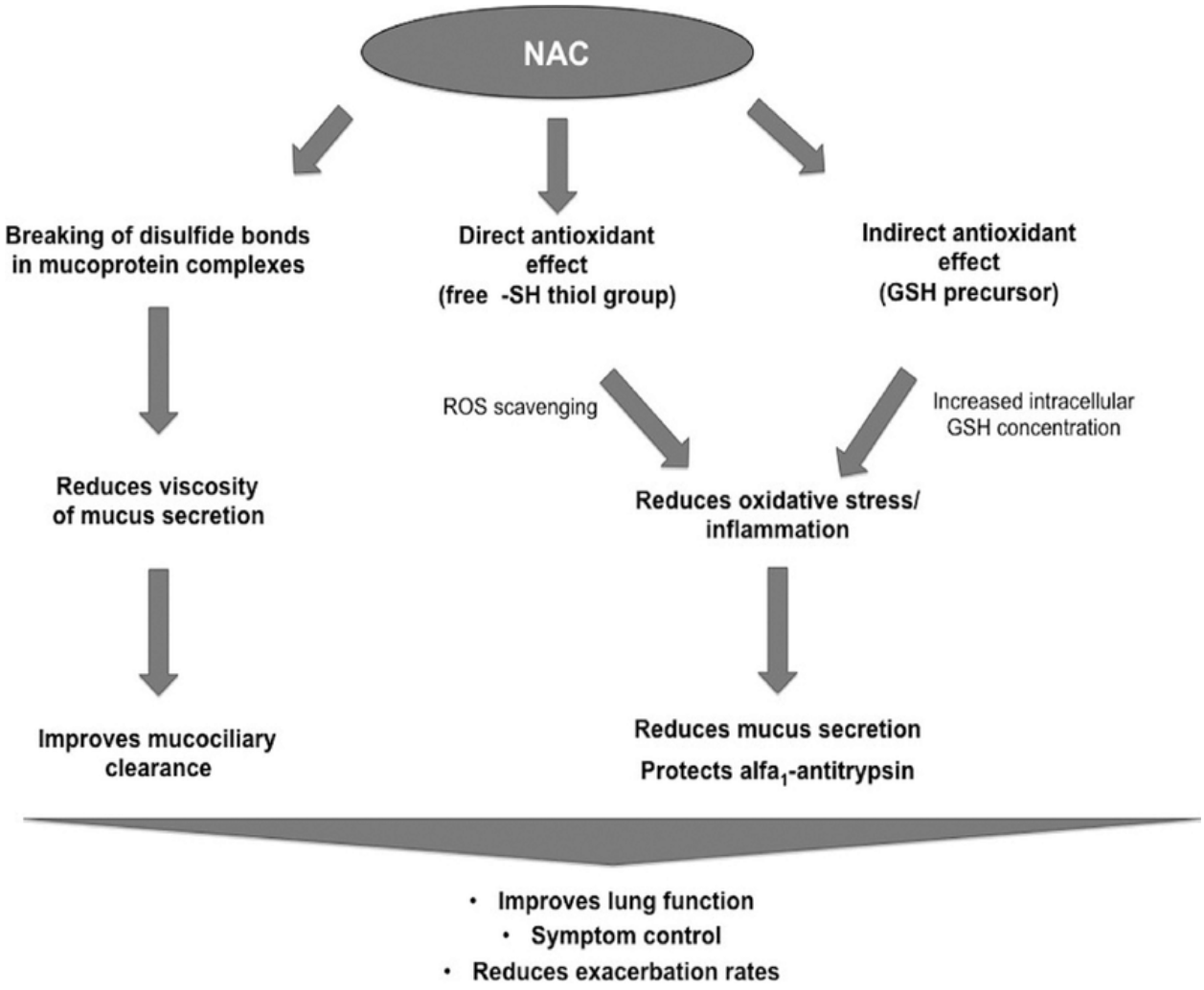

Figure 31: Flowchart showing mechanism of action of N-acetylcysteine or NAC (Santus et al., 2014)

3.12.3.5 Montelukast

Montelukast is quinolones member being a monocarboxylic acid and an aliphatic sulfide. It functions as a leukotriene antagonist, showing anti-asthmatic and anti-arrhythmia effects. It is a conjugate acid of a montelukast(1-).

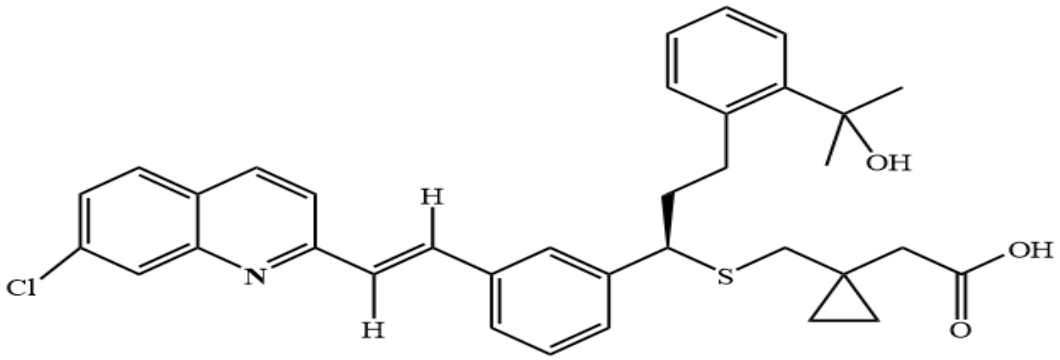

Figure 32: Structure of Montelukast

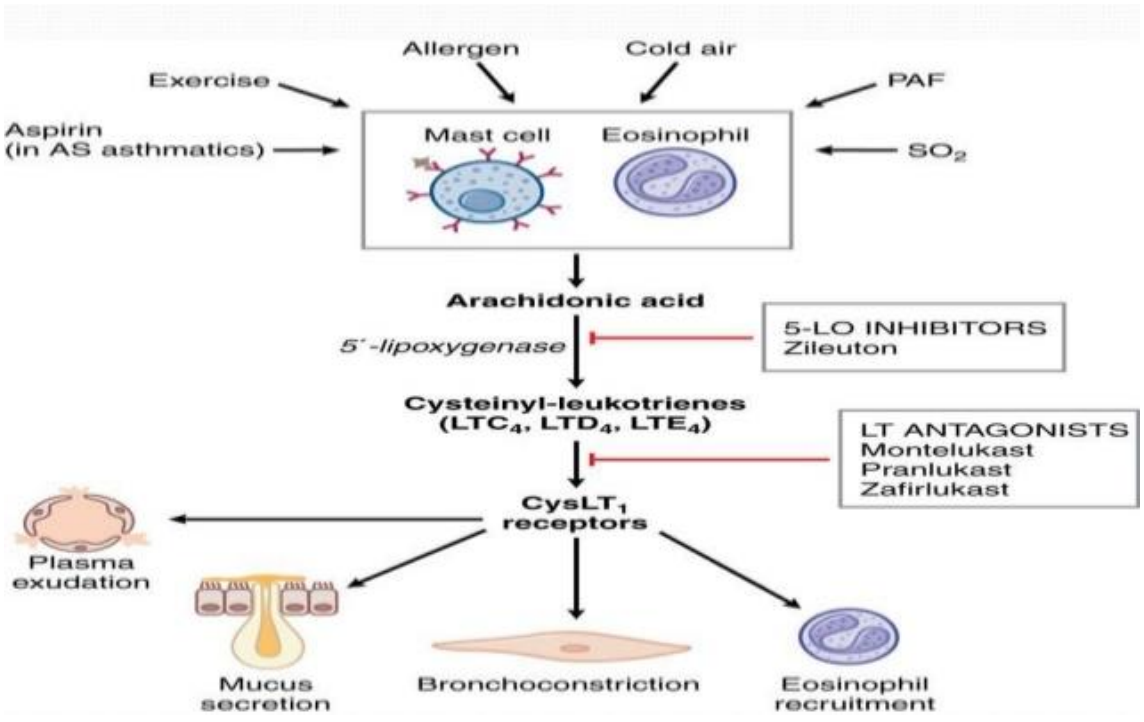

Figure 33: Mechanism of action of Montelukast

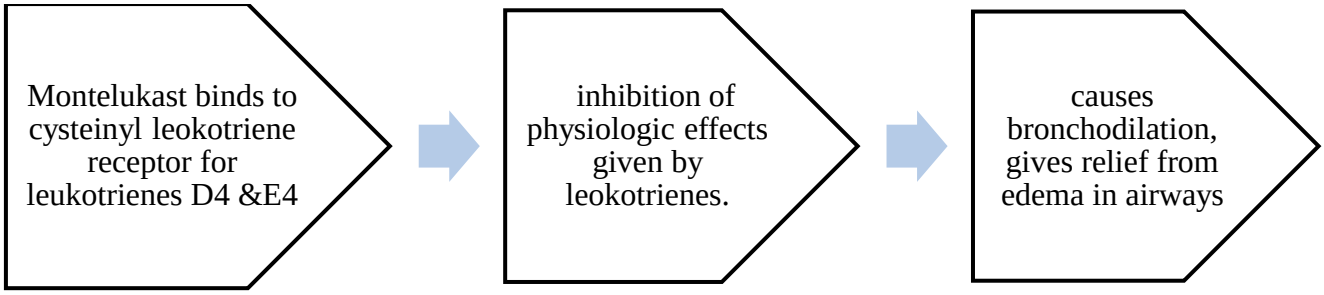

Figure 34: Flowchart showing mechanism of action of Montelukast

3.12.3.6 Salbutamol

Salbutamol, a moderately selective beta-2 adrenoreceptor agonist have a similar structure to terbutaline and is widely works as a bronchodilator to manage asthma and other chronic obstructive airway diseases. Salbutamol also known as Albuterol is found to be the racemic mixture of the r-isomer levalbuterol and s-albuterol which is a short-acting sympathomimetic agent with bronchodilator activity. Albuterol acts on beta-2 adrenergic receptors in the lungs majorly but also stimulates beta-1 adrenergic receptors to a lesser extent, thereby increasing the force and rate of myocardial contraction.

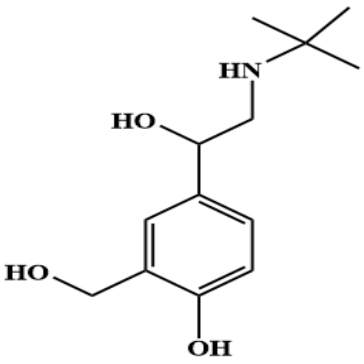

Figure 35: Structure of Salbutamol

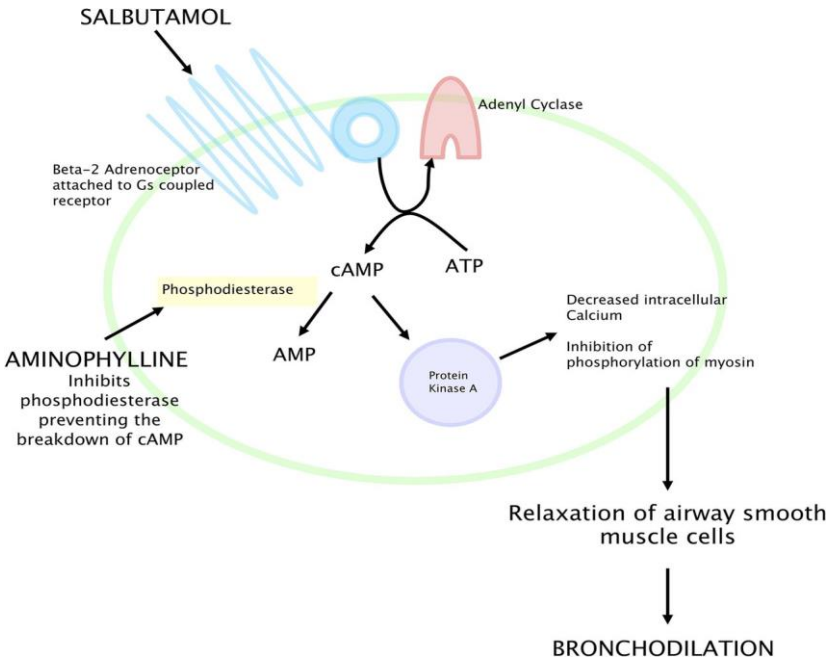

Figure 36: Mechanism of action of Salbutamol

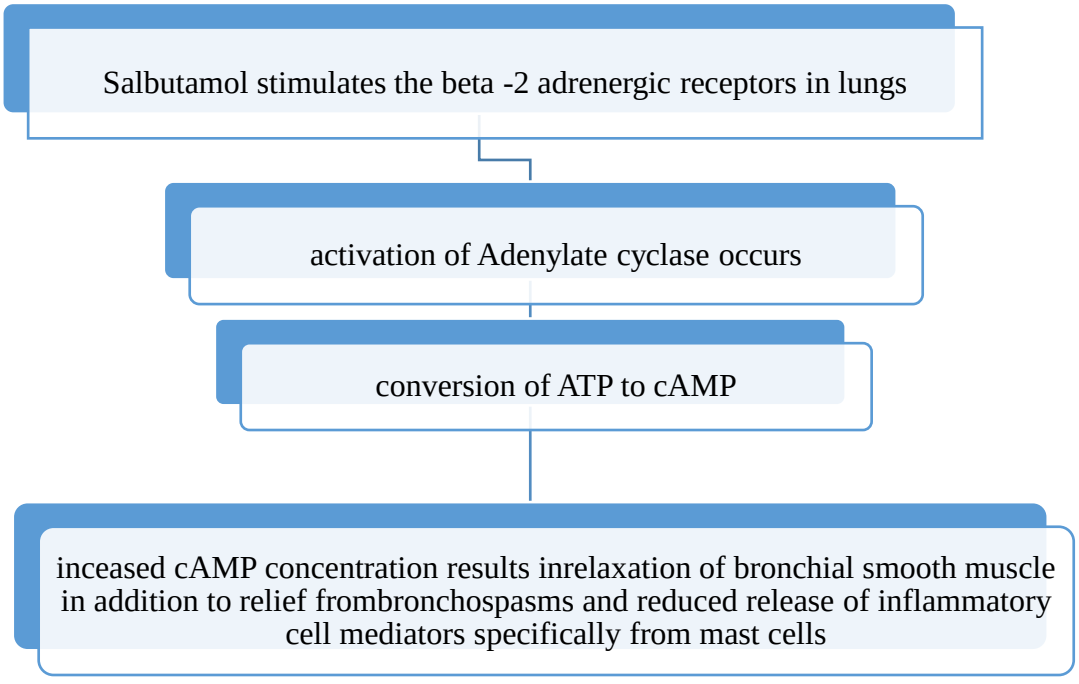

Figure 37: Flowchart showing mechanism of action of Salbutamol (Neame et al., 2015)

Chapter 4

Discussion

The study was done based on the parameters that are part of the questionnaire made for the survey and the result found from the survey performed in a hospital in Dhaka city. The survey was performed on only men participants. Thus the condition and analysis of condition of female COPD patients could not be identified by this study. Majority of the patients were found to be nonsmokers who were smoker formerly. They had quit smoking totally due to diseased conditions for more than 5years at least and thus considered nonsmokers. Few patients are found to continue being smokers even despite their condition.

Among the patients different age groups were found but all being 40years and above as COPD patients ought to be aging likely. During the survey it was observed that most number of patients were above even 50 years old with different severity of the disease condition.

Lifestyle behaviors of the participants were studied in the process. As one of the major aspect of the study was to determine the exposure of patients to household smokes prepared from different possible sources, this parameter was included in the questionnaire with utmost importance. The patients were exposed to smoke for at least about three hours in a single day up to 7 hours a day. Sources might differ in nature. A majority of patients were seen to be using biomass fuel instead of stoves that work with either liquid paraffin or natural gas. These stoves create way more smoke and causes harm to the patients. Choice of cooking oil used in the patient differs in patients. It is found that soybean oil majorly, and other options were mustard oil, rice bran oils etc.

Moreover, a great source of the household smokes is found to be usage of different forms of mosquito repellants. Of those repellants, mosquito coils are used mostly all over the year.

Mosquito repellant sprays are also used in a small number of participants either alone or alteration with the coils occasionally. Some participants were found to be exposed to air pollutants and industrial dust due to the location of their residence.

Usage of perfume & room fresheners were found to be present but in a negligible percentage. Patients were asked about their effort to avoid the exposure to household smokes and none were found to take steps like changing stove type, appointing ventilators or kitchen chimney etc. A small number of participants changed to using mosquito net instead of any type of repellants in their daily lives.

A range of symptoms were found to be faced by patients having different severity of the disease for example shortness of breath, sneezing, wheezing, coughing etc. In presence of smokes, symptoms like burning sensation in eyes were noticed. Patients were asked about members of their family having COPD and other lung diseases. The answer came out with a minor percentage of patients having tuberculosis and asthma, either former or current.

For diagnosis of the disease a couple of tests were asked to be done for individual patients by the physicians as a particular test might not prove to gather sufficient knowledge needed for further judgment about the disease. Here, spirometry, sputum tests, chest X-ray being the mostly used ones. Patients were found to visit a physician in varying frequency because the conscious participants visited once in a month or once in three months. And other ones visit once in 6months or more. It was noticed that patients tend to attend the physician whenever they feel the need due to disease progression rather than following up on the schedule suggested for them individually.

A couple of medicines were prescribed commonly to the patients in different doses according to the severity of the disease, age and other concurrent diseases. The commonly used medicines have different mechanism of action in the body that help the patients improve their

condition. Medicines prescribed had different dosage forms such as tablet, capsules and nebulizers. Oxygen inhalation was suggested to patients having severe conditions of the disease. Also, some drugs were prescribed to be continued and some were prescribed for a certain period. The elderly patients were found to be taking medicines for diseases like diabetes, heart disease, liver malfunction, prostate related disorders etc.

Consultation about avoiding the smokes generated from house and adjacent outdoor locations of patients could have helped the unaware patients but it seemed that consultation regarding the exposure to household smokes and alternative measures to be taken does not exist at all.

Chapter 5

Conclusion

COPD being a preventable and treatable disease has several periods of worsening in terms of disease progression. With increasing age additional diseases add to the frequency of symptomatic attacks and declined lung function. The significant concurrent diseases involve in the comorbidity of the disease. The additional diseases such as cardiovascular problems, kidney diseases, skeletal muscle dysfunction, some metabolic disorders and lung cancer occurring in COPD patients with increasing age may increase the chances of hospitalizing the patients. Thus management of those diseases with individualized attention may help stabilizing the disease progression of COPD patients. COPD is a disease which might be prevented from exaggeration of symptoms which proper counseling of patients about changes in their lifestyle behaviors. Quitting to smoke as well as choosing better options of stove system, mosquito repellants used in households as well as maintaining least level of exposure to those smokes may bring significant changes in severity and frequency of symptoms & disease progression. The patients must be prepared as educated individuals about the disease and the ways how to avoid symptomatic progression of the disease. Patients must be awaked about self-management ways such as understanding the risk factors, withdrawal of smoking and intentional exposure to any source of smokes that contain noxious particles. The patients must know about recognizing stages of exacerbation, when to take necessary decisions about hospitalization, seeking extra help etc. The patients must develop themselves as individuals who are aware about motivating themselves in adapting behaviors that help in better and accelerated management of the disease.

Chapter 6

Future plan of the work

The study is performed in a very confined manner with participation of only 50 patients and also only in a hospital of Dhaka city. If the study could be brought up to the whole population of COPD patients in Dhaka city might depict a sign of severity of effect of smoke on patients. The study could be done in way where each patient is closely monitored starting from their lifestyle choices to treatment choices made for them over a time for example over a year. Then the condition of patients after any changes brought in that period, any improvement happening or the stability of symptoms and severity of disease could be discussed upon. Also, the study can be done on different areas of the country to area-specific comparison of the factors.

Patients are not aware of the factors in consideration of this study and their relation to the disease. Awareness campaigns could be designed in participation of doctors, pharmacists, pharmaceutical companies, nongovernment organizations and also students studying life science.

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