" TO STUDY THE SERUM MAGNESIUM LEVELS IN ACUTE EXACERBATION OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE "

By

DR. MANOHAR GOWDA B G

Dissertation submitted to the

Sri Devaraj Urs Academy of Higher Education and Research,

Tamaka, Kolar, Karnataka,

IN PARTIAL FULFILLMENT OF THE REQUIREMENT FOR THE DEGREE OF

DOCTOR OF MEDICINE (M.D.)

IN

GENERAL MEDICINE

Under The Guidance Of

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SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR, KARNATAKA.

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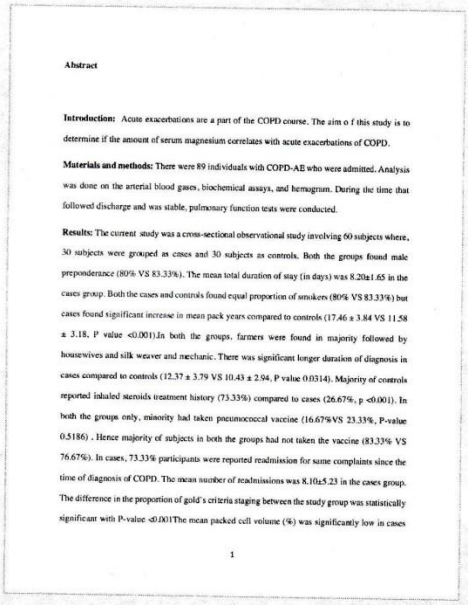

Abstract

Introduction: Acute exacerbations are a part of the COPD course. The aim o f this study is to determine if the amount of serum magnesium correlates with acute exacerbations of COPD.

Materials and methods: There were 89 individuals with COPD-AE who were admitted. Analysis was done on the arterial blood gases, biochemical assays, and hemogram. During the time that followed discharge and was stable, pulmonary function tests were conducted.

Results: The current study was a cross-sectional observational study involving 60 subjects where, 30 subjects were grouped as cases and 30 subjects as controls. Both the groups found male preponderance (80% VS 83.33%). The mean total duration of stay (in days) was 8.20±1.65 in the cases group. Both the cases and controls found equal proportion of smokers (80% VS 83.33%) but cases found significant increase in mean pack years compared to controls (17.46 ± 3.84 VS 11.58 ± 3.18, P value <0.001).In both the groups, farmers were found in majority followed by housewives and silk weaver and mechanic. There was significant longer duration of diagnosis in cases compared to controls (12.37 ± 3.79 VS 10.43 ± 2.94, P value 0.0314). Majority of controls reported inhaled steroids treatment history (73.33%) compared to cases (26.67%, p <0.001). In both the groups only, minority had taken pneumococcal vaccine (16.67%VS 23.33%, P-value 0.5186) . Hence majority of subjects in both the groups had not taken the vaccine (83.33% VS 76.67%). In cases, 73.33% participants were reported readmission for same complaints since the time of diagnosis of COPD. The mean number of readmissions was 8.10±5.23 in the cases group. The difference in the proportion of gold's criteria staging between the study group was statistically significant with P-value <0.001The mean packed cell volume (%) was significantly low in cases

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PRIOR PERMISSION TO START OF STUDY

The Institutional Ethics Committee of Sri Devaraj Urs Medical College, Tamaka, Kolar has examined and unanimously approved the synopsis entitled **"To study the serum magnesium levels in acute exacerbation of chronic obstructive pulmonary disease"** being investigated by **DR. MANOHAR GOWDA B G**, Dr. Raveesha A in the Department of Medicine at Sri Devaraj Urs Medical College, Tamaka, Kolar. **Permission is granted by the Ethics Committee to start the study.**

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- **DR MANOHAR GOWDA B G**

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Glossary	Abbreviations
COPD	Chronic Obstructive Pulmonary Disease
CRD	Chronic Respiratory Disease
DALY	Disability Adjusted Life Years
CRP	C-Reactive Protein
IL	Interleukin
TNF	Tumor Necrosis Factor Factor
SP	Substance – P
COPD	Chronic Obstructive Pulmonary Disease
PFT	Pulmonary Function Testing
SABA	Short-acting beta2-agonist
SAC	short-acting anticholinergic
FEV1/FVC	forced vital capacity ratio
NHLBI	National Heart, Lung, and Blood Institute
WHO	World Health Organization
GOLD	Global Initiative for Chronic Obstructive Lung Disease
CAT	COPD Assessment Test
mMRC	Medical Research Council
TCR	T-cell antigen receptors
HIV	Human Immunodeficiency Virus
SIV	Simian Immunodeficiency Virus
TGP	tobacco glycoprotein
NIV	non-invasive ventilation

ABSTRACT

Introduction: Acute exacerbations are a part of the COPD course. The aim of this study is to determine if the amount of serum magnesium correlates with acute exacerbations of COPD.

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significantly higher compared to controls (14.69 ± 3.11 VS 9.74 ± 2.13, P value <0.001. The mean serum magnesium (mg/dL) with in cases was significantly less compared to controls (1.45 ± 0.29 VS 2.23 ± 0.52 P value <0.001). The mean pulmonary function test (forced expiratory volume) in cases was significantly low compared to controls (41.13 ± 16.31 VS 60.00 ± 12.11 P value <0.001). In cases, 36.67% participants had reported normal chest Xray and 19 (63.33%) had reported non-homogenous opacities chest Xray. In controls, all of them 30 (100.00%) participants had reported normal chest Xray.

Conclusions: Hence the study results found that the low magnesium levels was substantially related with acute exacerbation of COPD with less pulmonary function and longer duration of disease.

INTRODUCTION

INTRODUCTION:

A potentially fatal lung condition, chronic obstructive pulmonary disease (COPD) is the third leading cause of death globally. The Global Burden of Disease Study estimates that there are over 251 million cases of COPD.[1] Over 90% of COPD-related fatalities occur in emerging countries.[2] In India, COPD is the 2nd factor in fatalities from non-communicable illnesses.[3] The exacerbation of COPD is becoming a more significant issue for patients as well as clinicians due to the disease's rising prevalence on a global scale.[4]

Nearly 65 million individuals worldwide are estimated to have moderate to severe COPD, which contributes for 5% of all mortality (41.9 / 100,000) and continued to be the most common illness-specific chronic respiratory disease (CRD) in 2017.[5] COPD also imposes a major burden in terms of health-care expenses and health-related quality of life. In 2016, it was the second greatest contributor of Disability Adjusted Life Years (DALY) and the main cause of disability among chronic respiratory disorders. [6] COPD caused about 32% of worldwide DALYs in 2016, and it is responsible for 75.6 percent of overall DALYs among chronic respiratory diseases in India.[5] From 2007 to 2017, COPD-related mortality was found to be 39%. The majority of known COPD data comes from high-income nations, whereas 90% of fatalities occur in poor and middle-income countries. 33 percent of the world's population and 66 per cent of COPD deaths were in India and China.[7,5]

COPD risk factors include smoking, the use of firewood or biomass fuel for cooking, outdoor air pollution, increasing age, occupation, gender, lung damage from TB, and socioeconomic status. [8]Smoking was shown to be linked with older age, poorer socioeconomic position, level of education, lack of understanding about the risks of smoking, and living in rural regions.[9] Multiple studies found that lower socioeconomic level, air pollution, and occupational or environmental tobacco/dust exposure all increase the risk of COPD.[10,11]

In most cases, the chronic damage caused by risk factors leads mucus buildup, bronchiolar fibrosis, and local inflammation (development of lymphoid follicles and infiltration of inflammatory cells). Along with continuous low-grade systemic inflammation and high levels of affecting molecules (C-reactive protein (CRP), interleukin (IL)-6, tumor necrosis factor factor (TNF), and blood leukocytes), people with moderate to severe stable COPD typically also have lung inflammation.[12]

Exacerbations follow infections, irritability, and changes in the surrounding temperature. Depending on the severity, exacerbations are frequently accompanied by an increase in neutrophilic or eosinophilic infiltration. A slight increase in airflow restriction occurs in mild exacerbations, whereas respiratory muscle fatigue, ventilation perfusion mismatch, and severe exacerbations affect pulmonary gas exchange. A severe exacerbation is characterized by bronchoconstriction, mucous hypersecretion, oedema, and airway inflammation. The pulmonary arterioles' subsequent hypoxic vasoconstriction reduces perfusion as a result.[13] As a result, there is growing interest in developing the best COPD treatment options as well as strategies for avoiding exacerbations.[14]

Magnesium and inflammatory response are closely related, according to several studies. Animals deficient in magnesium for three weeks have been shown to have raised levels of cytokines that are aggravating (Interleukin 6, Tumor Necrosis Factor). During the first week of magnesium deficiency, researchers also found plasma Substance - P (SP), a well-known stimulator of cytokine production. Interleukin-2, Interleukin-10, and Interferon gamma can reach their peak levels five or seven days after magnesium deficiency, respectively, depending on the cytokine.[15] One of the causes of the inability to clear secretion is bronchospasm. Reduced pulmonary gas exchange could have negative effects on one's quality of life and require frequent hospital stays. It has been proposed that magnesium helps

to maintain the patency of airways by lowering bronchial smooth muscle tension, even if the precise mechanism of action is uncertain.[16]

Need of the study

An intracellular cation called magnesium (Mg2+) controls the tone of the bronchial tubes and the activity of the respiratory muscles. In certain research, the part magnesium plays in long-term respiratory illnesses is examined. Magnesium is the second-most frequent cation in cellular fluid. Magnesium is a cofactor in many enzyme systems that regulate a number of biochemical processes within the body, such as the creation of proteins, the preservation of blood glucose levels, the blood pressure control, and the function of nerves and muscles. Magnesium is also required for the manufacture of ATP. Calcium and potassium are actively transported across cell membranes by magnesium.[17]

Airway hyperactivity is increased and pulmonary function is hampered by hypomagnesemia. A lower magnesium level is thought to increase COPD exacerbations because of its bronchodilator properties. [17] An increasing amount of evidence shows that magnesium shortage contributes to asthma attacks, and as a result, magnesium helps these patients' bronchospasm.[18,19] However, it is unclear exactly how this action works. According to some theories, magnesium helps to keep the smooth muscles in the bronchi open by relaxing them.[20] A component of asthmatic bronchitis is present in patients with chronic obstructive pulmonary disease (COPD), which is a combination of chronic bronchitis and emphysema. They are unable to expel secretions due in part to bronchospasm. Reduced pulmonary gas exchange could be the result, which could have negative effects on one's quality of life and require frequent hospital stays. As a result, magnesium may help COPD patients' diseases stay stable. [21] Hence the present study aimed to assess study the variation of serum Mg levels in subjects with COPD with acute exacerbation.

AIMS AND OBJECTIVES:

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1. To assess the COPD patients and COPD subjects with acute exacerbation.
2. To estimate the Serum Mg Levels in patients with COPD and COPD patients with acute exacerbation.
3. To correlate the serum Mg levels in stable COPD subjects and acute exacerbated COPD patients.

REVIEW OF LITERATURE

REVIEW OF LITERATURE:

COPD

A common, preventable, and treatable condition known as COPD is characterised by recurrent breathlessness and airflow restriction brought on by respiratory system and/or alveolar deformities, which are typically brought on by prolonged exposure to hazardous particles or gases.

Chronic airflow restriction, which is the defining feature of COPD, is brought on by a mix of parenchymal damage (emphysema) and small airway disease, the proportions of which differ from individual to individual. Chronic inflammation leads to structural modifications, narrowing of small airways, and tissue loss in the lungs. Airflow limitation and mucociliary malfunction, two signs of the illness, may be exacerbated by small airway loss.[22]

Acute respiratory episodes may coexist with chronic respiratory symptoms ahead of the onset of airflow limitation.[22]Even those with normal spirometry results might develop chronic respiratory problems. Additionally, a sizable number of cigarette smokers who do not suffer from airflow restriction have anatomical signs of lung illness, including as hyperinflation, thickening of the airway walls, and gas entrapment. [23]

Epidemiology

A systematic review by Verma, A et al[6] presented the data from published studies on COPD prevalence and risk factors undertaken among people over the age of 30 in India between 2000 and 2020. Using the meta-analysis data, it was found that, COPD prevalence of 7.0 percent based on estimates from 23 studies with a total of 80 138 study participants in India. These findings showed a lower prevalence of COPD than the worldwide incidence, which ranges from 10.7 percent to 12.1 percent.[24] The systematic analysis found study's pooled COPD prevalence lower than that reported in South-East Asia (8.80 percent), but it is similar

to the spirometry-diagnosed COPD prevalence.[24] In contrast, the review found a higher prevalence of COPD (5.87 percent) than that reported in a meta-analysis.

Notably, the stratified prevalence calculation revealed a greater prevalence of COPD (8%) among those identified using spirometry vs those diagnosed using a non-spirometry approach (7 percent). These findings are consistent with meta-analysis estimates from Africa, which revealed a greater COPD prevalence on spirometry data (13.4 percent) compared to non-spirometry data (4.0 percent).[25] Furthermore, in comparison to our findings, studies from Nepal (15.4%),[26] Pakistan (11.31%),[27] Sri Lanka (16.4%,[28] and Bangladesh (13.5%) [29] found greater prevalence.

The review observed a variation with the prevalence of COPD in other study settings, including South Asian countries, when comparing the prevalence of other studies with this review. This could be due to differences in geographical settings, criteria for COPD diagnosis, exposure to COPD risk factors, diversity of COPD diagnostic definitions, sampling method, and study population. Evidence suggests that 50 percent to 90 percent of persons with COPD go undetected due to a shortage of spirometers or educated health practitioners to identify the disease. Programs to address NCDs in India are mostly focused on diabetes, cardiovascular disease, and hypertension; however, enough attention should also be paid to diagnosing and managing COPD.[30]

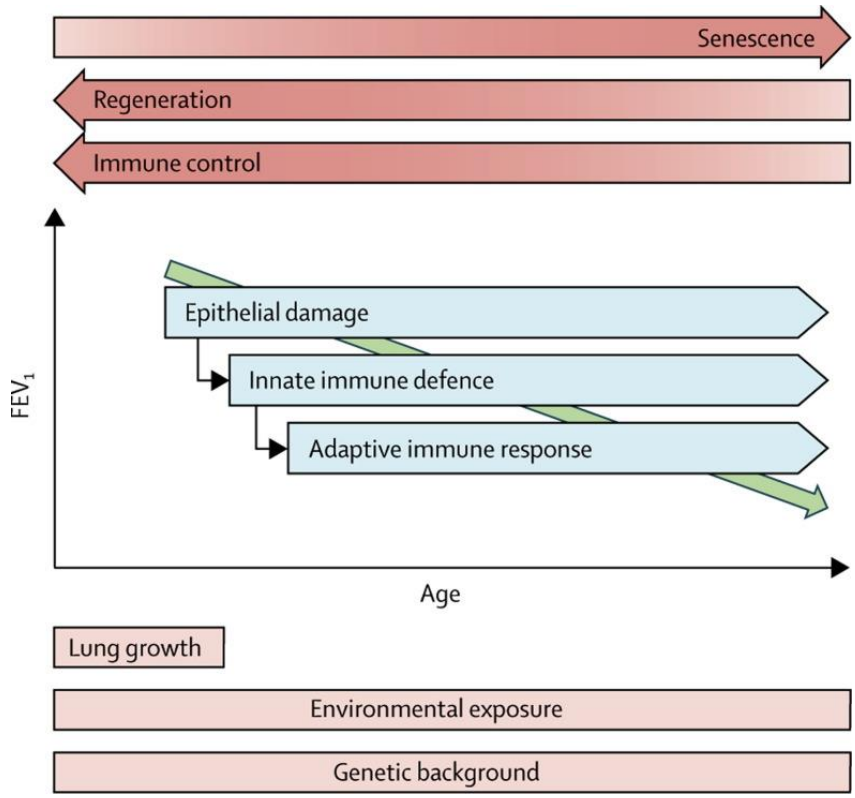
Etiology, risk factors, pathophysiology

COPD is distinguished by a restriction of airflow that is not totally reversible. Remodeling of the small-airway compartment and loss of elastic recoil due to emphysematous degradation of the parenchyma result in a gradual drop in FEV1, insufficient lung emptying on expiration,

and subsequent static and dynamic hyperinflation.[31] At the pathogenic level, smoking causes inflammatory cells to infiltrate the mucosa, submucosa, and glandular tissue. Increased mucus production, epithelial cell hyperplasia, and disturbed tissue regeneration with wall hypertrophy in the smaller air passages are features of COPD.[32] The progressive compression, complete destruction, and even removal of the bronchial tubes are symptoms of emphysema, which frequently starts in the bronchi.[33]

Small-airway wall widening and lung tissue loss is thought to be caused by a number of immunopathology processes that interact against a multifaceted background of genetic determinants, lung development, and environmental cues. However, the exact mechanisms causing these changes remain unclear. [34]

Figure 1: Schematic representation of the mechanisms involved in the pathogenesis of chronic obstructive pulmonary disease.



The process is essentially characterised by a decline in FEV_1 with increasing age. FEV_1=forced expiratory volume in 1 s.

Smoking cigarettes causes airway epithelial cells to become directly damaged, which causes endogenous intracellular compounds or danger-related molecular patterns to be released. A non-specific inflammatory reaction occurs when these signals are detected by sequence receptors on epithelia, such as Toll-like ligands 4 and 2.[35] To regulate the innate immune response, early cytokines (such as tumour necrosis factor and interleukins 1 and 8) direct macrophages, neutrophil, and dendritic cells to the site of inflammation. If proteolytic enzymes and reactive oxygen molecules are not properly balanced by antioxidants and antiproteases, they will create more damage.[36]

Immature dendritic cells collect self-antigens generated by injured tissue as well as foreign antigens from entering pathogens and deliver them to naïve T cells in draining lymph nodes. Once activated, antigen-specific CD4 and CD8 cells, as well as antibody-producing B cells, are attracted to the lungs to neutralise the antigens. Tertiary lymphoid aggregates, involving an oligoclonal selection of the B and T cells involved, form around the tiny airways as the illness advances.[37] Although the specific structure and function of these aggregates are unknown, adaptive or autoimmune responses are thought to keep the inflammation going even after smoking is stopped.[38]

Clinical presentation and Diagnosis

Any patient with dyspnea, a chronic cough, phlegm production, and/or a record of susceptibility to illness risk factors should have their COPD evaluated. Spirometry is necessary in this clinical setting to make the diagnosis. [39]In patients with the appropriate symptoms and risk factors, a post-bronchodilator FEV1/FVC ratio of less than 0.70 confirms the occurrence of chronic airflow limitation and identifies the presence of COPD.

The symptoms of COPD usually appear in maturity, frequently in the winter. Patients typically complain of persistent, chronic dyspnea, a coughing, and phlegm production. The chest may feel constricted and the patient may also wheeze. While cigarette history is present in the majority of instances, many people lack it. They should be questioned about their familial history, occupational and environmental hazards, including exposure to secondhand smoking. COPD patients should be questioned about past exacerbations, nightly awakenings, inhaler use, and how the condition affects level of activity. Individuals should be questioned about any prior medical conditions they may have had, such as asthmatic, allergies, or respiratory infections as a kid. Alpha-1 antitrypsin deficiency should be suspected in those with liver illness, basilar emphysema, and a genetic predisposition of emphysema. The typical symptoms of an acute COPD exacerbation include wheezing, more dyspnea, and a productive cough.[40]

Individuals who have COPD may exhibit several clinical findings, including the following:

In common [40]

• Severe respiratory discomfort in exacerbations;

• Muscle atrophy

Respiratory system [41]

• Clenched breathing; extended expiration; utilisation of auxiliary respiratory system;

Chest [41]

• A larger chest wall's with respect to anteroposterior dimensions (barrel chest)

Skin [42]

• When arterial supply of oxygen is poor, central cerebral hypoxia can occur.

Extremities [40]

- Digital clubbing
- Right heart failure with edoema in the lower extremities

Note: If any of these indications are present in a person aged more than 40, consider COPD and do spirometry. These symptoms are not diagnostic in and of themselves, but the presence of many critical markers improves the likelihood of a COPD diagnosis. Spirometry is essential to make a COPD diagnosis.

Table 1: Important signs to examine for diagnosing COPD

Dyspnoea ie…	• Progression with time; Typically becomes worst and activity; Consistent
Chronic cough	• Could be infrequent and unsuccessful • Repeated wheezing
Chronic sputum production	• With any pattern
Recurrent lower respiratory tract infections History of risk factors	• Host characteristics, including heredity, congenital anomalies, and developmental anomalies, etc. Combustion from household heating and cooking fuels and from tobacco • Occupational chemicals, hydrocarbons, and noxious fumes
Family history of COPD and/or childhood factors	For instance, reduced birth weight and respiratory problems in children

Diagnosis

Individuals with relevant signs and health conditions are frequently tested for COPD. Spirometry is utilized to confirm the diagnosis. Other examinations might consist of a 6-minute walk assessment, lab examinations, and radiographic image analysis.[40]

It is crucial to diagnose, stage, and monitor COPD using pulmonary function testing (PFT). Before and after giving an inhaled bronchodilator, spirometry is done. Short-acting beta2-agonist (SABA), short-acting anticholinergic (SAC), or a mixture of both types of drugs can be used as inhaled bronchodilators. The diagnosis of COPD is confirmed if the forced expiratory volume in one second to forced vital capacity ratio (FEV1/FVC) is less than 0.7.

Pulse oximetry or arterial blood gas analysis should be used to assess oxygenation in patients with a markedly decreased FEV1 and indications of dyspnea.[43,44]

The National Heart, Lung, and Blood Institute (NHLBI) and the World Health Organization (WHO) launched the Global Initiative for Chronic Obstructive Lung Disease (GOLD) initiative. The programme is renowned across the world for offering up-to-date and comprehensive updates on the suggestions for the diagnosis and treatment of COPD. It is common practise to evaluate illness severity and treatment options using the GOLD criteria. [40]

The 2019 GOLD report describes a streamlined process for assessing and selecting the initial COPD medication for patients. The GOLD group categorization and illness severity are determined by the healthcare professionals using the sophisticated ABCD evaluation method. The severity of COPD is assessed using the FEV1 once spirometry has verified the diagnosis (FEV1/FVC 0.7). (GOLD classification 1-4). The degree of symptom intensity and the history of exacerbations are then used to define the GOLD group (A-D).[40]

The COPD Assessment Test (CAT) and the modified British Medical Research Council (mMRC) survey are used to assess the severity of symptoms (Table 2). The mMRC questionnaire rates the severity of shortness of breath on a scale from 0 to 4, with 4 being the worst. The COPD Assessment Test (CAT) assigns a grade based on eight functional criteria to assess how the illness affects a patient's day-to-day activities.

A 6-minute walk test is frequently used to evaluate a participant's sub – maximal functional ability. On a level, straight surface indoors, this test is conducted. The corridor is typically

100 feet long, and the test evaluates the participant's walking distance over the course of six mins.[45]

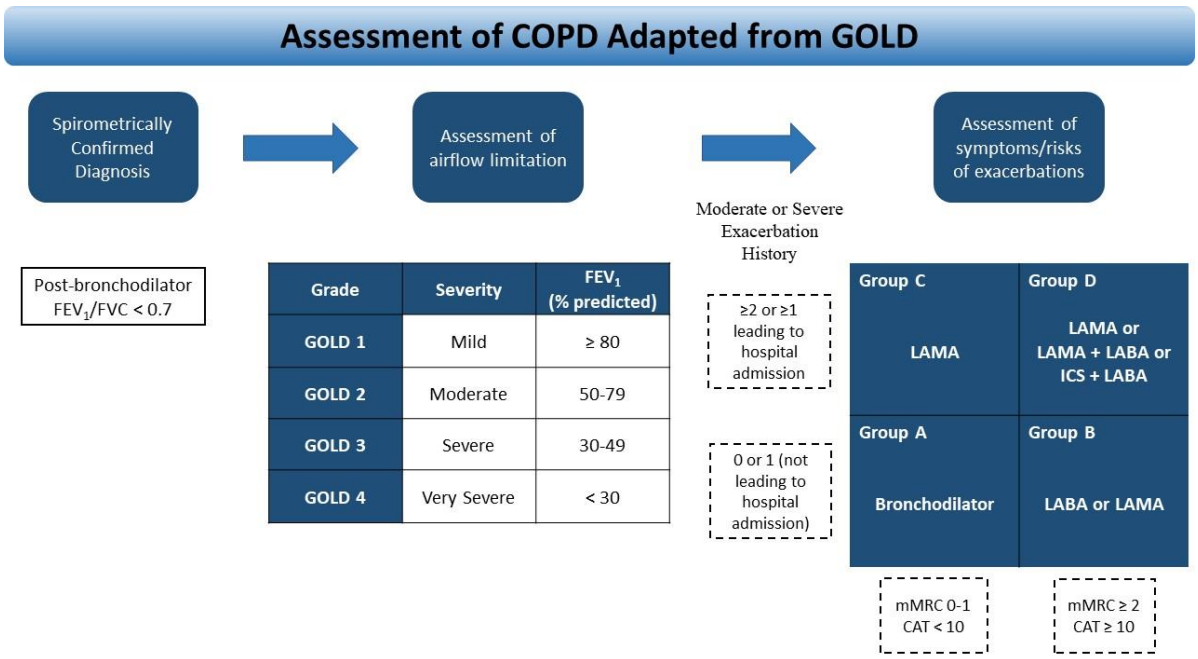
A total blood count is frequently needed as part of laboratory testing to check for infections, anaemia, and polycythemia. For further COPD reasons, α1 antitrypsin values should be examined.

Chest radiography and computed tomography are examples of radiographic imaging (CT). On chest x-rays, hyperinflation, diaphragmatic flattening, and greater anterior-posterior diameter may all be seen. Bronchial wall hypertrophy may be observed in situations of chronic bronchitis. Patients with bronchiectasis, cancer patients, or those contemplating surgical operations may find CT imaging helpful. Centrilobular emphysema will be substantial on a CT of the chest in individuals with COPD. The subpleural areas may include bullae. [46]

The evaluation of COPD does not require a biopsy. An upsurge in proinflammatory cytokines, structural modifications, and lymphoid follicles are among the histopathologic findings.

An immediate increase of respiratory symptoms is referred to as an acute exacerbation of COPD. The model created by Anthonisen and colleagues, which categorises severity by the presence of increasing breathlessness, phlegm volume, and purulence, is frequently used for assessing severity. An upper respiratory infection within five days, increased wheezing, increased coughing, fever without additional cause, an elevation in heartbeat or breathing rate from the patient's baseline, or the presence of two or several of these symptoms together, are considered mild exacerbations. When two or all three of the symptoms are present, an exacerbation is deemed moderate or severe. Patients may have physical symptoms of hypoperfusion and hypercapnia as well as severe respiratory failure. Pulse oximetry, chest radiography, and artery blood gas analysis are recommended. [44]

Figure 2: COPD assessment adapted from GOLD 2022 report.[47]



GOLD criteria (recent staging, 2022 staging criteria)

Spirometry and medical history, including symptom history and the existence of risk factors, are used to diagnose COPD. Spirometry is a non-invasive, easily accessible, and objective measure of airflow restriction. Spirometry is necessary to provide an authoritative diagnosis of COPD, with a postbronchodilator FEV1/FVC (FEV1/FVC) of 0.70 demonstrating ongoing airflow restriction. Smoking status and occupational or environmental exposures are important risk factors. Dyspnea, cough, sputum production, wheezing, and chest tightness are all common symptoms of COPD. As indicated by the new Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommendations, it is critical to consider differential diagnosis while examining symptoms, especially during the COVID-19 epidemic.[48]

The GOLD recommendations for 2021 propose that spirometry be used exclusively for patients who require urgent or necessary testing for diagnosis and/or to assess lung function for interventional treatments or surgery, as such testing may result in virus transmission. A safer approach may be to employ home peak expiratory volume measurement and verified

patient surveys. These questionnaires are administered during an interview and are used to measure respiratory health, symptoms, comorbidities, and risk factors for developing COPD.[49]

COPD symptoms and COVID-19 infection symptoms may overlap. Coughing and shortness of breath are the two most common overlapping symptoms. Fever, hypoxia, loss of smell or taste, migraines, and lymphopenia are some of the symptoms that favour COVID-19. Pathophysiologic alterations caused by the SARS-CoV-2 virus include vascular damage, pneumonitis linked with hypoxemia, coagulopathy, high levels of systemic inflammation, and multiorgan involvement.[48]

The GOLD guidelines classify patients into four different categories: GOLD 1 (mild), GOLD 2 (moderate), GOLD 3 (severe), or GOLD 4 (very severe) based on their level of airflow limitation. This is assessed by evaluating a postbronchodilator FEV_1/FVC. Refer to TABLE 1 for more information regarding FEV_1 values and GOLD classification.[50]

Figure 3: 2022 GOLD classification of COPD.[50]

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

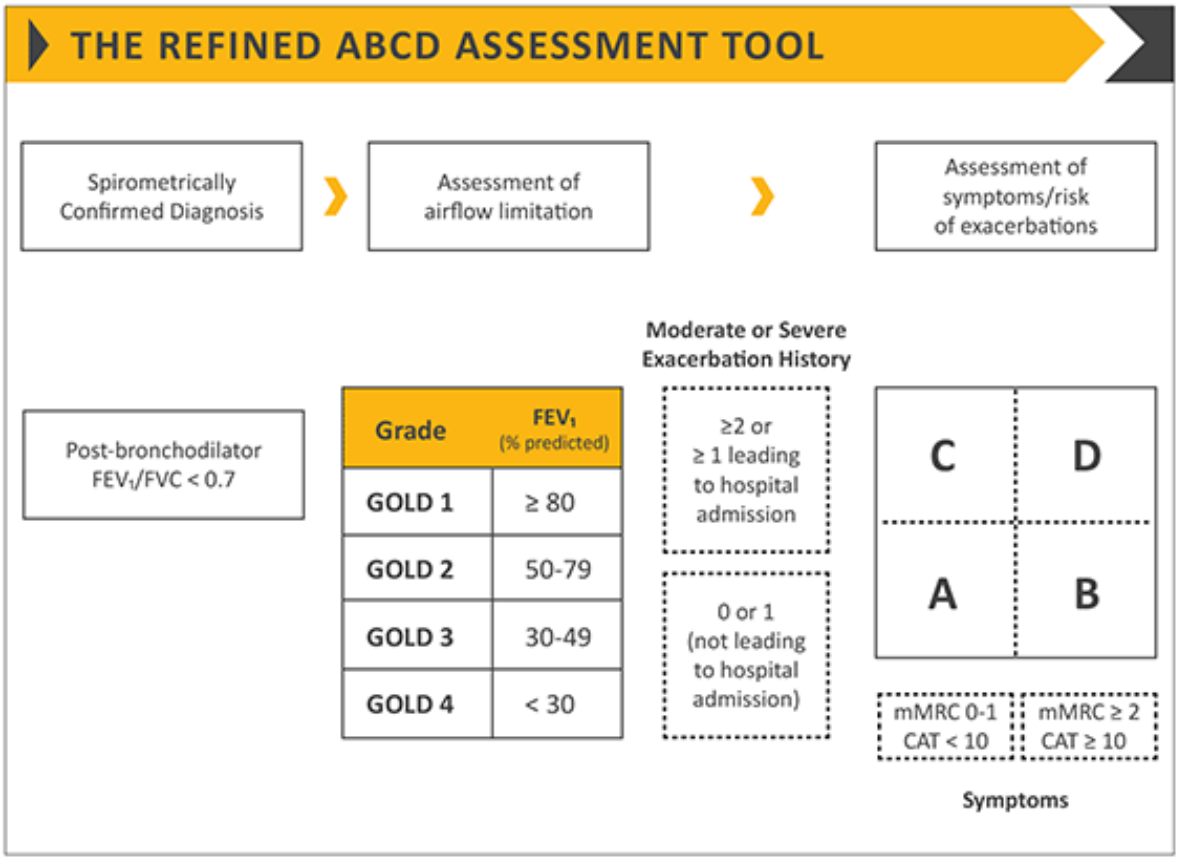
COPD: chronic obstructive pulmonary disease; FEV1: forced expiratory volume in 1 second; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease. Source: Reference 1. Reprinted with permission.

The Modified British Medical Research Council (mMRC) Questionnaire and the COPD Assessment Test (CAT) are the two most often used assessments for assessing COPD

symptoms. The mMRC is used to measure COPD patients' breathlessness. It is graded from 0 to 4, with 0 suggesting merely hard activity and 4 indicating dyspnea that impacts daily tasks as well as the ability to leave the house. The CAT is an eight-item test of COPD impairment with scores ranging from 0 to 40. Higher CAT scores imply a greater impact of COPD on the patient's life.

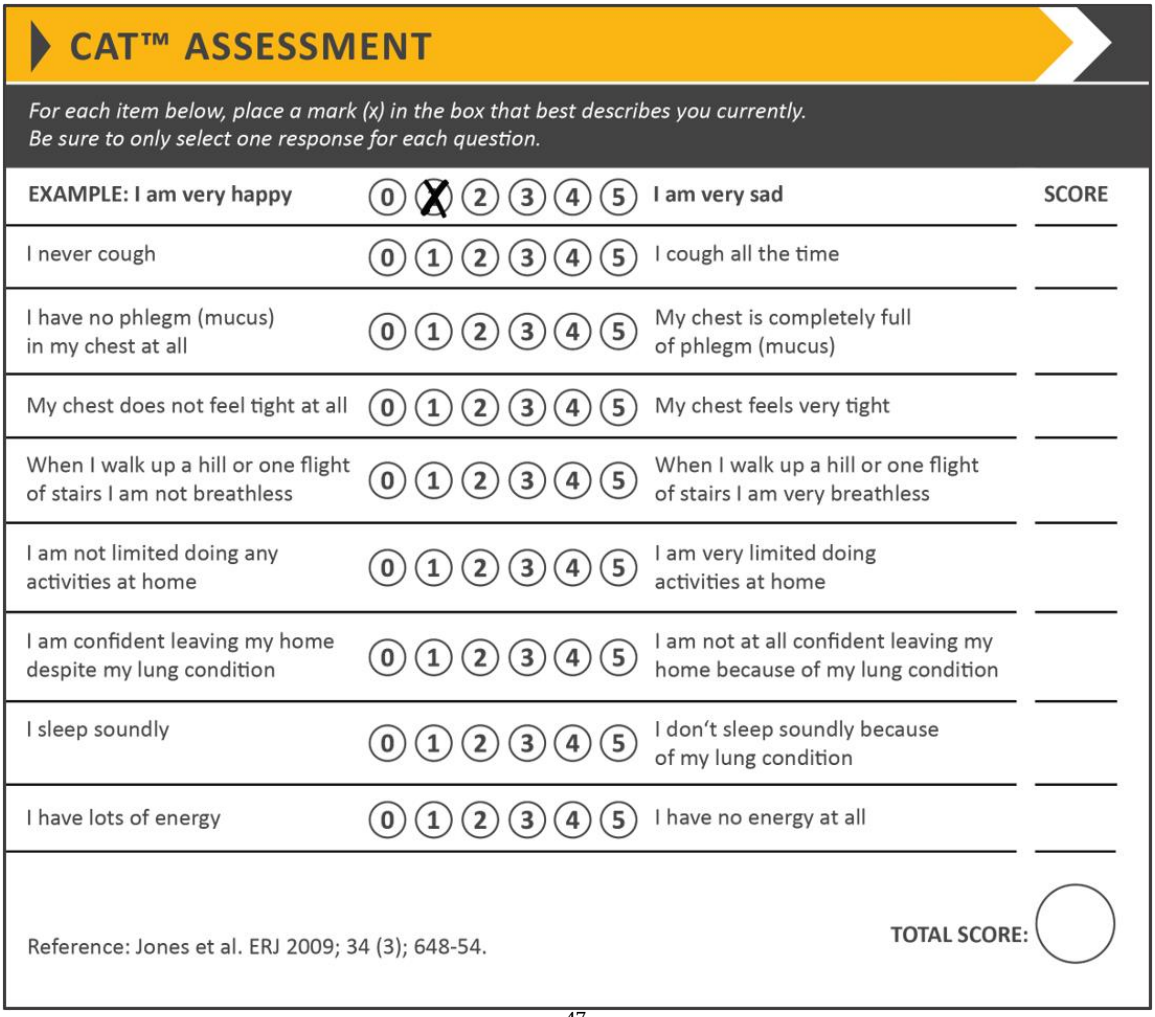
GOLD categories A through D, which are used to direct therapy, are also used to categorise the severity of symptoms and the chance of aggravation. Them patient's categorization is unique to them, and the treatment strategy for each should be customised to meet their particular needs.[50]

Figure 4: GOLD group classification algorithm.[50]



ABCD: Group A low risk/low symptoms, Group B low risk/high symptoms, Group C high risk/low symptoms, Group D high risk/high symptoms; CAT: COPD Assessment Test; FEV_1: forced expiratory volume in 1 second; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; mMRC: modified British Medical Research Council. Source: Reference 1. Reprinted with permission.

Figure 5: COPD Assessment Test (CAT)[47]



CAT™ ASSESSMENT

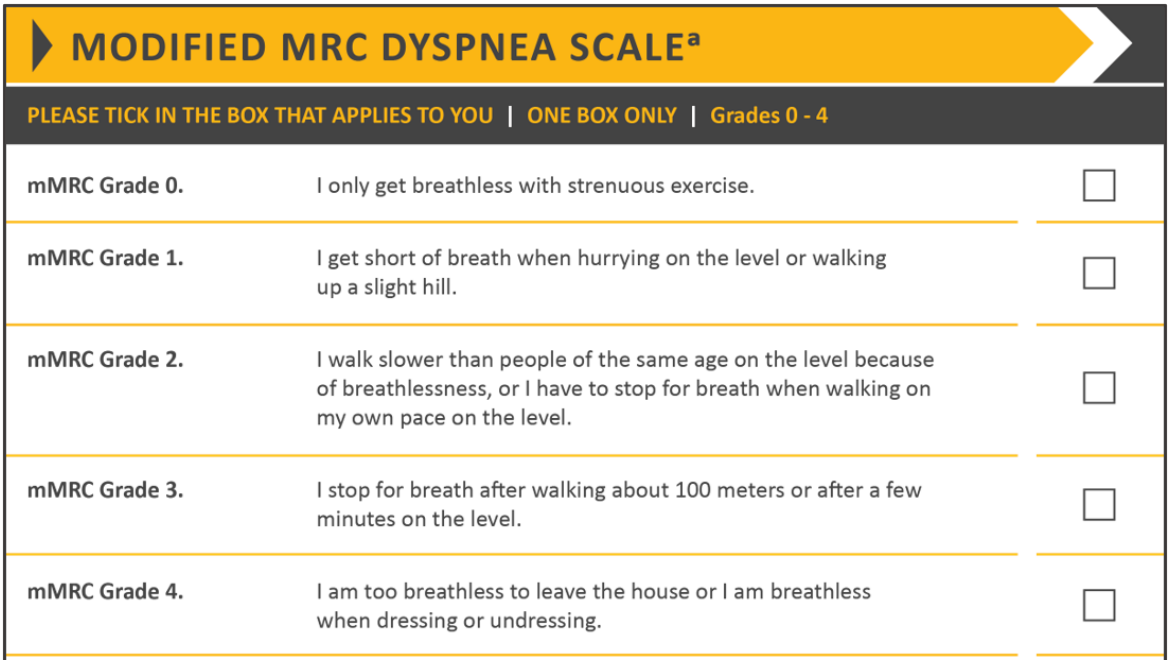
For each item below, place a mark (x) in the box that best describes you currently.
Be sure to only select one response for each question.

EXAMPLE: I am very happy	0 **X** 2 3 4 5	**I am very sad**	**SCORE**
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

TOTAL SCORE: ◯

Figure 6: Modified MRC Dyspnoea Scale[47]



MODIFIED MRC DYSPNEA SCALE[a]

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0.	I only get breathless with strenuous exercise.	☐
mMRC Grade 1.	I get short of breath when hurrying on the level or walking up a slight hill.	☐
mMRC Grade 2.	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	☐
mMRC Grade 3.	I stop for breath after walking about 100 meters or after a few minutes on the level.	☐
mMRC Grade 4.	I am too breathless to leave the house or I am breathless when dressing or undressing.	☐

1. Pro-inflammatory and anti-inflammatory mediators in individuals with COPD

Since a long time ago, it has been known that Patients with copd have intrapulmonary inflammation, and it has also been assumed that the innate immune system's stimulated macrophages and megakaryocytes leukocytes play a role in the accumulation and development of the illness.[51] Recent studies indicate that the development of COPD may be influenced by the adaptive immune response. The cellular signaling pathways of innate immune are lymphocytes, which comprise B- and T-cells. The system's distinctive characteristics include antigenicity, clone proliferation of antigen-activated leukocytes, and the development of immunologic memory.[52] More effective disease intervention strategies, such as antigen eradication or elimination, antigen tolerance induction, manipulation of immunoregulatory mechanisms, or targeted depletion of particular disease-associated lymphocyte subpopulations, may result from a deeper understanding of adaptive immune processes in COPD.[53]

The probable role of T-cells in COPD was initially emphasised by histopathologic studies that found associations between disease severity and the extent of intrapulmonary lymphocyte infiltrates. Immune cells and monocytes are the most prevalent following key features of inflammatory reaction within the upper airway of COPD patients, as per Finkelstein et al. [54]These results were confirmed by the discovery that the number of CD8+ lymphocytes in COPD lungs was inversely correlated with the degree of airflow obstruction. The quantity of T-lymphocytes in operative lung lobectomy of emphysema individuals was revealed to be much greater than in smoking without signs of airflow limitation or non-smokers, according to numerous studies.[55]

T-lymphocytes have the ability to directly lyse tissue or release pro-inflammatory mediators that draw in and activate various immune cell types (eg, phagocytic cells and B-cells). Emphysematous lung tissue-derived pulmonary lymphocytes are frequently activated and capable of secreting mediators implicated in the pathogenesis of COPD.[56]At least a portion of these disease-specific lymphocytes travel via lymphatic and blood circulations when T-cells move between inflammatory foci in organs and local lymph nodes. Peripheral T-cells, particularly CD8+, are more frequently activated and release more mediators in COPD patients, according to research on peripheral blood T-lymphocytes, and many of these T-cell abnormalities are strongly associated with the severity of the illness.[57]

Peptide antigens

Although there is growing evidence that T-lymphocytes play a part in the genesis of COPD, it is still unclear what triggers these cells to become activated. According to several studies, certain peptide antigens cause the lymphocyte proliferation observed in COPD patients. The identification of this antigen(s) would significantly advance our knowledge of COPD and virtually certainly enhance efforts to avoid illness or develop more potent treatments. The adaptive immune system is distinguished by antigen recognition and lymphocyte activation specificity, as was already mentioned.

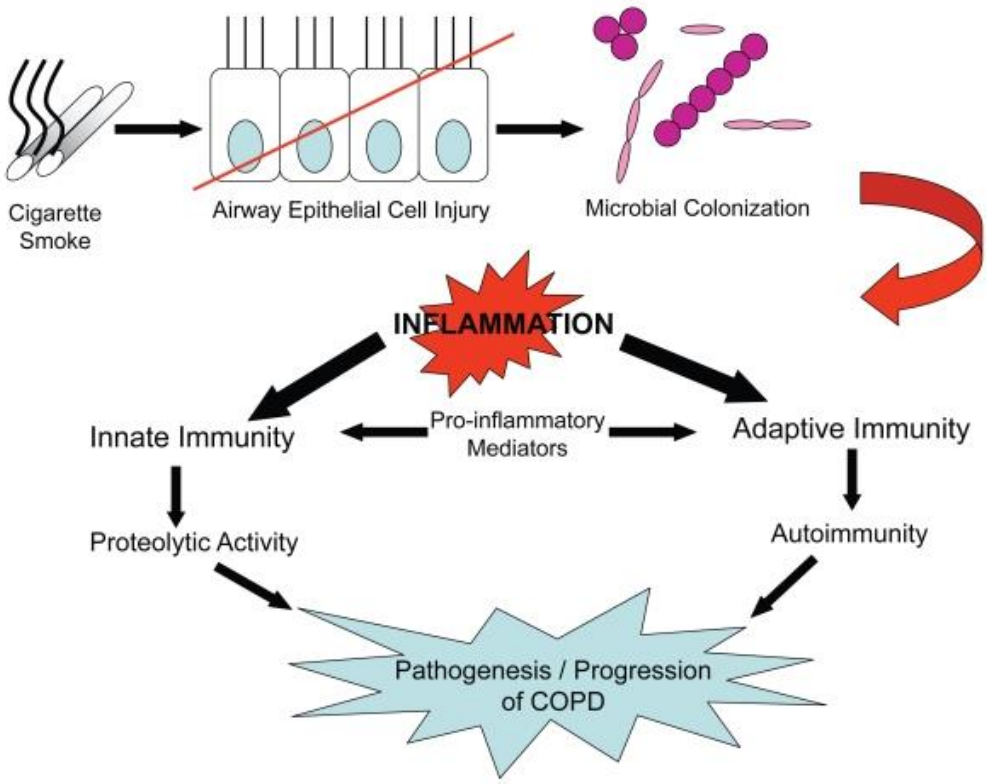
During maturation, developing B- and T-cells randomly rearrange the gene segments encoding the corresponding antigen receptors. As a result of these various genetic sequences, lymphocytes develop highly individualised antigen receptors on their cell surfaces, such as immunoglobulins (Ig) on B-cells and T-cell antigen receptors (TCR). Each cell can only bind a restricted variety of distinct peptides since the avidity of these antigen receptors is controlled by their structural characteristics. As a result, only a tiny percentage of cells with

surface Ig or TCR specificity for that antigen are activated during adaptive immune responses to any given antigen.[53]

It is possible to investigate lymphocyte populations to determine the portion of these cells which have shared ancestors, as suggested by antigen specific sequence commonality, since antigen receptor patterns may be characterised by several cellular DNA and mRNA tests. In a T- or B-cell infiltration, the existence of daughter cells made from a small number of extension of existing lymphocyte founders (i.e., mono- or oligoclonality) suggests that a peptide antigen has triggered these cellular proliferations. [58] Conversely, lymphocytes that are proliferating promiscuously due to causes other than antigen receptor specificity (such as mitogens and growth factors) or that are non-specifically recruited to and engulfed in inflammatory foci would be made up of cells without a common ancestor (ie, polyclonal populations).

Few studies have examined the lymphocytes antigen receptor repertoires in COPD patients. According to Sullivan et al. T-lymphocytes isolated from emphysematous lung tissue were shown to include oligoclonal T-cells.[56] The findings of Korn et al., who found that clonal expansions were more pronounced in CD8+ T-lymphocytes in both the lung and blood of chronic smokers, confirmed this result.[59]Another, albeit less visible, effect of persistent antigen exposure and repeated cell divisions is the down-regulation of CD28, a co-stimulatory molecule, in circulating T-lymphocytes and those isolated from COPD lungs.[56] CD28 downregulation has been seen in a number of studies.

Figure 7: A schematic representation of the putative function of microbial organisms in the propagation of pathogenic processes in COPD.[53]



Additionally, viral infections are more common in COPD patients, and the formation of COPD has even been related to viral infections in children. One study found that severe emphysema was associated with a 40-fold greater prevalence of adeno - associated viral E1A protein production in alveolar epithelia, providing evidence that various viral infections may be connected to COPD.[60]

Pneumocystis jiroveci is another organism that has a role in the pathogenesis of COPD. Compared to 5% of samples from healthy controls or patients with less severe illnesses, it has been found that this bacteria colonises 36% of the lung tissues of people with end-stage COPD.

Human Immunodeficiency Virus (HIV)-infected smokers frequently have a quicker emphysema development, especially when their BAL fluid CD8+ lymphocyte numbers are

high.[61] Pneumocystis colonisation in the lungs of Simian Immunodeficiency Virus (SIV)-infected rhesus macaques resulted in CD8-lymphocyte and neutrophil predominant cellular inflammation, progressive airflow limitation, and local increases in IL-8, IFN-, and TNF- similar to the findings in emphysematous patients. [62]

- **Tobacco associated antigens**

  Exogenous antigens may be one of the many intricate components of cigarette smoke. It was initially discovered that tobacco glycoprotein (TGP), a polyphenol-rich glycoprotein produced from cured tobacco leaves, increased T-cell activation and proliferation in cell culture. However, as far as we are aware, there is no strong evidence linking TGP or other smoking-related factors to cellular immunological activation in COPD. Furthermore, unless an immune response initially elicited by such an antigen later expanded to cover self-antigens, the persistence of intrapulmonary inflammation even after smoking cessation puts into doubt COPD's reliance on antigenic stimulation provided by a smoke constituent.

  Like several other air pollutants, tobacco smoke contains highly reactive compounds that can change the structure of lung proteins (eg, glycosolation, oxidation). It is also conceivable, though not yet shown, that some lung proteins changed by these processes may function as haptens or perhaps be enough changed to cause autoimmune responses since immune cells would no longer recognise them as self.

- **Elastin peptides**

  According to a new study, elastin peptides may represent antigens that stimulate adaptive immune responses in COPD patients. [63] Elastin is a protein found in the extracellular matrix that aids in the structural stability of the lung and other tissues. In pathologic conditions, elastin is destroyed and digested by matrix MMP, which has been demonstrated to have enhanced activity in advanced emphysema. In a cigarette

smoke model of murine emphysema, elastin fragments enhance monocyte chemotaxis and disease development.[64] Circulating T-lymphocytes from COPD subjects were seen to grow and release more IFN- and IL-10 when incubated with elastin digestion fragments.[63]

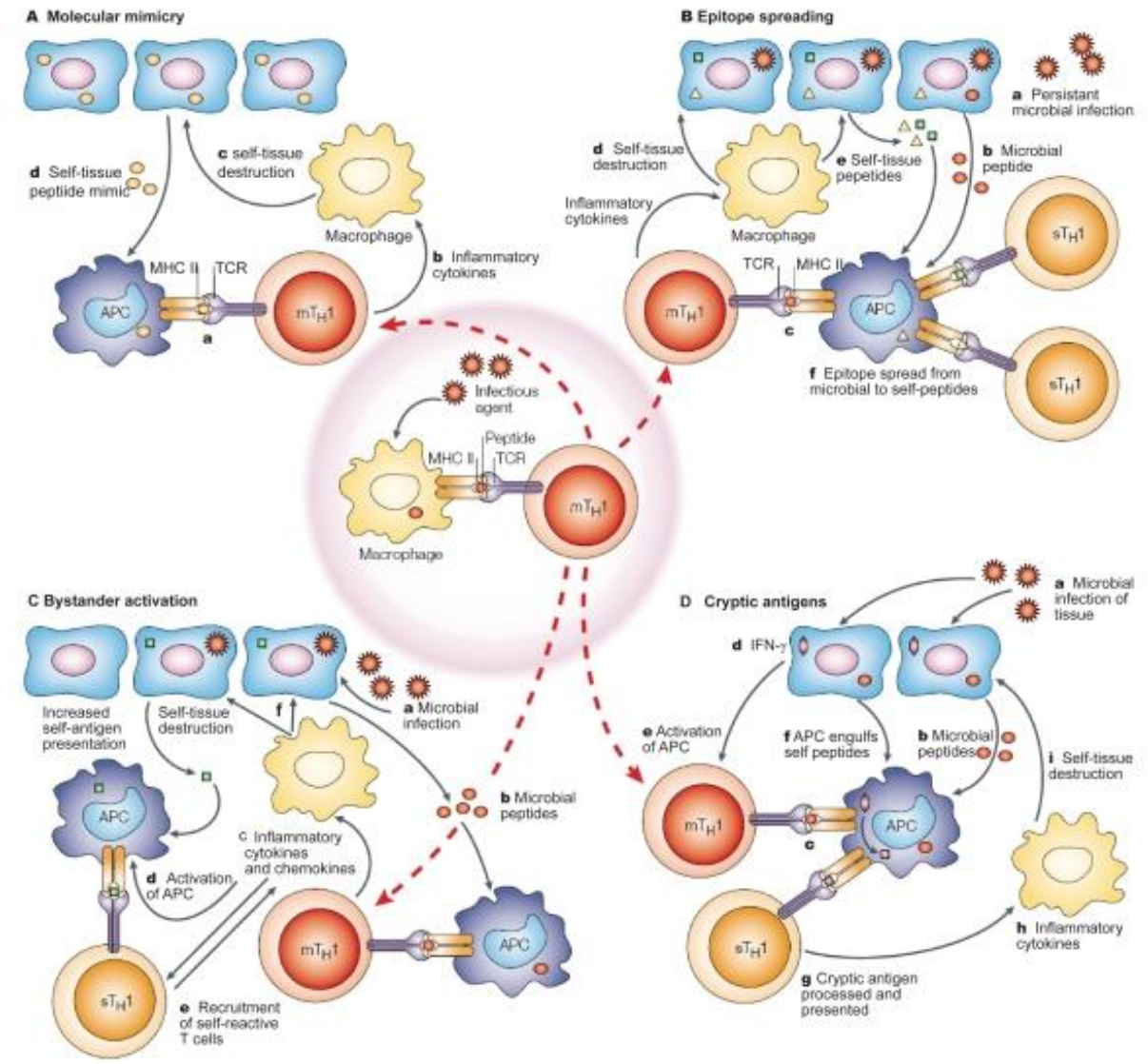
Research is currently ongoing to determine the importance of the adaptive immune response to elastin in the emergence of COPD. Furthermore, evidence of identical anti-elastin responses in a variety of immunological disorders, some healthy individuals, and COPD patients, as well as evidence of various intracellular autoantigens, may imply that anti-elastin reactions are not always integral components of pathophysiology. [66]

- **Autoantigens**

  Additionally, autoreactivity can happen during immune responses that are initially and more effectively directed against potential pathogens. In some situations, it seems that instigating antigen's structural characteristics clone or resemble those of identity, which later become the focus of immune responses triggered and guided by the foreign antigen.[65] Furthermore, by using functional specificity errors or epitope spreading, highly focused and suitable reactions against foreign antigens may include the targeting of typically dormant self-antigens.

  As was already mentioned, various bacteria that might activate the immune system frequently colonise and/or infect the airways of COPD patients. Accordingly, innate immune responses created to eradicate these pathogens may eventually result in self-reactivity through microbiological imitation and/or epitope spreading, especially in those who have been exposed to these species continuously.[65,66]

Figure 8: Infection-induced autoimmunity mechanisms Activated microbe-specific TH1 (mTH1) cells move to the affected organ following a microbial infection.



The activation of crossreactive TH1 cells that recognise both the microbial epitope (mTH1) and the self epitope (sTH1) is referred to as molecular mimicry (a). When crossreactive T cells are activated, they produce cytokines and chemokines (b), which attract and activate monocytes and macrophages, resulting in self-tissue injury (c). The subsequent release of self-tissue antigens and their absorption by APCs contributes to the persistence of the autoimmune illness (d). (B) A chronic microbial infection (a) triggers the activation of

microorganism-specific TH1 cells (b,c), which inflict self-tissue damage (d). As a result, self -peptides (e) are released, which are swallowed by APCs and delivered to self-reactive TH1 cells (f). Continuous self-peptide destruction and release results in the spread of the self-reactive immune response to many self-epitopes (f). C Nonspecific stimulation of self-reactive TH1 cells is known as bystander activation. Activation of microorganism-specific TH1 cells (a,b) causes inflammation (c,d), resulting in enhanced T cell infiltration at the site of infection and activation of self-reactive TH1 cells via TCR-dependent and -independent processes. (e) Self-reactive T cells activated in this manner cause self-tissue damage and contribute to the perpetuation of the autoimmune response (f). (D) Autoimmunity is initiated by differential processing of self peptides, according to a cryptic antigen concept. Following microbial infection (a), both activated microbe-specific TH1 cells (b,c) and microbe-infected tissue cells release IFN- (d). This activates APCs (e), which can result in APCs engulfing self-antigens (f). When APCs are activated by cytokines, they produce more proteases and handle captured self-antigens differently, resulting in the display of cryptic epitopes. These cryptic epitopes can activate self-reactive TH1 cells (g), resulting in self-tissue damage (h,i). APC stands for antigen-presenting cell; MHC II stands for major histocompatibility complex class II; and TCR stands for T-cell receptor.[66]

COPD and T-cell mediators

Inflammatory cells are assisted in their functions by the extracellular signalling proteins cytokines and chemokines. The aetiology of COPD has been linked to a wide range of possible effector molecules, and the course of the illness is likely influenced by an imbalance between the many pro- and anti-inflammatory mediators. This ongoing pro-inflammatory chemokines milieu may also be responsible for COPD patients' evident propensity for cardiovascular disease and bronchogenic malignancy.[67]

The majority of studies using COPD clinical samples have shown a Th1 dominant pattern of cytokine production (e.g., IFN-), while Th2 biassed responses (e.g., IL-4, IL-10) were also seen.[68] The apparent disparities between these studies may be due to individual heterogeneity in terms of sickness severity (or medicines), confounding brought on by relatively small sample sizes, or a combination of these factors. Furthermore, efforts to pinpoint COPD as a particular Th are probably oversimplified, as is the case with the most of complex disease processes. Th1 and Th2 lymphocytes overlap significantly in the mediator environment that is most likely responsible for the onset of this illness.

Interferon-gamma (IFN-γ)

Interferon-gamma is a pro-inflammatory mediator that is mostly produced by Th1/Tc1 monocytes and natural killer cells. Among other things, it is a potent activator of phagocytes and epithelial cells. As previously mentioned, IFN- has been demonstrated to be elevated in lymphocytes isolated from granulomatous lung clinical specimens, bronchoalveolar saline fluid, and peripheral blood. Additionally, IFN- secreting CD8+ T-cells are identified more often in COPD sputum.[69]

Tumor necrosis factor (TNF)

TNF-, a cytokine that promotes apoptotic, has been found to be greater in the blood of people with stable COPD and to increase even further during exacerbations. Although further research hasn't been able to confirm this finding, a TNF- gene variant that causes higher TNF- values has been identified in a population that is more prone to the onset of COPD. It's interesting to note that the subset of COPD patients who have malnutrition or weight loss had particularly high blood TNF- concentrations and TNF- production by monocytes.[70]

IL-1 (interleukin-1)

IL-1, which functions similarly to TNF, is a potent stimulator of alveolar macrophages. Several pro-inflammatory mediators implicated in the pathogenesis of COPD, such as IL-2,-6,-8, RANTES, GM-CSF, IFN-, and TNF-, are stimulated by this mediator. Elastolytic proteases like MMP-9, which may contribute to the onset of emphysema, appear to be under the control of IL-1. Interleukins double receptor knockout mice displayed increasing and more severe emphysema in response to intratracheal application of neutrophil elastase than cytokine single knockout animals or wild-type mice.[71]

Interleukin-8 (IL-8)

Numerous parenchymal and immune effector cells, such as lymphocytes and monocytes, generate the C-X-C chemokine IL-8, a potent chemoattractant for neutrophils and lymphocytes. Given that lymphocytic infiltrates within lung tissue are strongly associated with disease severity and that monocytes are the most prevalent inflammation cell in COPD airspaces, it makes sense that IL-8 may have a role in the onset of emphysema. IL-8 levels are increased in the sputum of COPD patients, and they rise much more during copd exacerbations, probably in tandem with bacterially-induced neutrophilic aggravation. It has been shown that the amount of IL-8 secreted by epithelial cells in response to airway pathogens correlates with the load of airway bacteria.[72]

Acute COPD exacerbations, chronic and acute respiratory distress, pulmonary hypertension, cor pulmonale, weight loss, bacterial infections, and adverse responses to glucocorticoids are all COPD consequences.

Acute exacerbation and its management, associated risk factors, and classification of exacerbation:[73]

COPD is characterised by a steady reduction in lung function, escalating symptoms, functional impairment, and vulnerability to respiratory infections known as exacerbations. Clinically, episodes of worsening dyspnea and productive cough (AECOPD) are recognised as an acute aggravation of chronic obstructive lung disease and call for more aggressive therapy. This disease's subgroup of individuals is especially susceptible to such exacerbations. The term frequent exacerbators is used to describe these patients. These patients are thought to represent a distinct phenotype because they have a various natural history with a more chronic condition and a worse progression than those who get flare ups infrequently, despite still being poorly characterised in terms of host features, including any genetic basis.

Although non-infectious agents like polluted air and other irritants may also be significant, it appears that the majority of exacerbations are linked to infectious stimuli, either bacterial or viral. Numerous factors influence flare susceptibility. There are several risk factors known, some of which may be changed. Exacerbations of COPD have a significant role in health status, patient-centered outcomes, and the need for hospitalisations and admissions to critical care units. These are linked to significant short- and long-term death and morbidity. These periods have negative effects on both the individual and the illness, including a heavy financial burden, higher mortality, deteriorating health condition, activity limitations, and complications like CVD, osteomalacia, and neurodevelopmental disorders that worsen. Exacerbations also speed up the disease's course, which worsens the prognosis and accelerates the rate at which lung function declines each year. In addition to the commonly used pulmonary function measure, FEV in one second, assessment of the risk of relapses is

now incorporated as a significant part of the first examination of an individual with COPD (FEV1). One of the main therapeutic objectives of COPD care is to lower the risk of relapses and avoid them.

Management:

Several therapy and managements exist for acute exacerbation of chronic pulmonary disease (AECOPD) patients and in severe cases require hospitalization. Acute management typically involves the use of short-acting bronchodilators, and systemic corticosteroid antibiotics and, if severe, requires oxygen and non-invasive ventilation (NIV). More research is needed to evaluate the many forms of nonpharmacological therapies available immediately after AECOPD, as well as a pharmacotherapy to prevent future risk of exacerbations, to identify the beneficial components and overall cost-effectiveness.

2. Magnesium

Magnesium is the second most prevalent intracellular cation after potassium and the fourth major most prevalent element in the human body after calcium, sodium, and potassium. A 70 kilogram person has 25 g of magnesium stored in reserve on average, with 53% of it in bone, 27% in muscle, 19% in fatty tissue, and less than 1% in the blood. Although the normal blood value for magnesium (SMC) is between 75 and 95 mmol/L, some study suggests that serum levels below 85 mmol/l should be regarded as inadequate. Critical values obtained are less than 0.5 mmol/L (or 1.0 mg/L) more than 2.0 mmol/L (or 4.9 mg/dL). Small variations in values might not be clinically important.[74]

Although the symptoms (hot flashes, muscular spasms, paresthesia, and fibrillation) only manifest when the threshold value is exceeded, hypomagnesemia is rather common. On the

other side, hypermagnesemia is an uncommon but severe electrolytic condition that, if not identified and treated right once, can be deadly. [75]

Vasodilation, neuromuscular blockade, vasopressor resistance, extreme fatigue, paralytic, respiratory distress, and coma are all indicators of hypermagnesemia, along with diminished tendon reflexes. Other signs of magnesium poisoning include paralytic ileus, flushing, pupil dilation, paradoxical bradycardia, cardiogenic shock, and extended PR, QT and QRS intervals.[76]

Role in the body:

Rossello, Pia, and Haury employed magnesium as a bronchodilator for the first time between 1936 and 1940. The bronchodilatory effect was also linked to interfering with parasympathetic activation and potentiating the impact of 2-agonists. The suggested mechanism involved a calcium antagonist that prevents smooth-muscle contraction. Other hypothesised methods include preventing mast cell histamine release and preventing cholinergic activation, as well as its soothing properties. Magnesium is a catalyst in more than 300 enzymatic reactions and is necessary for many essential functions, including the synthesis of nucleic acids and the creation of energy. The mitochondria, which contain abundant intracellular Mg reserves, are essential for the production of ATP (adenosine triphosphate) from ADP (adenosine diphosphate) and pyrophosphate. Additionally, it is predicted that 3571 human proteins may bind to Mg+2, which is produced when Mg is coupled to ATP to produce the bioactive form of ATP (Mg-ATP). Mg has a biological half-life in the body of approximately 1000 hours (42 days).[77]

Magnesium is necessary for the formation of DNA, RNA, and polymers as well as for the control of blood pressure, insulin metabolism, and muscle contraction, especially that of the

heart. Magnesium plays a critical role in the nervous system's ability to transmit signals efficiently, coordinate neuromuscular contractions, and defend off neurotoxic effects. [78]

1. Magnesium is essential and uses Energy, or adenosine triphosphate. We are aware that ATP serves as the energy source for a variety of cells and chemical processes.
2. It participates in the contraction of cardiac muscle.
3. It participates in the smooth muscle contraction.
4. It aids in the absorption of minerals.
5. It promotes the production of proteins.
6. It also contributes to the coagulation process.
7. It supports insulin's functionality.
8. According to research, taking a magnesium supplement can lower blood pressure and reduce the risk of stroke.
9. A diet high in potassium and magnesium helps older folks use less medicine to regulate their blood pressure.
10. Magnesium, along with calcium and potassium, causes the vascular smooth muscles to relax, which aids in maintaining blood channel openness and blood pressure regulation.
11. I/V magnesium reduces pain and other symptoms of migraine attacks.
12. According to controlled research, taking a magnesium supplement reduces the incidence of migraine attacks.
13. Patients with migraines are advised to take magnesium supplements.
14. Individuals with heart failure and heart attacks benefit from magnesium.
15. It benefits women with H/O preeclampsia.
16. It also alleviates situations of exhaustion.

Role in respiratory diseases – asthma, COPD:

Asthmatics have been found to have lower magnesium levels, while the underlying causes are still unclear. Inadequate lung function, airway hyperreactivity, and an increased prevalence of wheeze have all been linked to hypomagnesemia. Mg2+ sulphate (MgSO4) administered intravenously is advised by international recommendations for the management of acute, severe asthma. This is crucial if the patient's FEV1 at presentation is between 25 and 30 percent of the expected value or if they have a deprived response to short-acting 2-agonists. However, it is unclear exactly how hypomagnesemia affects adult individuals with chronic stable asthma. Despite the fact that the aetiology was unknown, hypomagnesemia was shown to be widespread in individuals with chronic asthma. When compared to asthmatic patients with normal serum Mg2+ levels, those with low Mg2+ levels had more severe asthmatic symptoms, a greater frequency of asthma exacerbations, and were more likely to require hospitalisation.[79]

By causing a rapid spasm of the bronchial muscles, hypomagnesemia might develop in increasing the symptoms of pulmonary illnesses including COPD. There hasn't been much research done on the connection between elevated blood Mg2+ levels and worsening COPD symptoms. Additionally, there have only been a few investigations on the impact of Mg2+ on the incidence of acute COPD exacerbations documented. In a research investigation, the levels of blood Mg2+ were further lowered in cases of hypomagnesemia (acute exacerbation of COPD) with each stage of the disease progressing, indicating a rise in the severity of the condition. Additionally, the frequency of exacerbations increased. Among the later phases, there were more acute exacerbations in patients with low blood Mg2+ levels. This was an important discovery. Similar findings were also found in other investigations. Serum Mg2+ appears to have a lower bioavailability in COPD patients. Low dietary magnesium intake,

heavy smoking, decreased dietary Mg intake, or usage of medications that might enhance Mg2+ deficiency are the most likely causes of low blood magnesium levels in COPD patients (e.g. cortisones and beta-agonists).[1]

Role on other diseases:

Various clinical conditions emerge due to insufficiency of magnesium such as:

- Low dietary intake:
    - Malnutrition, including anorexia nervosa.
- Malabsorption:
    - Coeliac disease.
    - Inflammatory bowel disease.
    - Chronic diarrhoea.
    - Steatorrhea.
    - Short bowel syndrome.
- Parathyroid disorders.
- Chronic alcoholism.

Although non-infectious factors like irritants and dirty air may also be important, it seems that most exacerbations are connected to infectious factors, either viral or bacterial. Flare susceptibility is influenced by a variety of variables. Numerous risk factors are identified, some of which could be altered. The health, patient-centered outcomes, and necessity for hospitalization and admissions to intensive care units are all greatly affected by COPD exacerbations. These have a considerable short- and long-term mortality and morbidity associated with them. These times have detrimental impacts on the patient as well as the sickness, such as a significant financial burden, increased mortality, a decline in health,

activity restrictions, and comorbidities including CVD, osteopenia, and neurodevelopmental abnormalities that worsen. Exacerbations also hasten the progression of the illness, which makes the prognosis worse and hastens the annual reduction in lung function. Evaluation of the likelihood of relapses is now included as a substantial component of the first evaluation of a person with COPD in addition to the often used pulmonary function test, FEV in one second (FEV1). Relapse prevention and reduction are two of the key therapeutic goals of COPD treatment.

According to studies, magnesium may be crucial to the pathophysiology of various inflammatory illnesses. The functional role of Mg has been investigated in a number of clinical studies and laboratory studies. In this work, we evaluate a few inflammatory illnesses whose pathophysiology is affected by magnesium. Obesity, asthmatic, preeclampsia, atherosclerosis, heart disease, and rheumatoid arthritis have been emphasised among these illnesses.

Magnesium is necessary for all human cells, including neurons, to function properly. It is involved in 100s of enzyme reactions, intracellular transmission, the myelination process, synapses' formation and maintenance, as well as the control of serotoninrgic, dopaminergic, and cholinergic transmission, among other processes. Because it has been demonstrated to lower cytotoxicity in a mouse model of generated oxygen starvation and to decrease synapses loss in a murine model of Alzheimer's disease, magnesium is consequently an ingredient required to retain neurons healthy and alive. The maturation of freshly formed brain cells and the involvement of Mg in these processes are also supported by research. In fact, mg has been shown to effectively promote the expansion of oligodendrocytes and neurite outgrowth. Magnesium has also been demonstrated to improve learning capacity, working memory,

short- and long-term memory in rats by inducing synaptic plasticity and potentiating synaptic transmission. [80]

Relationship between sustained COPD and COPD with exacerbation and blood Mg levels:

The role of blood magnesium levels in lung illness is becoming more widely known. The reasonably well-established role of Mg in the management of acute asthma is a major driver for the identification of Mg++ as a risk factor and a possible therapeutic reagent in people who have COPD. A reduction in magnesium levels in COPD patients is a factor that is harmful to respiratory function because low magnesium levels cause muscular fatigue. Mg is implicated in muscle strength.[81] In a retrospective research, Aziz et al. compared the high serum Mg levels of people who had stable COPD to a different group of individuals with severe illness.[15] In comparison to the acute flare group, serum Mg levels significantly greater in the steady period group. Gumus et alprospective.'s analysis found.[82] Nearly 89 individuals who were hospitalised with COPD-AE underwent a year of follow-up at three-monthly intervals. Serum magnesium levels and the frequency of exacerbations showed a strong positive connection. The frequent readmissions brought on by an acute exacerbation of COPD are independently predicted by serum magnesium levels. Despite this, there hasn't been much research done on the connection between blood Mg+2 level and outcomes for illness flares in COPD patients. AECOPD readmission is independently predicted by low serum Mg levels. [83]

A typical finding in acute COPD exacerbations is hypomagnesaemia, which is commonly seen in patients who arrive at the hospital late. Over than 50% of COPD patients who were having an acute relapse had hypomagnesemia. Over the past few decades, COPD exacerbations have become more frequent and severe. Acute COPD exacerbations also cause

a steadily rising hospital admission rate, particularly during the winter months. Exacerbation relapses of COPD are frequently caused by inappropriate use of prednisolone and salbutamol, inappropriate use of antibacterial agents, reduced pre-treatment FEV1 (forced expiration output during the first sec), background of more than 3 episodes of acute episode in the prior 2 years, and co - occurring or immunosuppressed state. When compared to people with stable COPD, the risk of mortality is greater in a group of individuals who frequently require hospitalisation or have a history of numerous bouts of acute exacerbation. Although not statistically significant, the length of hospital stay (and over 7 days) was significantly greater in hypomagnesemia participants than in normomagnesemia patients. In patients with an acute COPD exacerbation, the level of Mg was found to be linked with the duration of hospitalization but not with death. [84]

3. **Correlation between serum Mg levels and COPD exacerbation** P**athophysiology pf magnesium in COPD exacerbation**

Exacerbations happen after an infection, an irritant, or a change in the surrounding temperature. Depending on the severity, eosinophilic or neutrophilic infiltration is frequently increased during flare-ups. While there is only a slight increase in airflow restriction during mild exacerbations, pulmonary gas exchange is negatively impacted during severe exacerbations because of respiratory muscle tiredness and a mismatch in ventilation permeability. The defining characteristics of a severe exacerbation include airway inflammation, oedema, mucous hypersecretion, and bronchoconstriction. Perfusion is hampered by the resulting hypoxic vasoconstriction of pulmonary arterioles.[85]

The two primary signs of COPD are airflow limitation brought on by the constriction of tiny airways brought on by immune cytokines entering them and inflation carried on by the degeneration of the elastic tissue of pulmonary parenchyma (COPD). The development of

inflammation is the consequence of a defensive response to ingested toxins that's become sluggish and exacerbated, resulting in persistent structural and inflammatory change that lasts also after access to the pathogen has ended, resulting in chronic airway blockage.[13] Long acting bronchodilators are the most effective treatment for chronic stable COPD.

Stopping the pathogenesis and reversing any possible triggering causes, notably infections, are the two main objectives of managing a COPD acute exacerbation. Despite the absence of data from controlled trials, short - acting beta beta agonists that are inhaled, either alone or with anticholinergics, improve respiratory metrics in individuals with COPD and reduce dyspnea. When infection is repressed and inflammation is decreased, correspondingly, by corticosteroids and antimicrobial agents, the acute exacerbation is simpler to treat. Respiratory assistance and admittance to an ICU may be required based on the patient's state.[22]

In addition to bronchodilators, IV MgSO4 is helpful for acute asthma attacks or when bronchodilators are ineffective.[86] Bronchial smooth muscle relaxation is thought to be the cause of this bronchodilator effect. More study is needed to assess the effectiveness of inhaled MgSO4 in treating acute asthma exacerbations, either alone or in conjunction with bronchodilators, as there is inadequate trial data to support its usage.[87]Acute severe COPD exacerbations have also been treated with intravenous and/or inhaled magnesium sulphate, with varying degrees of success.[13]

Relationship between blood magnesium levels and individuals with steady and severe COPD episodes

Inflammation affects the major and minor airways, together with the alveoli, to variable degrees, leading to an increase in secretion of mucus, airway constriction, and, accordingly,

alveolar destruction. Exacerbations are events where the type of injury is increased given this backdrop of moderate inflammatory, despite the fact that the mechanisms involved and their consequences are poorly understood. [88]There is strong evidence between magnesium with the inflammatory process, according to several research. Interleukin 6 and tumour necrosis factor levels were found to be higher in rats whose magnesium levels were decreased over three weeks. Researchers also discovered that plasma Substances - P (SP), a well-known activator of inflammatory cytokines, increased within the 7 days of Mg deprivation.

Five days following a magnesium deficit, Interleukin-4 and Interleukin-5 secretion can peak, whereas Interleukin-2, Interleukin-10, and Interferon-gamma secretion peak seven days later. Bronchospasm is one of the factors contributing to the difficulty to remove secretion. Decreased pulmonary gas exchange may impair quality of life and still need repeated hospital admissions. Despite the lack of a clear mechanism of action, it has been proposed that magnesium aids in maintaining the openness of the airways by calming the bronchial smooth muscle.[89]

Table 2: Comparison of mean serum Mg levels among stable and exacerbated COPD among study population across various studies

Studies	Stable COPD	Exacerbation
Sanowara, R. et al[89]	2.09±0.11 mEq/L	1.69±0.27 mEq/L
Azis et al[15]	0.91±0.10 mmol/L	0.77±0.10 mmol/L
Kumar, G et al	2.33 mg/dl	1.69g/dl

4. MOST RELEVANT STUDIES:

A cross-sectional study Mkwana S et al.[84] 2022, aimed to assess the serum Mg levels in acute exacerbation of COPD. The involved100 subjects with COPD of acute exacerbation. The study considered a cut-off of less than 1.7 mg/dl as hypomagnesemia. The study

populations found 57% of subjects with acute exacerbations of COPD with hypomagnesemia. In addition, the length of hospital stay was longer in majority (80.7%) of subjects with hypomagnesemia among COPD with acute exacerbations. A higher mortality rate was found in subjects with hypomagnesemia among COPD with acute exacerbations. The study results found that hypomagnesaemia is a frequent finding among COPD with acute exacerbations.

A prospective study by Kshirsagar, K et al[1] 2022, aimed to assess the function of serum Mg concentration in acute exacerbation of COPD. The study considered 100 subjects with acute exacerbation of COPD. The study population found 72% of subjects with acute exacerbation of COPD with hypomagnesemia. In addition, the subject with serum magnesium levels less than 1.7 mg/dl exhibited a 9.34-fold greater incidence of acute exacerbations. Hence, the study results found that hypomagnesemia is associated with an increased incidence of acute exacerbations in COPD.

A prospective study by Sreekumar, A et al[90] 2021, aimed to assess a relationship between hypomagnesemia and its influence on COPD exacerbation. The study considered 100 COPD subjects, during an exacerbation the subject's blood serum Mg content, oxygen saturation (SpO2) and peak expiratory flow rate test were measured. The study population found a difference in serum Mg concentration in an exacerbation that was lower than the values of a regular check-up. Hence the study results determined low serum Mg concentrations have a defined connection with COPD exacerbation.

A case-control study by Parimala Sundari et al[91] 2019, aimed to assess the link between Serum Mg level and exacerbation of COPD. The study considered subjects more than the age of 18 years. The study population found that the occurrence of low serum magnesium levels

is comparatively higher in cases than in control with a 1.57 mg/dl level of serum Mg in COPD exacerbation and 2.10mg/dl in stable COPD. Hence, the study results found that low serum Mg levels are related with COPD exacerbation.

A prospective study by Saswat Subhankar et al [21]2018, aimed to assess the function of baseline blood Mg level in respiratory management. The study considered 80 subjects and divided equally into diagnosed COPD with exacerbation and stable COPD over a period of two years. The study population found that blood Mg level was significantly lower in COPD with exacerbation subjects compared to stable COPD where none of them was <1.5 mg/dl. The study results found that low serum Mg levels was related with COPD exacerbation.

GP Vignan Kumar et al[17] 2017, aimed to assess the variation in blood Mg level in AE-COPD. The study considered 40 subjects divided equally into 20 cases and 20 control COPD, where their blood Mg level was measured and tracked for the duration of two months. The study population found that among the cases of COPD with exacerbation had significantly < 1.5mg/dl but none of the subjects in the stable group had blood Mg levels < 1.5 mg/dl. Therefore, the study implies a probable link between blood Mg level and AE-COPD. The study results found that the subjects with respiratory conditions must be frequently examined for blood Mg levels.

A study by Anand Agrawal et al[92] 2017, study considered 150 divided equally into case and control of COPD and appropriate parameters used to analyse the values. The study population found that the values of serum magnesium levels were reduced in severe COPD compared to the stable COPD category. The study results found that a decrease in the serum magnesium level in acute exacerbation of COPD is strongly related, and also it increases the duration of hospital stay.

A study by Murthy, M.G.Krishna et al [93]2016, aimed to assess the association between serum Mg level and its impact on COPD with exacerbation and Stable COPD. The study considered 50 subjects with exacerbation in COPD and stable COPD. The levels of serum Mg in COPD acute exacerbation were observed at the time they were admitted and before discharge. The study population found that those with exacerbations had low serum Mg levels, whereas subjects with stable COPD had high amounts of serum Mg content. Hence the study results found that the incidence of hypomagnesemia in COPD with exacerbation is a significantly high chance in an exacerbation.

A prospective observational study by Gumus, A et al[82] 2014, study considered 89 subjects hospitalized with COPD with acute exacerbation. Complete blood count, biochemical tests and level of oxygen, carbon dioxide and pH level in blood were all measured along with the level of PFT at a recovered stage. The study population found that in the occurrence of COPD with acute exacerbation the forced expiratory volume, Level of Mg in blood and globular protein were the sovereign indicators. Hence, the study results found that throughout exacerbation, serum Mg concentration was the most important interrelation incidence of COPD-AE.

JP.Singh et al[81], 2012 aimed to assess the correlation between the exacerbation of COPD and the level of Mg in blood. The study considered 50 subjects of exacerbation of COPD according to guidelines of Anthonisen and GOLD staging criteria. A low level of magnesium was seen among 34% of the subjects and 88% of them progressed to stages two and three compared to a normal level of magnesium. The study population found that the length of stay in the hospital, prolongation symptoms and requirement of mechanical ventilation in 17.64 %

of subjects were more significant in subjects with a low level of magnesium. The study results found that low levels of magnesium are a frequent finding in acute COPD exacerbations. Furthermore, these subjects typically have progressed to late illness stages, require a longer hospital stay, and require mechanical breathing more frequently.

Shah, B et al [94]2010, considered 77 subjects with an severe COPD including cases and control based on the presence of one or more of 2 cardinal symptoms. The study population found that the investigation revealed that cases had considerably shown lower serum magnesium levels than controls. Also, subjects with an acute exacerbation of COPD and a longer period of symptoms progressed to stage 3 COPD. Therefore, the study infers that COPD exacerbation is linked to hypomagnesemia. Low Mg concentration levels are related to a prolonged time of symptoms, the third stage of COPD, and elevated MCV levels. Hence, the study results found that serum Mg levels be observed in COPD patients with flares.

A retrospective study by Aziz, H et al[15] 2005, study considered 50 subjects with COPD excerbation and 50 steady COPD subjects. The study population found that exacerbation subjects exhibited considerably lower serum levels. Therefore, the study results found that findings imply that low magnesium levels in COPD patients are related to an increased risk of symptom exacerbation. Also, decision level was proposed as an indicator to operate a goal value for the treatment of COPD with exacerbation.

LACUNAE IN LITERATURE:

Serum magnesium levels during an acute exacerbation period have been linked to COPD-AE frequency in the literature up to this point. The majority of research discovered a stronger association between blood magnesium levels and steady COPD than they did with aggravated

illness. Therefore, hypomagnesemia is a frequent finding in COPD acute exacerbations and is commonly seen in patients who arrive at the hospital after the acute exacerbation has started. Patients also frequently have severe illness stages (stages II and III) when they arrive at the hospital, require mechanical breathing more frequently, and remain longer than seven days. There is no connection between the mortality rate and serum magnesium levels. Although some studies link the aggravation of chronic respiratory diseases with low serum magnesium levels, the exact reason why this reduction occurred is unknown. It would be much better if serum Mg levels in the same individuals were checked repeatedly throughout time. In such a situation, fluctuations in a patient's serum magnesium levels may be tracked during the course of the illness and the likelihood that magnesium could serve as a potential indicator of exacerbations can be evaluated.

MATERIAL & METHODS

MATERIAL & METHODS

Study site: The study was conducted in the department of Internal Medicine at R L JALAPPA HOSPITAL AND RESEARCH CENTRE – A tertiary care hospital Tamaka, Kolar.

Study population: All Adults admitted with COPD (Stable/ after stabilisation) to the Department of General medicine.

Study design: The current study was a case -control study.

Sample size: was calculated using the mean blood magnesium levels that differed between the case and control groups in the research by Keta et al., which were 1.58 ±0.3 mg/dl and 2.15 ±0.29 mg/dl.

By utilising the formula below and the MedCalc sample size programme, a sample size of 7 was determined for each group using these values at the 95percentage Confidence Limit and 90percentage Power.

with a required sample size of 7plus 0.78 individuals and a 10% non-response rate. 30 participants from each group were included.

Sampling method: Until the desired sample size was obtained, all of the eligible participants were sequentially recruited into the research using easy sampling.

Study duration: The study's data gathering period was one year, from January 2021 to December 2021.

Inclusion Criteria:

1. **CASE GROUP –**

The case group will consist of individuals who present to the Department of Internal Medicine with a COPD exacerbation that necessitates hospitalisation.

2. **CONTROL GROUP –**

The stable COPD patients who come for routine check up on outpatient basis

to Department of Internal Medicine

Patient characteristics :

a) According to the recommendations of the European Respiratory Society Task Force, the patients in the case groups after stabilization/after initial treatment and the control groups will be diagnosed with COPD based on the results of dynamic pulmonary function tests (ratio of 1-sec forced expiratory volume to forced vital capacity, FEV1/FVC70).

b) Using the criteria of Anthonisen et al., the patients in the case group will be classified with acute exacerbation, which includes either the presence of shortness of breath or a severe cough with or without an increase in sputum volume. Cases and controls will undergo blood tests to evaluate serum levels of magnesium after collecting a thorough history, rigorous examination, preliminary investigations, and stages of COPD.

Exclusion criteria:

Individuals who have any of the below conditions won't be included in the research:

1. Individuals with additional respiratory conditions brought on by pleural effusion and hyperinflation
2. Patients whose bronchiectasis has recently become acutely worse.
3. Patients who have any of the following conditions, each of which poses a danger for hyponatremia, will be disqualified.
4. Digestive disorders, including chronic diarrhea, pancreatitis, ulcer disease, and malabsorption syndrome.
5. Gestation and breastfeeding.
6. Endocrine disorders: thyriod disorders, and type 2 diabetes
7. Patients with COPD, CCF, or kidney failure who are hospitalised for other conditions
8. Drugs: systemic hypertension, thiazolidinediones, furosemide, and CAD

9. Malignancy

Ethical considerations: The organizational human ethics board approved the study. All research participants provided written informed consent, and only those who have signed consent were included in the study. Before the consent , the participants were informed about the study's risks and benefits as well as the voluntary nature of participation. The study participants' privacy was protected.

Data collection tools: A well-organized research proforma contained documentation of all pertinent parameters.

Methodology:

- There will be 30 subjects in each group who met the inclusion and exclusion requirements.
- A complete history was elicited and detailed examination was performed.
- All the subjects have undergone investigations, including 2 cc of blood drawn into a simple vacutainer to gather serum magnesium levels which was calculated using automated machine values and VITROS chemistry Mg slides.
- The stable control groups were immediately received a pulmonary function test at the time of presentation (Recorder and Medicare system Chandigarh computerised Spirometry), whereas patients with acute exacerbations had a pulmonary function test following first therapy and stabilization.
- At the time of Presentation, serum magnesium levels were estimated.
- After acquiring the blood magnesium levels, the GOLD criteria was used to correlate the COPD staging and serum magnesium levels.

STATISTICAL METHODS

Gold's criterion staging, the length of the diagnosis, and the number of readmissions were regarded as the main determinant of result. Case and control groups from the study were regarded as the main explanatory factor.

Age, gender, and laboratory results such as haemoglobin (gm%), red blood cell count (mil/cu.mm), packed cell volume (%), mean corpuscular volume (fl), white blood cell count (thousands/cu.mm), platelet count (thousands/cu.mm), etc. were all deemed to be pertinent research factors.

For quantitative variables, the relevant statistics (mean+/- SD) presented in the descriptive analysis, while frequency and percentage were used for categorical variables. The necessary graphics, such as bar graphs and pie charts, were also used to illustrate the data.

By visually inspecting histograms and normality Q-Q plots, all continuous measurements were examined to define the distribution as normal of each group of study. Additionally, the Shapiro-Wilk test was used to evaluate statistically. When the test's p value was >0.05, the distribution was regarded as normal.

The Independent sample t-test was used to define the mean values of quantitative parameters that were normally distributed amongst study groups (2 groups).

Chi square test reported the comparison of categorical outcomes between research clusters.

P value< 0.05 defined as significance statistically.[95]

RESULTS

RESULTS

Subjects taken into the study were 60.

Table 3: Summary of study groups (N=60)

Study group	Frequency (N)	Percentage
Cases	30	50.00%
Controls	30	50.00%

In the study, 30 (50.00%) samples were Cases and 30 (50.00%) participants Controls. (Table 3 and Figure 9)

Figure 9: Pie chart of cases and controls (N=60)

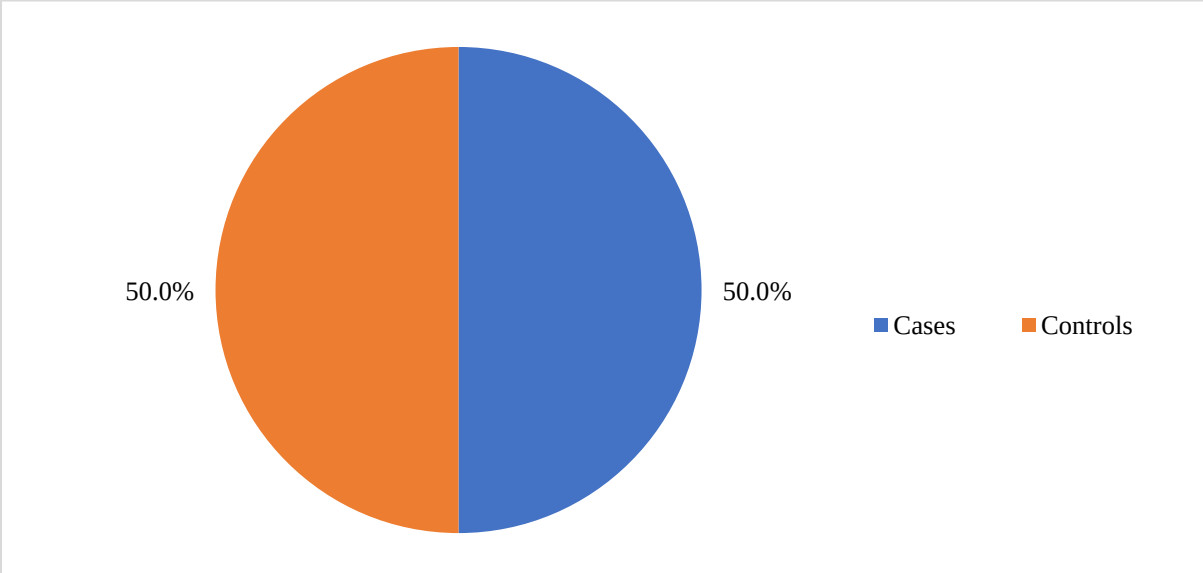


Table 4: Distribution of age (years) in each group of the study (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Age (years)	65.23 ± 7.08	59.57 ± 6.21	0.0017

The mean age (years) with in cases was 65.23 ± 7.08 and it was 59.57 ± 6.21 in controls. The mean difference of age (years) in study group did not show any significance statistically since the P value =0.0017. (Figure 10 and 4th Table)

Figure 10: Error bars age (years) distribution in each group (N=60)

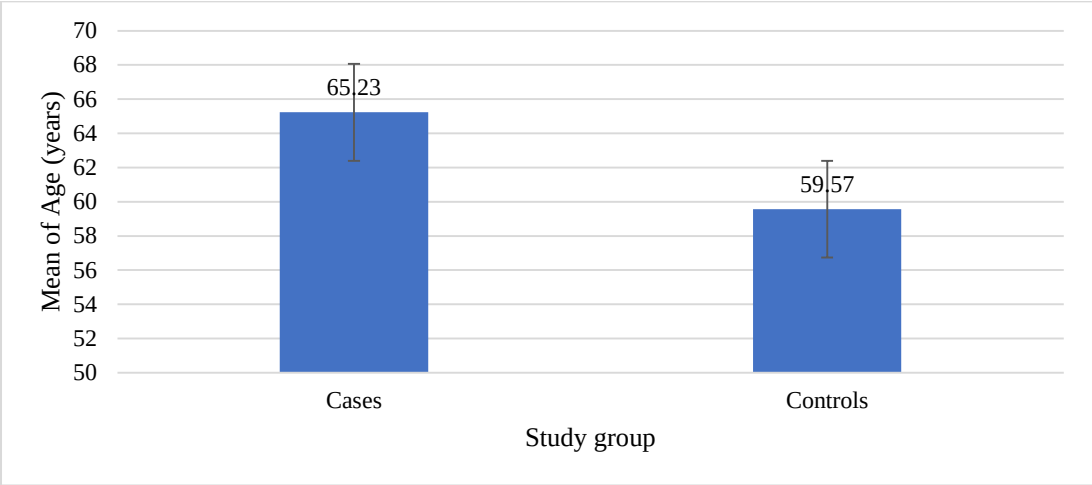


Table 5: Comparison of gender with study clusters (N=60)

Gender	Study group		Chi square value	P value
	Cases (N=30)	Controls (N=30)		
Male	24 (80.00%)	25 (83.33%)	0.11	0.7386
Female	6 (20.00%)	5 (16.67%)		

In cases, 24 (80.00%) participants were male and 6 (20.00%) were female. In controls, 25 (83.33%) were male and 5 (16.67%) were female. The male and female distribution invariably same in cases and controls and it was supported by P= 0.7386. (Table 5 & Figure 11)

Figure 11: Study clusters indicating gender distribution (N=60)

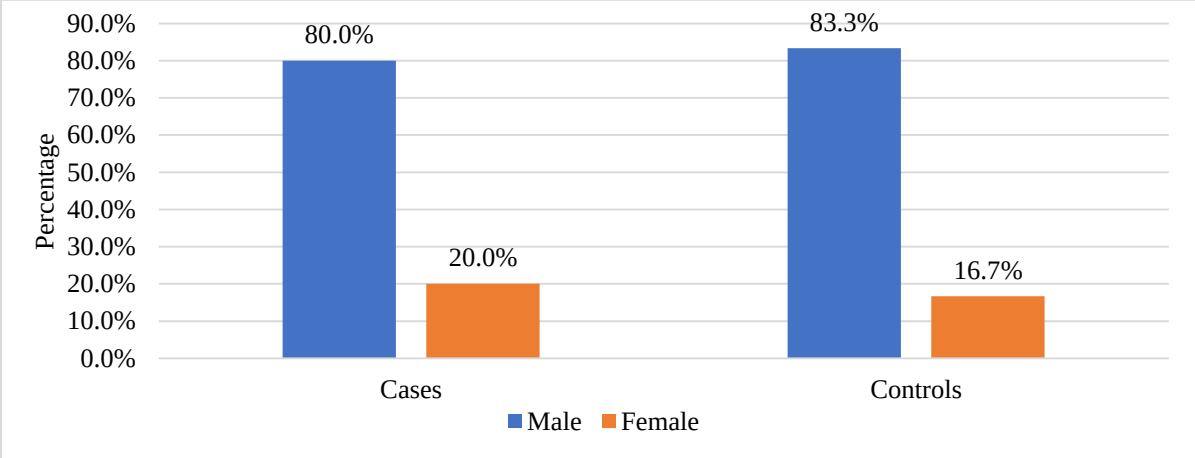


Table 6: Summary of total duration of stay (in days) in cases (N=30)

Measurement	Mean ± S. D	Median	Minimum	Maximum	95% CI	
					Lower	Upper
Total duration of stay (in days)	8.20±1.65	8.50	4.00	10.00	7.61	8.79

The mean total duration of stay (in days) was 8.20±1.65 in the cases group. Ranged between 4.0 to 10.0 (95 % CI 7.61 to 8.79). (Table 6)

Table 7: Comparison of risk factor as per cases Vs controls (N=60)

Risk factor	Study group		Chi square value	P value
	Cases (N=30)	Controls (N=30)		
Smoker	24 (80.00%)	25 (83.33%)	0.11	0.7386
Nil	6 (20.00%)	5 (16.67%)		

In cases, 24 (80.00%) participants were smokers and 25 (83.33%) in controls. The difference in the proportion of smokers was not significant between the two research clusters where P-value= 0.7386. (Table 7 & Figure 12)

Figure 12: Cluster bars for risk factor presentation group wise (N=60)

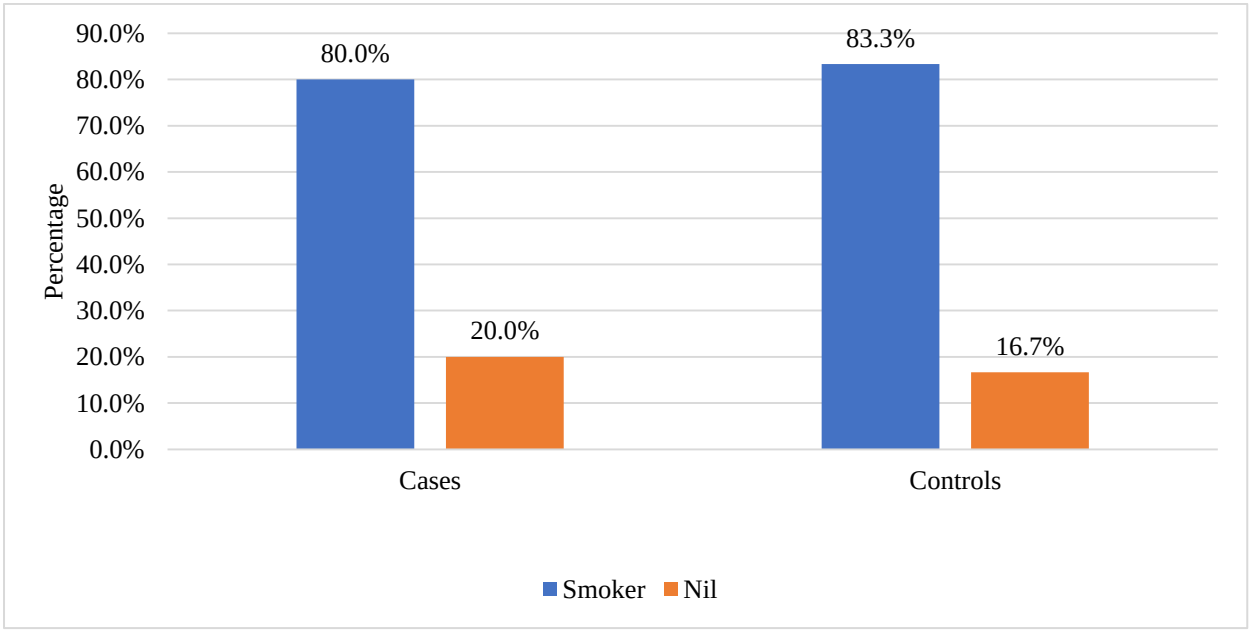


Table 8: Association of pack years with cases and controls in the smokers (N=49)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=24)	Controls (N=25)	
Pack years	17.46 ± 3.84	11.58 ± 3.18	<0.001

The mean pack years with in cases were 17.46 ± 3.84 and it was 11.58 ± 3.18 in controls. The mean difference of pack years was statistically significant as in cases and controls groups. (value of significance <0.001). (Figure 13 & Table 8)

Figure 13: Error bar graph of pack years with cases and controls in the smokers (N=49)

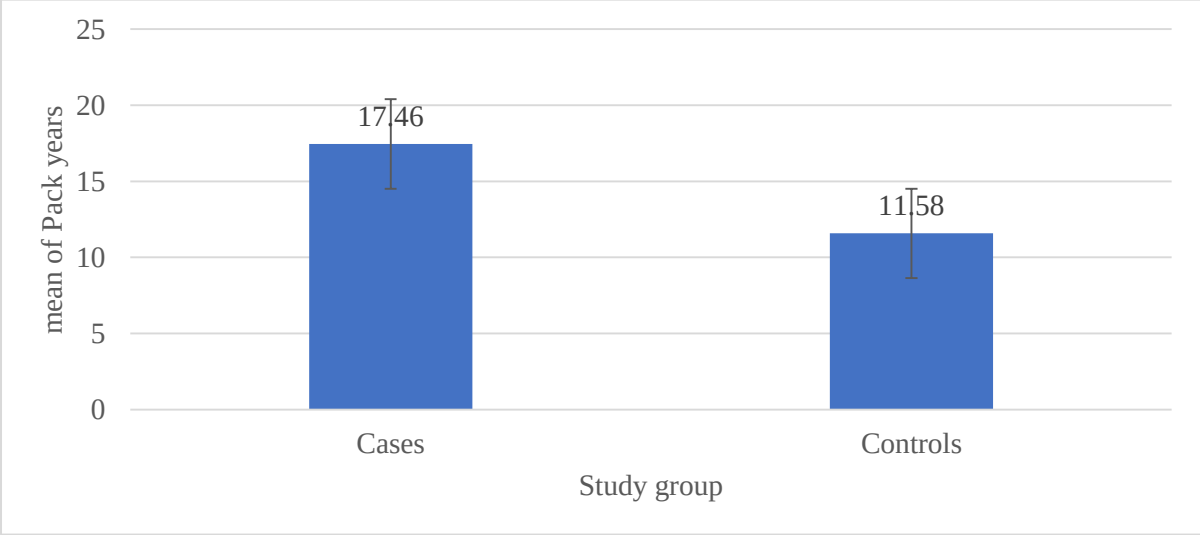


Table 9: Comparison of occupation with cases and controls (N=60)

Occupation	Study group	
	Cases (N=30)	Controls (N=30)
Farmer	14 (46.67%)	12 (40.00%)
Carpenter	1 (3.33%)	1 (3.33%)
Truck Driver	1 (3.33%)	1 (3.33%)
Housewife	4 (13.33%)	3 (10.00%)
Cashier	1 (3.33%)	0 (0.00%)
Silk Weaver	3 (10.00%)	2 (6.67%)
Mechanic	1 (3.33%)	3 (10.00%)
Engineer	1 (3.33%)	3 (10.00%)
Painter	1 (3.33%)	1 (3.33%)
Contractor	1 (3.33%)	0 (0.00%)
Coolie	1 (3.33%)	3 (10.00%)
RTO Officer	1 (3.33%)	0 (0.00%)
Financier	0 (0.00%)	1 (3.33%)

In cases, highest of 14 (46.67%) farmers, 4 (13.33%) were housewife and silk weaver, 3 (10.00%) respectively. In controls, the majority of 12 (40.00%) participants were farmers followed by housewife and mechanic with 3 (10.00%) each. (Table 9)

Table 10: Comparison of socioeconomic status with two cluster samples (N=60)

Socioeconomic Status	Study group	
	Cases (N=30)	Controls (N=30)
Class 1	1 (3.33%)	0 (0.00%)
Class 2	4 (13.33%)	4 (13.33%)
Class 3	16 (53.33%)	14 (46.67%)
Class 4	9 (30.00%)	12 (40.00%)

In cases, the majority of 16 (53.33%) participants socioeconomic class 3 followed by socioeconomic class 4 and socioeconomic class 2 were 9 (30.00%), 4 (13.33%). In controls, the majority of 14 (46.67%) participants had socioeconomic class 3 followed by socioeconomic class 4 and socioeconomic class 2 were 12 (40.00%), 4 (13.33%). (Table 10 & Figure 14)

Figure 14: Cluster bars depicting Socioeconomic Status distribution group wise (N=60)

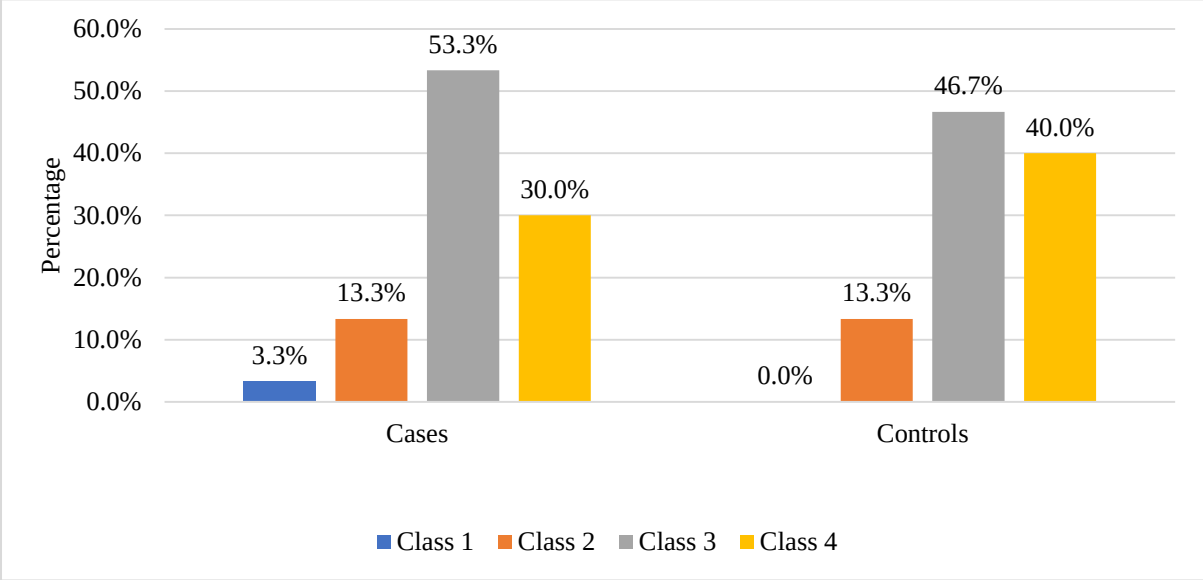


Table11: Comparison COPD as per cases and controls (N=60)

K/C/O COPD	Study group	
	Cases (N=30)	Controls (N=30)
Yes	30 (100.00%)	30 (100.00%)

In cases, all 30 (100.00%) participants diagnosing has having COPD and 30 (100.00%) diagnosing has having COPD in controls. (Table 11)

Table 12: Comparison of duration of diagnosis with cases and controls (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Duration of diagnosis (years)	12.37 ± 3.79	10.43 ± 2.94	0.0314

The mean duration of diagnosis (in years) with in cases was 12.37 ± 3.79 and it was 10.43 ± 2.94 in controls. The value of P (0,0314) indicated statistical significance in the mean difference of duration of diagnosis (in years) cluster wise. (Figure 15 & Table 12)

Figure 15: Error bars reporting duration of diagnosis (in years) with the study group (N=60)

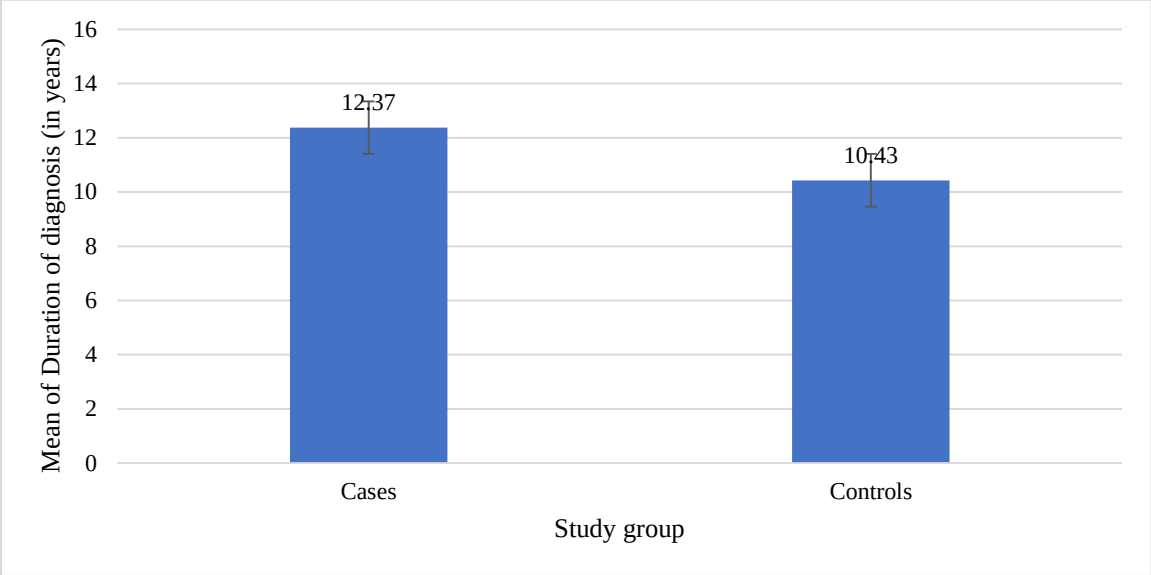


Table 13: Comparison of any treatment history with study group (N=60)

Any treatment history	Study group		Chi-square	P value
	Cases (N=30)	Controls(N=30)		
Inhaled steroids	8 (26.67%)	22 (73.33%)	13.07	<0.001
No	22 (73.33%)	8 (26.67%)		

In cases, 8 (26.67%) participants were reported inhaled steroids treatment history and 22 (73.33%) participants were reported inhaled steroids treatment history in controls. The variation in proportion of any treatment history as per each group was defined as significant statistically when the value of P as <0.001. (Figure 16 & Table 13)

Figure 16: Cluster bars indicating any treatment history comparison with cases and controls (N=60)

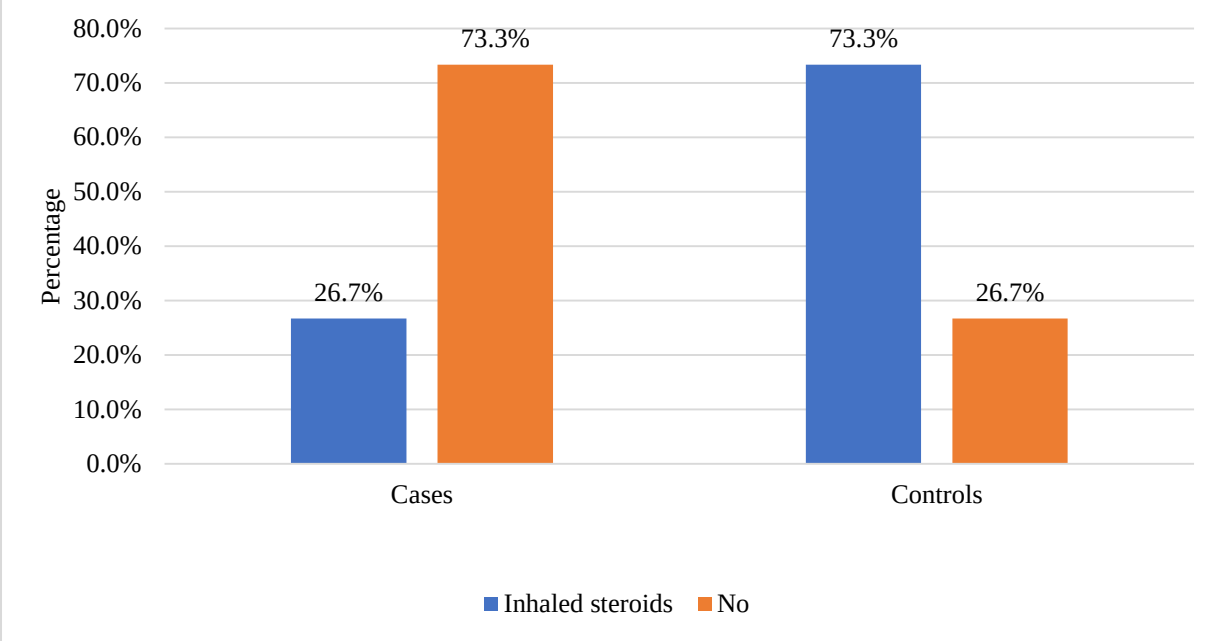


Table 14: Comparison of pneumococcal vaccine taken with study group (N=60)

Pneumococcal vaccine taken	Study group		Chi-square Value	P value
	Cases(N=30)	Controls(N=30)		
Taken	5 (16.67%)	7 (23.33%)	0.42	0.5186
Not taken	25 (83.33%)	23 (76.67%)		

In cases, 5 (16.67%) participants had taken pneumococcal vaccine and 25 (83.33%) had not taken. In controls, 7 (23.33%) participants had taken pneumococcal vaccine and 23 (76.67%) had not taken. The difference in the distribution of pneumococcal vaccine taken in each cluster was statistically proven insignificance since the P-value = 0.5186. (Figure 17 & Table 14)

Figure 17: pneumococcal vaccine taken in cases and controls reported with clustered bars (N=60)

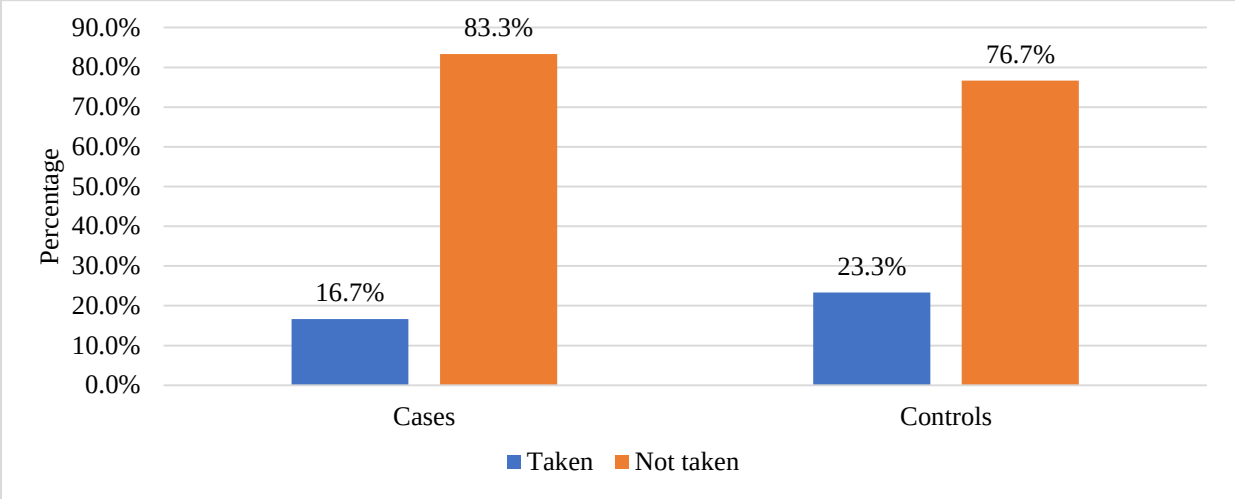


Table 15: Comparison of any readmission for same complaints since the time of diagnosis of COPD with study group in the study population (N=60)

Any readmission for same complaints since the time of diagnosis of COPD	Study group	
	Cases (N=30)	Controls (N=30)
Yes	22 (73.33%)	0 (0.00%)
No	8 (26.67%)	30 (100.00%)

In cases, 22 (73.33%) participants were reported readmission for same complaints since the time of diagnosis of COPD. (Table 15)

Figure 18: Indication through Cluster bars about any readmission for same complaints since the time of diagnosis of COPD as per cases and controls (N=60)

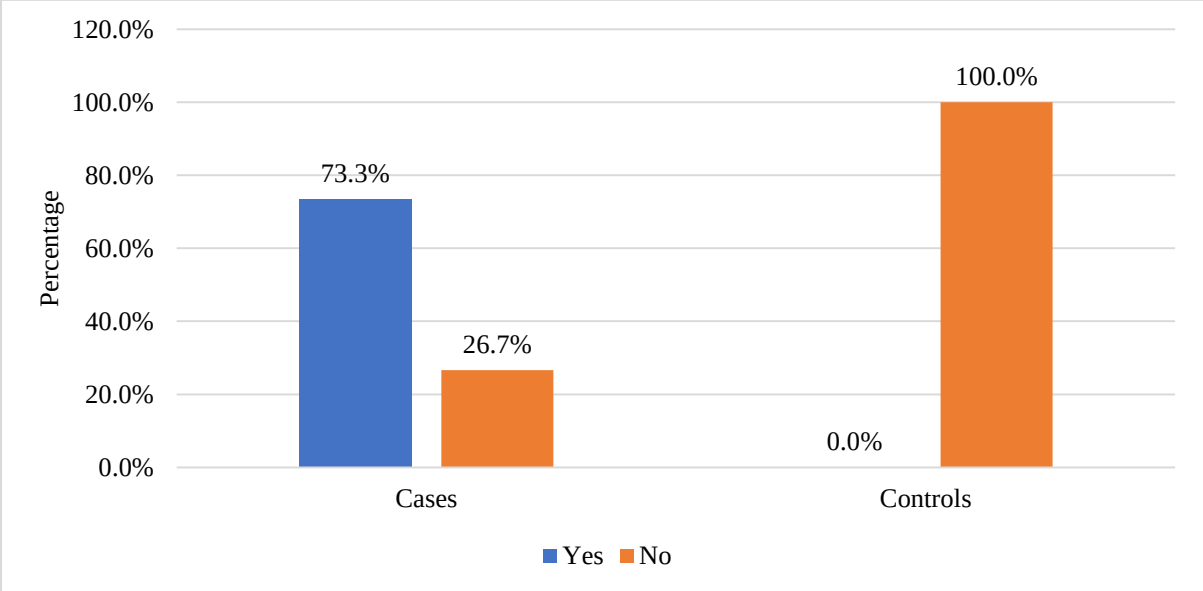


Table 16: Distribution of number of readmissions with cases (N=30)

Measurement	Mean ± S. D	Median	Minimum	Maximum	95% CI	
					Lower	Upper
Number of readmissions	8.10±5.23	10.00	0.00	15.00	6.23	9.97

The mean number of readmissions was 8.10±5.23 in the cases group. Ranged between 0.0 to 15.0 (95 % CI 6.23 to 9.97). (Table 16)

Table 17: Comparison of gold's criteria staging with study group in the study population (N=60)

Gold's criteria staging	Study group		Chi-square Value	P value
	Cases(N=30)	Controls (N=30)		
2	6 (20.00%)	21 (70.00%)	16.86	<0.001
3	15 (50.00%)	8 (26.67%)		
4	9 (30.00%)	1 (3.33%)		

In cases, 6 (20.00%) participants had gold's criteria staging 2, 15 (50.00%) had gold's criteria staging 3 and 9 (30.00%) had gold's criteria staging 4. In controls, 21 (70.00%) participants had gold's criteria staging 2, 8 (26.67%) had gold's criteria staging 3 and 1 (3.33%) had gold's criteria staging 4. The difference in the proportion of gold's criteria staging was significant as per the P value<0.001 in cases and controls. (P-value <0.001) (Figure19 & Table 17)

Figure 19: Cluster bar graph of gold's criteria staging with cases and controls (N=60)

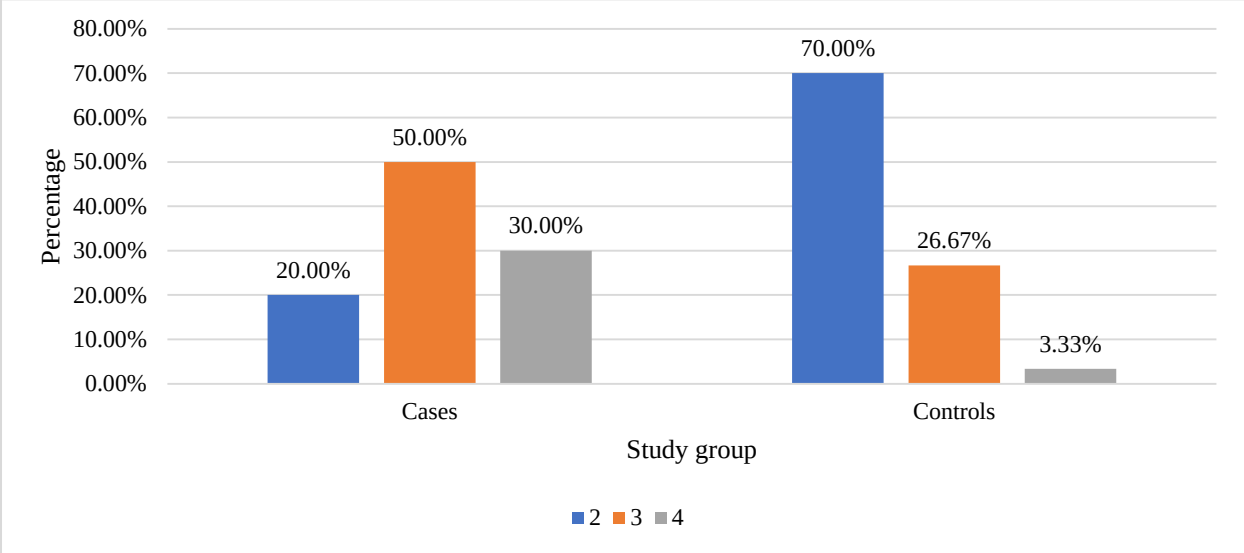


Table 18: Comparison of haemoglobin (gm%) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Haemoglobin (gm%)	12.67 ± 2.29	13.87 ± 2.44	0.0546

The mean haemoglobin (gm%) with in cases was 12.67 ± 2.29 and it was 13.87 ± 2.44 in controls. The mean difference of haemoglobin (gm%) in study group defined no significance as the value of P = 0.0546. (Figure 20 and Table 19)

Figure 20: Error bars depicting comparison of haemoglobin (gm%) as per study groups (N=60)

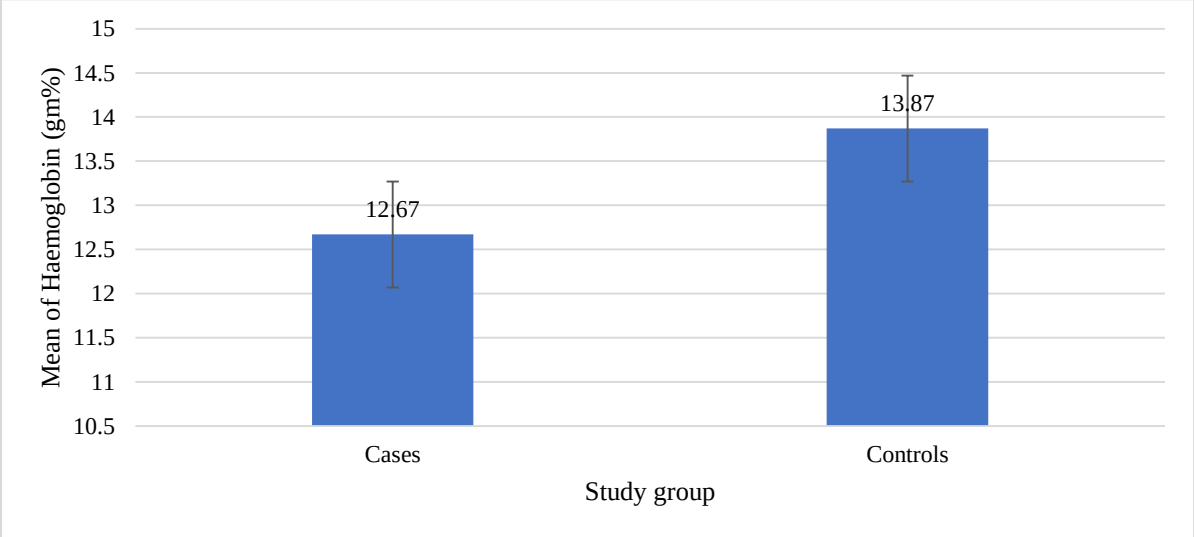


Table 19: Comparison of red blood cell count(mil/cu.mm) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Red Blood Cell Count(mil/cu.mm)	3.96 ± 0.31	4.12 ± 0.28	0.0427

The mean red blood cell count(mil/cu.mm) with in cases was 3.96 ± 0.31 and it was 4.12 ± 0.28 in controls. The mean difference of red blood cell count(mil/cu.mm) in two clusters was significant since the P value was 0.04. (19 Table and Figure 21)

Figure 21: Error bars reporting comparison of red blood cell count(mil/cu.mm) as per each gorup (N=60)

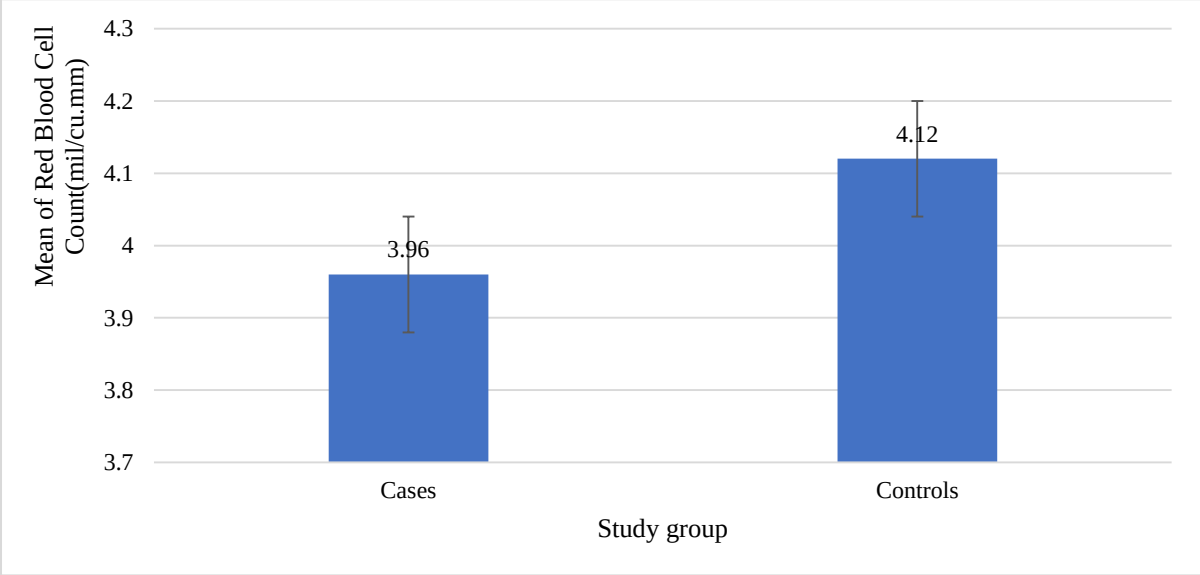


Table 20: Comparison of packed cell volume (%) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Packed Cell Volume (%)	37.90 ± 3.19	43.53 ± 5.32	<0.001

The mean packed cell volume (%) with in cases was 37.90 ± 3.19 and it was 43.53 ± 5.32 in controls. The mean difference of packed cell volume (%) was differed in two groups of the research statistically with value of significance as <0.001. (Figure 22 and Table 20)

Figure 22: Packed cell volume (%) distribution group wise using error bars (N=60)

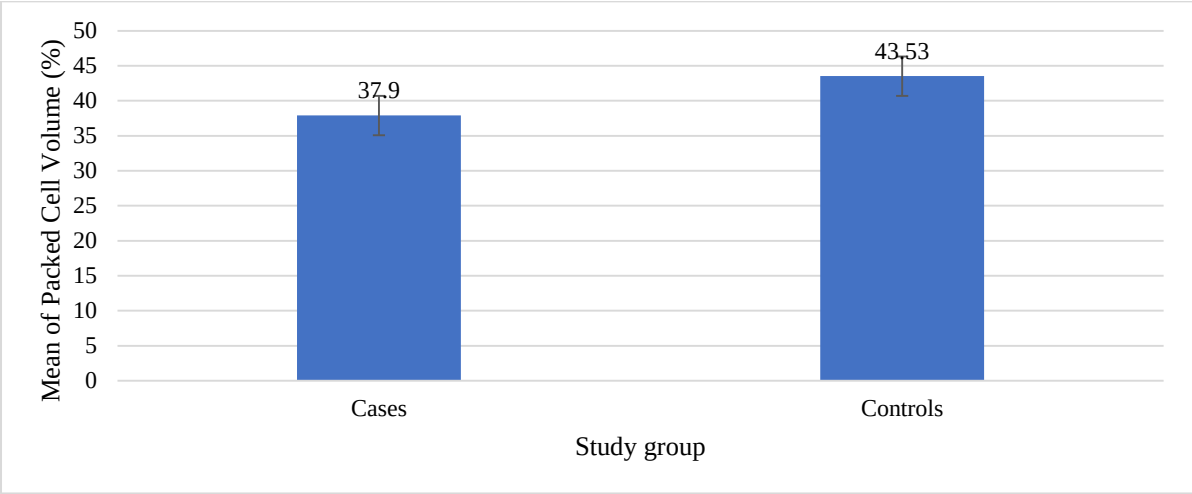


Table 21: Comparison of mean corpuscular volume (fl) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Mean Corpuscular Volume(fl)	78.87 ± 4.45	80.30 ± 4.54	0.2222

The mean corpuscular volume (fl) with in cases was 78.87 ± 4.45 and it was 80.30 ± 4.54 in controls. The mean difference reported as insignificant (P value=0.22) for mean corpuscular volume (fl) cluster wise. (19th Table 21 & Figure 23)

Figure 23: Error bars picture of comparison of mean corpuscular volume (fl) in study participants of groups (N=60)

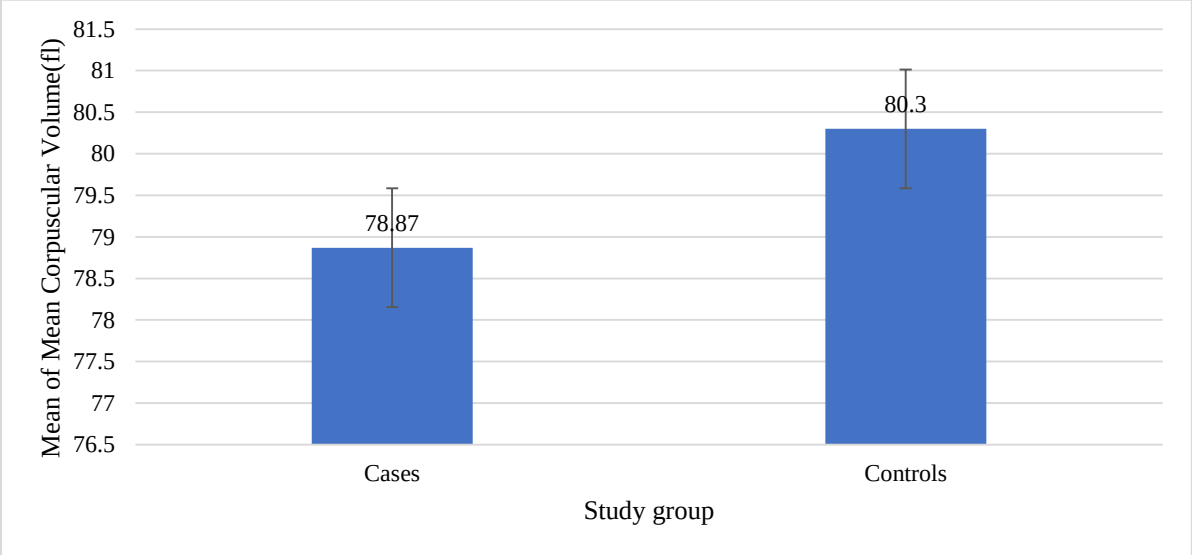


Table 22: Comparison of white blood cell count (thousands/cu.mm) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
White Blood Cell Count(thousands/cu.mm)	14.69 ± 3.11	9.74 ± 2.13	<0.001

The mean white blood cell count (thousands/cu.mm) with in cases was 14.69 ± 3.11 and it was 9.74 ± 2.13 in controls. The mean difference of white blood cell count (thousands/cu.mm) indicated as significant since the value of P was <0.001. (Table 22 & Figure 24)

Figure 24: Error bars comparing white blood cell count (thousands/cu.mm) between study groups (N=60)

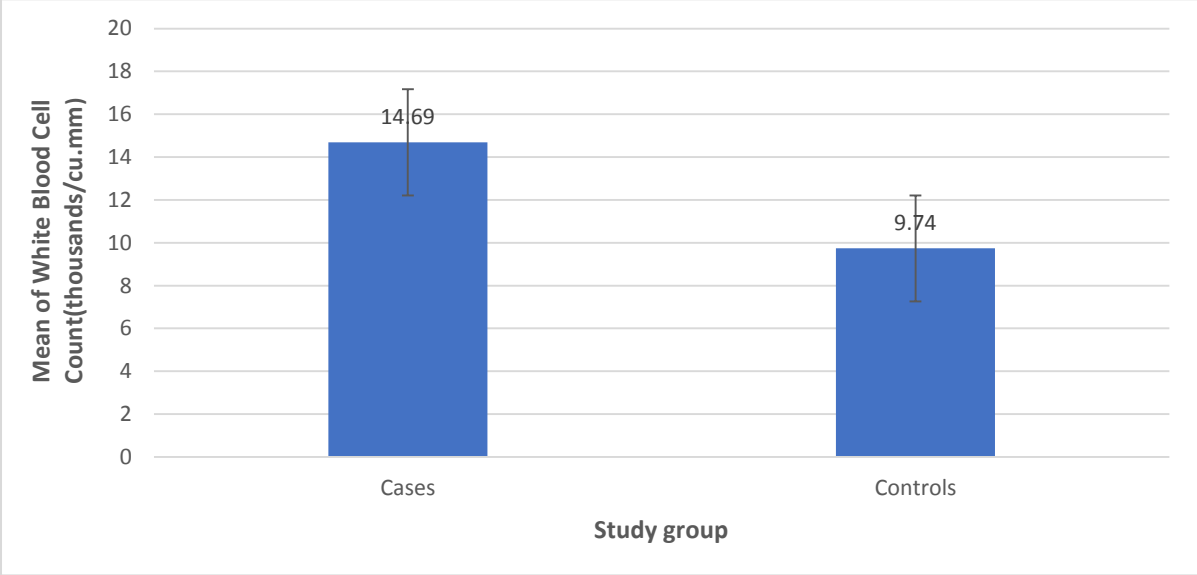


Table 23: Comparison of platelet count (thousands/cu.mm) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Platelet count(thousands/cu.mm)	278.83 ± 82.75	282.07 ± 82.72	0.8802

The mean platelet count(thousands/cu.mm) with in cases was 278.83 ± 82.75 and it was 282.07 ± 82.72 in controls. The difference in mean of platelet count (thousands/cu.mm) in

study group defined no significance as the significance value was 0.8802. (21st Table 23 with Figure 25)

Figure 25: Error bars indicating distribution of platelet count (thousands/cu.mm) with study group in the study population (N=60)

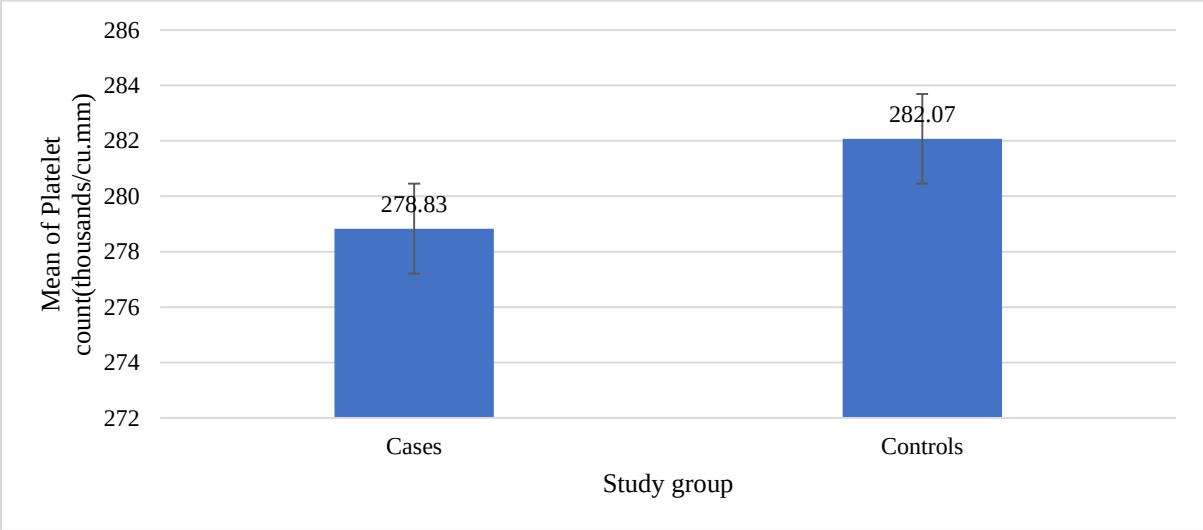


Table 24: Comparison of blood urea(mg/dL) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls(N=30)	
Blood Urea(mg/dL)	30.50 ± 8.87	26.77 ± 7.70	0.0872

The mean blood urea (mg/dL) with in cases was 30.50 ± 8.87 and it was 26.77 ± 7.70 in controls. The mean difference of blood urea (mg/dL) in study group was of no significance with value of P as 0.0872. (Table 24)

Figure 26: Error bars for the comparison of blood urea(mg/dL) in two clusters of the study (N=60)

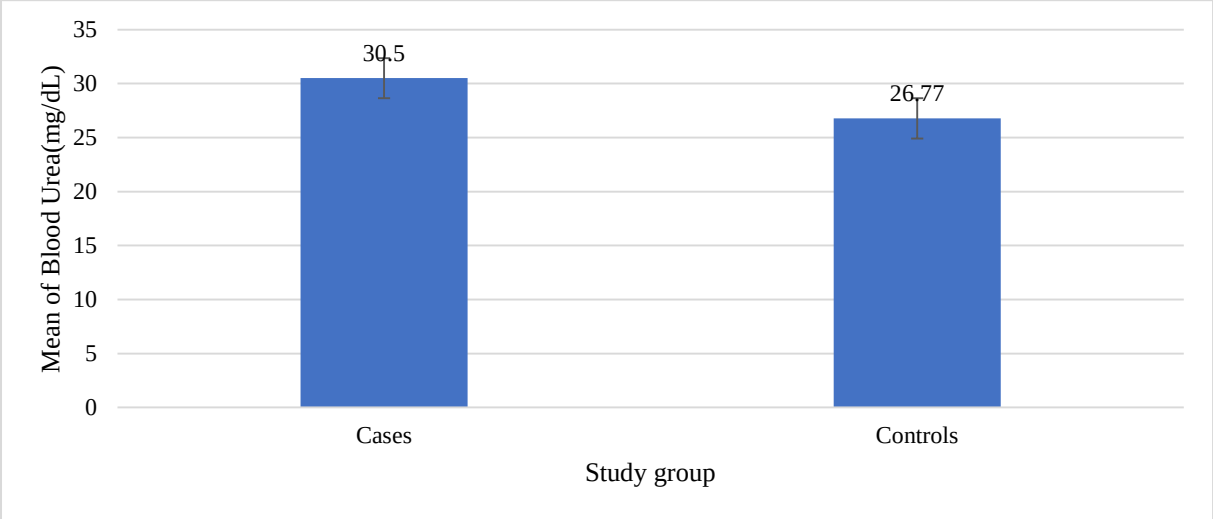


Table 25: Comparison of serum creatinine (mg/dL) with study cases Vs controls (N=60)

Measure	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Serum Creatinine (mg/dL)	0.79 ± 0.15	0.77 ± 0.16	0.5633

The value of central tendency (mean) serum creatinine (mg/dL) with in cases was 0.79 ± 0.15 and it was 0.77 ± 0.16 in controls. There was no significant difference in serum creatinine (mg/dL) as per cases Vs controls (P value>0.05). (Figure 27 and 25rd Table)

Figure 27: Indication of comparison of serum creatinine (mg/dL) using error bars in two groups (N=60)

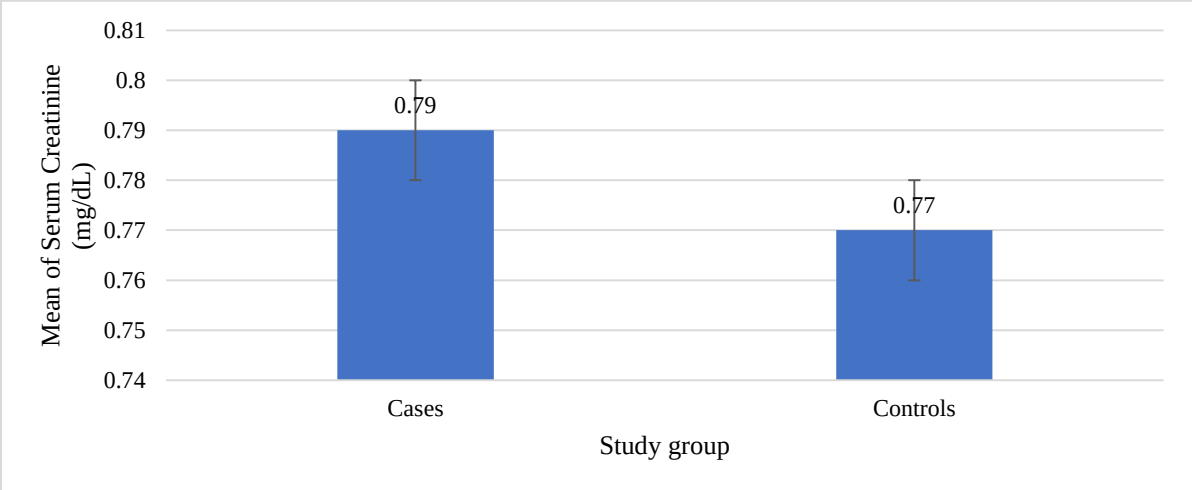


Table 26: Comparison of serum sodium (mEq/L) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Serum Sodium (mEq/L)	135.87 ± 3.88	134.67 ± 3.98	0.2419

The mean serum sodium (mEq/L) with in cases was 135.87 ± 3.88 and it was 134.67 ± 3.98 in controls. The reported P value (0.24) denotes no significant difference in mean of serum sodium (mEq/L) in cases and controls samples. (26th Table & Figure 26)

Figure 28: Serum sodium (mEq/L) distribution picturised by error bars (N=60)

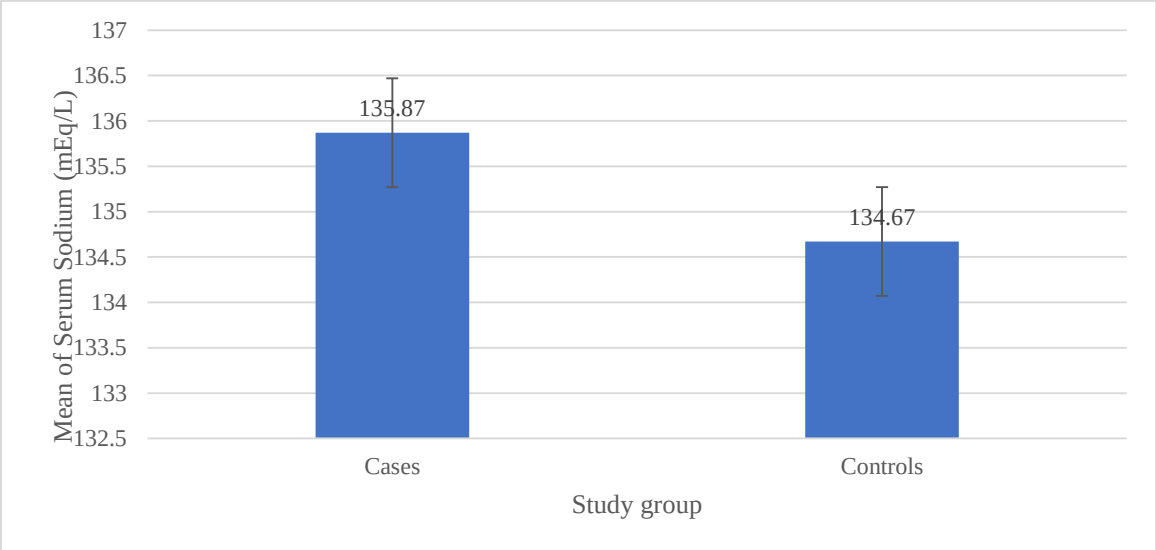


Table 27: Comparison of serum potassium (mEq/L) with the clusters of the study (N=60)

Continuous measurement	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Serum Potassium (mEq/L)	4.07 ± 0.42	4.15 ± 0.43	0.4880

Without major difference in serum potassium as per the P value in cases and controls the values were 4.07 ± 0.42 and 4.15 ± 0.43 respectively with the value of P as 0.4880. (29th figure and 27th table)

Figure 29: Error bars used to show the distribution of serum potassium (mEq/L) with study group (N=60)

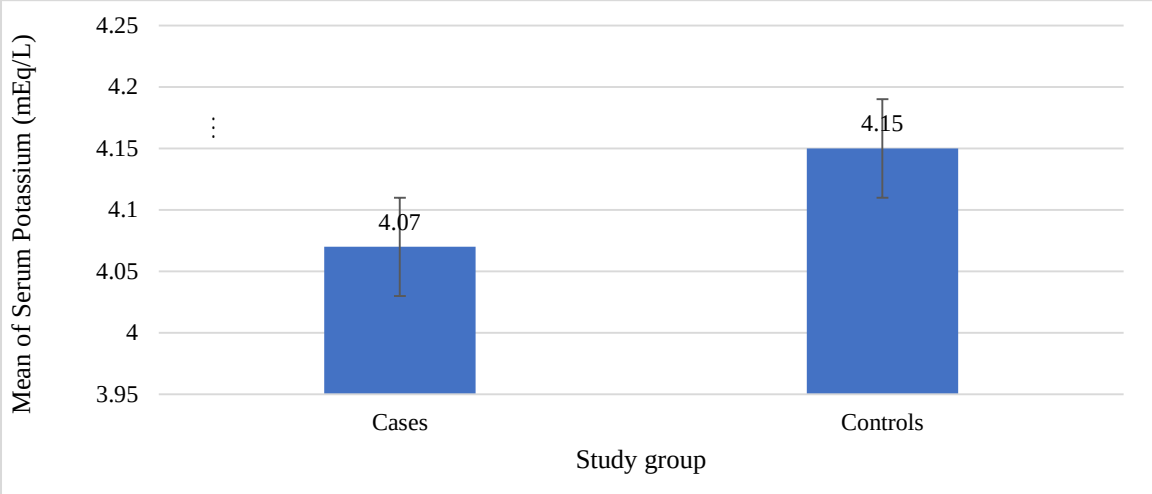


Table 28: Comparison of serum magnesium (mg/dL) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Serum Magnesium(mg/dL)	1.45 ± 0.29	2.23 ± 0.52	<0.001

The mean serum magnesium (mg/dL) with in cases was 1.45 ± 0.29 and it was 2.23 ± 0.52 in controls. The difference of mean serum magnesium (mg/dL) group wise indicate significance statistically where P value was <0.001. (28th Table 28)

Figure 30: Comparison of serum magnesium (mg/dL) with study group with error bars (N=60)

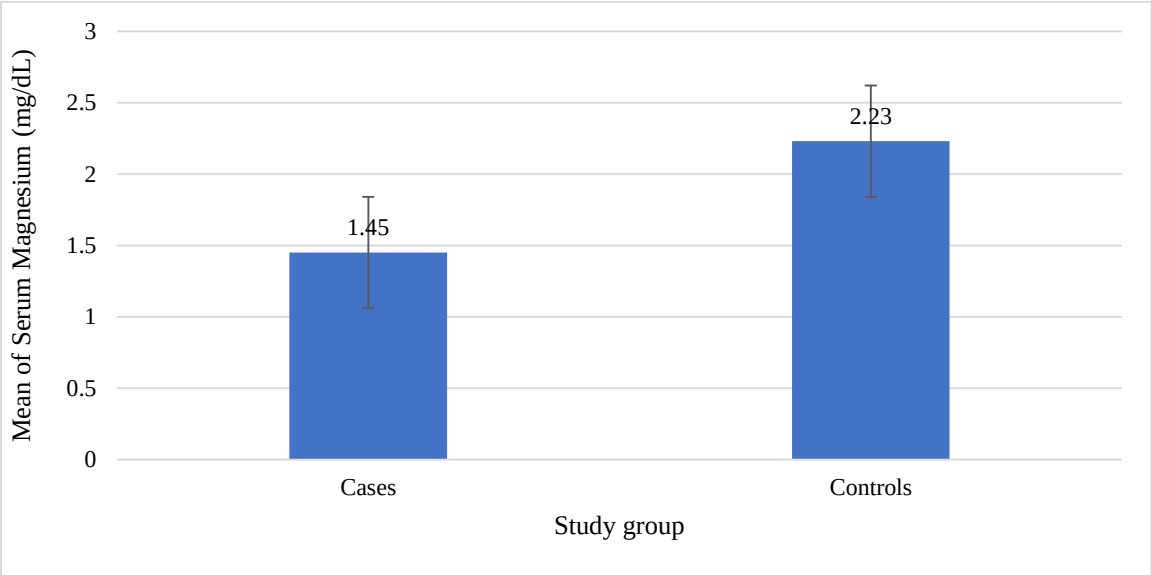


Table 29: Comparison of pulmonary function test (forced expiratory volume) with study group in the study population (N=60)

Parameter	Study group (Mean ± SD)		P Value
	Cases (N=30)	Controls (N=30)	
Pulmonary Function Test (Forced Expiratory Volume)	41.13 ± 16.31	60.00 ± 12.11	<0.001

The mean pulmonary function test (forced expiratory volume) with in cases was 41.13 ± 16.31 and it was 60.00 ± 12.11 in controls. Significant difference (P value<0.001) observed in mean of pulmonary function test (forced expiratory volume) in study groups. (29th Table & Figure 31)

Figure 31: Error bars depicting pulmonary function test (forced expiratory volume) comparison with study group (N=60)

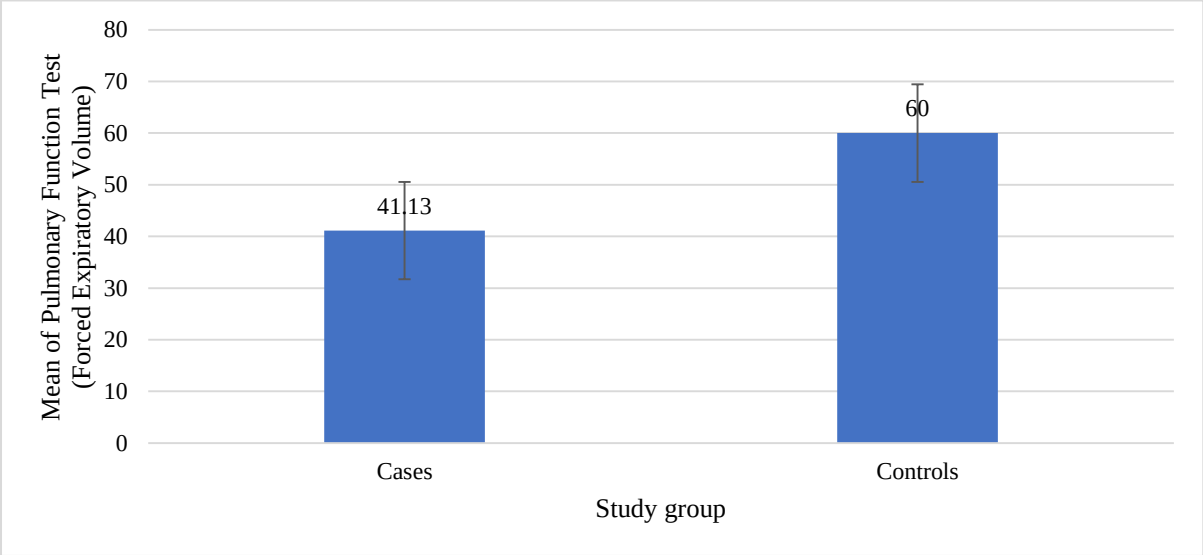


Table 30: Comparison of chest x-ray with study group (N=60)

Chest X-ray	Study group	
	Cases (N=30)	Controls (N=30)
Normal	11 (36.67%)	30 (100.00%)
Non-Homogenous Opacities	19 (63.33%)	0 (0.00%)

In cases, 11 (36.67%) participants had reported normal chest Xray and 19 (63.33%) had reported non-homogenous opacities chest Xray. In controls, all of them 30 (100.00%) participants had reported normal chest Xray. (Table 30 & Figure 32)

Figure 32: Cluster bars for the comparison of chest x-ray group wise (N=60)

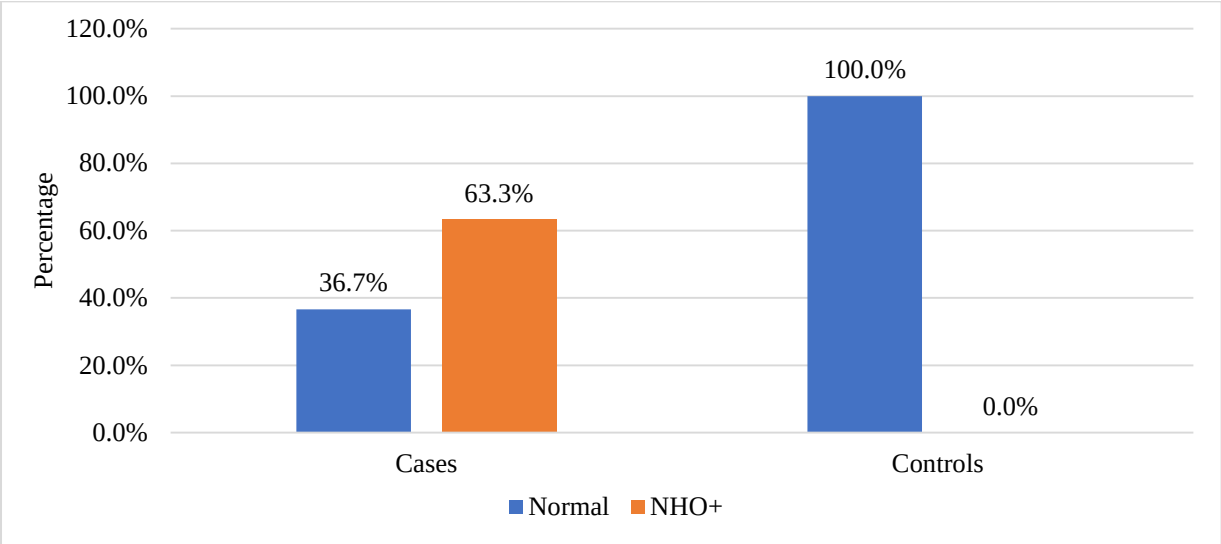
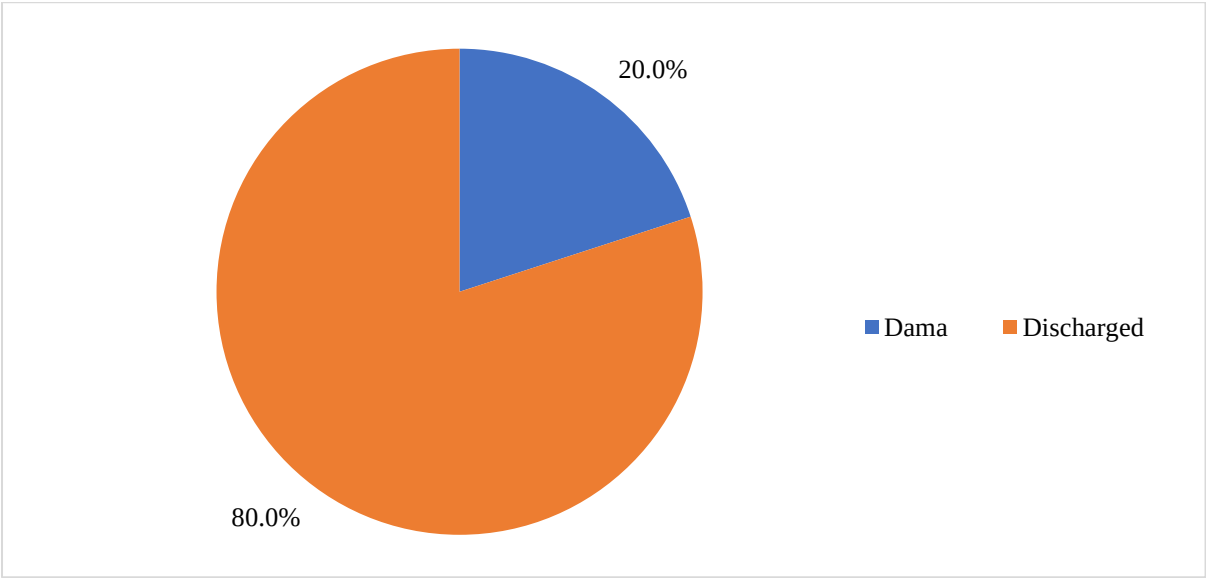


Table 31: Summary statistics of Status in the cases (N=30)

Status	Count	Proportion
Dama	6	20.00%
Discharged	24	80.00%

In cases group, 6 (20.00%) participants had reported dama status and remaining 24 (80.00%) had reported discharged status. (Table 31 & Figure 33)

Figure 33: Pie chart of status in the cases group (N=30)



DISCUSSION

DISCUSSION

Although it is preventable and controllable, COPD is a significant public health issue. The fourth most prevalent cause of death in the US is COPD, and its frequency is steadily rising around the world. There are thought to be 250 million people who have COPD already.[96] Global initiatives of chronic obstructive pulmonary disease (GOLD) defined COPD as a widespread, preventable, and treatable disease characterised by persistent respiratory symptoms and airflow restriction caused by anomalies in the air network and/or alveolar sacs, which are typically brought on by prolonged exposure to toxic particles or gases.[22] In a developing nation like India, smoking and non-smoking-related variables such workers exposed to dust and fumes, pollens, crop dust, exposure to biorefineries during cooking, lower socioeconomic level, and overcrowding are among the most prevalent risk factors for COPD.[97,98]

Magnesium is essential for several physiological activities occurring inside the cell, including membrane stability. Magnesium mostly exerts bronchodilator effects in COPD patients' airways. Different mechanisms underlie the bronchodilator actions of magnesium, including calcium's inhibitory influence on bronchial smooth muscle contraction, acetylcholine production from cholinergic nerve terminals, and mast cell release of histamine. A very low dietary level of magnesium has been found to increase the risk of acquiring asthma and COPD.[99]

Regarding the impact of magnesium on the incidence of COPD acute exacerbations as well as its contribution to lowering hospital stays and exacerbation-related mortality, information is, however, still lacking. In order to ascertain the serum magnesium levels in COPD patients experiencing an acute episode and its relationship to the exacerbation of COPD, the current investigation was carried out.

The present study was a cross-sectional observational study involving 60 subjects where, 30 subjects were grouped as cases and 30 subjects as controls. The cases group found significantly aged compared to controls (65.23 ± 7.08 VS 59.57 ± 6.21, P value 0.0017). Both the groups found male preponderance (80% VS 83.33%). The mean total duration of stay (in days) was 8.20±1.65 in the cases group. Both the cases and controls found equal proportion of smokers (80% VS 83.33%) but cases found significant increase in mean pack years compared to controls (17.46 ± 3.84 VS 11.58 ± 3.18, P value <0.001). In both the groups, farmers were found in majority followed by housewives and silk weaver and mechanic. (farmers: 46.67% VS 40%, housewife:13.33%VS 10%, silk weaver/ mechanics 10% VS 10%). In cases, the majority of 16 (53.33%) participants socioeconomic class 3 followed by socioeconomic class 4 and socioeconomic class 2 were 9 (30.00%), 4 (13.33%). In controls, the majority of 14 (46.67%) participants had socioeconomic class 3 followed by socioeconomic class 4 and socioeconomic class 2 were 12 (40.00%), 4 (13.33%).

In a similar study by Kshirsagar, K et al[1] involved 100 subjects with COPD where 72%had hypomagnesemia and 28% were normomagnesemia and found insignificant difference in the mean age (66.54±8.32 yrs VS 66.18±8.0 yrs), with male predominance in both groups (76.38 %VS 64.28%). Smokers were 73.61% and non- smokers were 26.39% in hypomagnesemia group and smokers were 64.28%, non -smokers were 35.72 in normomagnesemia group (p0.49).[1] Makwana, S et al.[84] involved 100 subjects with COPD with mean age of 60.1 ±11.7 yrs and male preponderance (78%) with majority 87% having smoking history, where 32% were present smokers, and 55% of subjects were not present smokers and had abstained for 6 months.[84] Parimala S et al[91] involved 116 subjects with 58 subjects each in cases and controls, with majority of the subjects belonging to 51-70yrs of age, male were 81.9% and female were 18.1%.

Clinical parameters

In cases, all 30 (100.00%) participants diagnosing has having COPD and 30 (100.00%) had K/C/O COPD in controls. The current study found significant longer duration of clinical features in cases compared to controls (12.37 ± 3.79 VS 10.43 ± 2.94, P value 0.0314). Majority of controls reported inhaled steroids treatment history (73.33%) compared to cases (26.67%, p <0.001). In both the groups only, minority had taken pneumococcal vaccine (16.67%VS 23.33%, P-value 0.5186). Hence majority of subjects in both the groups had not taken the vaccine (83.33% VS 76.67%). In cases, 73.33% participants were reported readmission for same complaints since the time of diagnosis of COPD. The mean number of readmissions was 8.10±5.23 in the cases group. The mean pulmonary function test (forced expiratory volume) in cases was significantly low compared to controls (41.13 ± 16.31 VS 60.00 ± 12.11 P value <0.001). The number of exacerbations and projected FEV1% have shown to be negatively correlated. The condition worsens often as it advances. Frequent exacerbations have been linked to poor FEV1%. [100–102]According to Coa et al.[103] frequent hospitalisation for acute exacerbations is correlated with FEV1% 50%. According to the findings of our study, the frequency of attacks increases as anticipated FEV1% declined.

Gumus, A et al[91] found the mean pack years to be 65 ± 34/year among COPD with acute exacerbation less than 3 years and 63 ± 35/ year among COPD with acute exacerbation greater than 3 yrs.

GOLD staging

In cases, 20.00% participants had gold's criteria staging 2, 50.00% had gold's criteria staging 3 and 30.00% had gold's criteria staging 4. In controls, 70.00% participants had gold's criteria staging 2, 26.67% had gold's criteria staging 3 and 3.33% had gold's criteria staging

4. The difference in the proportion of gold's criteria staging between the study group was statistically significant with P-value <0.001. Kshirsagar, K et al[1] found stage 2 in 34.7%, stage 3 in 48.6%, stage 4 in 16.7% in hypomagnesemia group. In normomagnesemia group, stage 1 were 3.6%, stage 2 were 71.4%, stage 3 were 17.9%, stage 4 were 7.1%.[1] Parimala S et al.[84] found 3.4 % subjects were in stage 1, 50.9% were in stage 2, 37.9% were in stage 3 and 7.8% were in stage 4.

Biochemical parameters

The mean red blood cell count(mil/cu.mm) was significantly low in cases compared to controls (3.96 ± 0.31 VS 4.12 ± 0.28, P value 0.0427). The mean packed cell volume (%) was significantly low in cases compared to controls (37.90 ± 3.19 VS 43.53 ± 5.32, P value <0.001). The mean white blood cell count (thousands/cu.mm) with in cases was significantly higher compared to controls (14.69 ± 3.11 VS 9.74 ± 2.13, P value <0.001. Anaemia is probably due to lower exercise ability, more severe respiratory issues, and more serious illnesses in persons with COPD. Additionally, research has indicated that anaemia increases the risk of long-term COPD mortality, and even moderate anaemia is linked to a considerable rise in risk.[104] Anemia may increase the risk of hospital mortality in people with severe COPD who require mechanical ventilator assistance and are experiencing acute COPD exacerbations.[105] However in our study we found that no variation in the haemoglobin count in cases, while the red cell count was significantly low in cases with acute exacerbation and long duration of COPD indicating the risk factor for hospitalization and readmission.

Koo, H et al[106] found that the severity of the COPD and current smoking status were independently correlated with the increase in WBC count. In their study, COPD patients had higher WBC counts than controls, and groups with greater levels of inflammatory markers displayed more exacerbations and had higher death rates. This finding was in comparison to present study.

The mean corpuscular volume (fl) between the groups was insignificant **(**78.87 ± 4.45 VS 80.30 ± 4.54, P value 0.2222). The mean haemoglobin (gm%) found insignificant between the cases and controls (12.67 ± 2.29 VS 13.87 ± 2.44, P value 0.0546). The mean difference in the platelet count(thousands/cu.mm) between cases and controls was insignificant (278.83 ± 82.75 VS 282.07 ± 82.72 P value 0.8802). In contrast to our findings was found in Gumus, A et al[91] study but increased platelet count in COPD with greater than 3 exacerbation.

The difference in the mean blood urea (mg/dL) between the groups was insignificant (30.50 ± 8.87 VS 26.77 ± 7.70, P value 0.0872). Similarly, the difference in the mean serum creatinine (mg/dL) between the groups (0.79 ± 0.15 VS 0.77 ± 0.16 P value 0.5633). The difference in the mean serum sodium (mEq/L) between the groups was insignificant (135.87 ± 3.88 VS 134.67 ± 3.98, P value 0.2419. The mean serum potassium (mEq/L) with in cases was 4.07 ± 0.42 and it was 4.15 ± 0.43 in controls. The mean difference of serum potassium (mEq/L) in study group was statistically not significant with P value 0.4880.

Magnesium levels

The mean serum magnesium (mg/dL) with in cases was significantly less compared to controls (1.45 ± 0.29 VS 2.23 ± 0.52 P value <0.001). The mean pulmonary function test (forced expiratory volume) in cases was significantly low compared to controls (41.13 ± 16.31 VS 60.00 ± 12.11 P value <0.001). In cases, 36.67% participants had reported normal chest X-ray and 63.33% had reported non-homogenous opacities chest Xray. In controls, all of them 100.00% participants had reported normal chest Xray.

In Rajab et al.[94] study.'s found that the mean blood magnesium levels of patients with acute exacerbations of COPD were statistically substantially lower than the serum magnesium levels of stable COPD patients, who had serum magnesium levels of 2.30±0.36 at 1.88± 0.67 mg/dl. They also concluded that an increase in hospital stays is closely correlated with

chronic hypomagnesaemia.[94] Similarly the present study found longer duration of COPD and hypomagnesemia in cases.

In Singh, J et al.[81] study, individuals with hypomagnesemia had a longer history of COPD than those with normomagnesemia (6.9± 4.3 years). This discovery was not made in prior investigations, which may be due to the frequent use of medications, which has been linked to hypomagnesemia and magnesium depletion. Emphysema was the most frequent finding on the chest x-ray in 38%, following by infiltrates in 20%, hyperinflated lungs in 16%, consolidation in 16%, and cardiomegaly in 10%.[81]

In cases group, 6 (20.00%) participants had left prematurely and remaining 24 (80.00%) had reported discharged status.

CONCLUSION

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This cross-sectional study had predominant male participants with age greater than 50 yrs. The history of smoking was equal among the cases and controls while the smoking pack years was significantly greater in cases. On x-ray finding cases found significant changes. The biochemical parameters such as mean PCV and red cell count was significantly low in the cases. However, the mean white cell blood count was significant high in cases. The mean magnesium (mg/dL) and pulmonary functional test (FEV) with in cases was significantly less compared to controls. Hence the study results found that the low magnesium levels were substantially connected with acute exacerbation of COPD with reduced pulmonary function.

Limitations and Recommendations

- Our patient follow-up was shorter in duration, and we only evaluated a small subset of patients.
- To find a greater association, further study to be done with a bigger sample size and longer duration of follow up .
- In addition, a significant portion of our patients smoked, which is a typical cause of COPD. Therefore, in order to show a clear link between serum magnesium and COPD exacerbations, more patient data is needed that includes non-smokers as well.

SUMMARY

SUMMARY

The present study was a cross-sectional observational study involving 60 diagnosed COPD subjects where, 30 subjects were grouped as cases and 30 subjects as controls. The cases group found significantly aged compared to controls (65.23 ± 7.08 VS 59.57 ± 6.21, P value 0.0017). Both the groups found male preponderance (80% VS 83.33%). The mean total duration of stay (in days) was 8.20±1.65 in the cases group. Both the cases and controls found equal proportion of smokers (80% VS 83.33%) but cases found significant increase in mean pack years compared to controls (17.46 ± 3.84 VS 11.58 ± 3.18, P value <0.001).

In both the groups, farmers were found in majority followed by housewives and silk weaver and mechanic. (farmers: 46.67% VS 40%, housewife:13.33%VS 10%, silk weaver/ mechanics 10% VS 10%). In cases, the majority of 16 (53.33%) participants socioeconomic class 3 followed by socioeconomic class 4 and socioeconomic class 2 were 9 (30.00%), 4 (13.33%). In controls, the majority of 14 (46.67%) participants had socioeconomic class 3 followed by socioeconomic class 4 and socioeconomic class 2 were 12 (40.00%), 4 (13.33%). In cases, all 30 (100.00%) participants diagnosing has having COPD and 30 (100.00%) participants diagnosing has having COPD in controls. The current study found significant longer duration of diagnosis in cases compared to controls (12.37 ± 3.79 VS 10.43 ± 2.94, P value 0.0314). Majority of controls reported inhaled steroids treatment history (73.33%) compared to cases (26.67%, p <0.001). In both the groups only, minority had taken pneumococcal vaccine (16.67%VS 23.33%, P-value 0.5186). Hence majority of subjects in both the groups had not taken the vaccine (83.33% VS 76.67%)

In cases, 73.33% participants were reported readmission for same complaints since the time of diagnosis of COPD. The mean number of readmissions was 8.10±5.23 in the cases group. In cases, 20.00% participants had gold's criteria staging 2, 50.00% had gold's criteria staging 3 and 30.00% had gold's criteria staging 4. In controls, 70.00% participants had gold's

criteria staging 2, 26.67% had gold's criteria staging 3 and 3.33% had gold's criteria staging 4. The difference in the proportion of gold's criteria staging between the study group was statistically significant with P-value <0.001. The mean haemoglobin (gm%) found insignificant between the cases and controls (12.67 ± 2.29 VS 13.87 ± 2.44, P value 0.0546). The mean red blood cell count(mil/cu.mm) was significantly low in cases compared to controls (3.96 ± 0.31 VS 4.12 ± 0.28, P value 0.0427). The mean packed cell volume (%) was significantly low in cases compared to controls (37.90 ± 3.19 VS 43.53 ± 5.32, P value <0.001).

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30 (100.00%) participants had reported normal chest Xray. In cases group, 6 (20.00%) participants had left prematurely and remaining 24 (80.00%) had reported discharged status.

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ANNEXURES

INFORMED CONSENT FORM

Date:

I, Mr/Mrs _____ ,have been explained in my own vernacular language that I/We will be included in **To Study the Serum Magnesium Levels in Acute Exacerbation of Chronic Obstructive Pulmonary Disease A Case Control Study,** hereby I/We give my valid written informed consent without any force or prejudice for recording the observations of haematological and clinical parameters . The nature and risks involved have been explained to me, to my satisfaction. I have been explained in detail about the study being conducted. I have read the patient information sheet and I have had the opportunity to ask any question. Any question that I have asked, have been answered to my satisfaction. I provide consent voluntarily to allow myself / my relative as a participant in this research. I hereby give consent to provide history, undergo physical examination, undergo the procedure, undergo investigations and provide its results and documents etc to the doctor / institute etc. For academic and scientific purpose the operation / procedure, etc may be video graphed or photographed. All the data may be published or used for any academic purpose.

_____

Name of Patient/Guardian

(Relation with patient)

_____

(Signature of Patient / Attendant)

(Signature & Name of Research doctor)

ಒಪ್ಪಿಗೆ ಪತ್ರ

ದಿನಾಂಕ:

ನಾನು, ಶ್ರೀ / ಶ್ರೀಮತಿ _____, ದೀರ್ಘಕಾಲದ ಅಬ್ಸ್ಟ್ರಕ್ಟಿವ್ ಪಲ್ಮನರಿ ಡಿಸೀಸ್ ಎ ಕೇಸ್ ಕಂಟ್ರೋಲ್ ಸ್ಟಡಿಯನ್ನು ತೀವ್ರವಾಗಿ ಉಲ್ಬಣಗೊಳಿಸುವುದರಲ್ಲಿ ಸೀರಮ್ ಮೆಗ್ನೀಸಿಯಮ್ ಮಟ್ಟವನ್ನು ಅಧ್ಯಯನ ಮಾಡಲು ನಾನು / ನಮ್ಮನ್ನು ಸೇರಿಸಲಾಗುವುದು ಎಂದು ನನ್ನದೇ ಆದ ಸ್ಥಳೀಯ ಭಾಷೆಯಲ್ಲಿ ವಿವರಿಸಲಾಗಿದೆ. ಹೆಮಟೊಲಾಜಿಕಲ್ ಮತ್ತು ಕ್ಲಿನಿಕಲ್ ನಿಯತಾಂಕಗಳ ಅವಲೋಕನಗಳನ್ನು ದಾಖಲಿಸಲು ಯಾವುದೇ ಬಲ ಅಥವಾ ಪೂರ್ವಾಗ್ರಹವಿಲ್ಲದೆ ತಿಳುವಳಿಕೆಯುಳ್ಳ ಒಪ್ಪಿಗೆ. ಒಳಗೊಂಡಿರುವ ಸ್ವರೂಪ ಮತ್ತು ಅಪಾಯಗಳನ್ನು ನನ್ನ ತೃಪ್ತಿಗೆ ವಿವರಿಸಲಾಗಿದೆ ನಡೆಸುತ್ತಿರುವ ಅಧ್ಯಯನದ ಬಗ್ಗೆ ನನಗೆ ವಿವರವಾಗಿ ವಿವರಿಸಲಾಗಿದೆ. ನಾನು ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆಯನ್ನು ಓದಿದ್ದೇನೆ ಮತ್ತು ಯಾವುದೇ ಪ್ರಶ್ನೆ ಕೇಳುವ ಅವಕಾಶ ನನಗೆ ಸಿಕ್ಕಿದೆ. ನಾನು ಕೇಳಿದ ಯಾವುದೇ ಪ್ರಶ್ನೆಗೆ ನನ್ನ ತೃಪ್ತಿಗೆ ಉತ್ತರಿಸಲಾಗಿದೆ. ಈ ಸಂಶೋಧನೆಯಲ್ಲಿ ಪಾಲ್ಗೊಳ್ಳುವವನಾಗಿ ನನ್ನ / ನನ್ನ ಸಂಬಂಧಿಯನ್ನು ಅನುಮತಿಸಲು ನಾನು ಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ. ಇತಿಹಾಸವನ್ನು ಒದಗಿಸಲು, ದೈಹಿಕ ಪರೀಕ್ಷೆಗೆ ಒಳಗಾಗಲು, ಕಾರ್ಯವಿಧಾನಕ್ಕೆ ಒಳಗಾಗಲು, ತನಿಖೆಗೆ ಒಳಗಾಗಲು ಮತ್ತು ಅದರ ಫಲಿತಾಂಶಗಳು ಮತ್ತು ದಾಖಲೆಗಳನ್ನು ಡಾಕ್‌ಗೆ ಒದಗಿಸಲು ನಾನು ಈ ಮೂಲಕ ಒಪ್ಪಿಗೆ ನೀಡುತ್ತೇನೆ

_____

ರೋಗಿಯ ಹೆಸರು / ರಕ್ಷಕ

(ರೋಗಿಯೊಂದಿಗಿನ ಸಂಬಂಧ)

_____

(ರೋಗಿಯ / ಅಟೆಂಡೆಂಟ್‌ನ ಸಹಿ)

(ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ)

PATIENT INFORMATION SHEET

Study title : To Study the Serum Magnesium Levels in Acute Exacerbation of Chronic Obstructive Pulmonary Disease Case Control Study

Principal investigator: Dr Manohar Gowda B G /Dr.Raveesha A

I Dr.MANOHAR GOWDA B G , Post graduate student in Department of general medicine at Sri Devraj Urs Medical College, will be conducting a study titled**"To Study the Serum Magnesium Levels in Acute Exacerbation of Chronic Obstructive Pulmonary Disease Case Control Study"** . This study will be useful for further management of Acute Exacerbation of COPD in the near future. The funds needed for the pulmonary function tests and serum magnesium levels will be done at my own expense .2 ml of blood will be drawn for estimation of serum magnesium levels , from each of the participating patients in this study . This study will be done under the guidance of Dr.RAVEESHA A,HOD & Professor of Department of GENERAL MEDICINE .

All the data will be kept confidential and will be used only for purpose specified by the institution. You are free to provide consent for the participation of yourself in this study. You can also withdraw yourself from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution.

In case of any clarifications are needed you are free to contact me on this mobile number - 9591147245

Name and Signature of the Principal Investigator

Date-

Patient or patient bystanders Signature

ರೋಗಿಯ ಮಾಹಿತಿ ಹಾಳೆ

ಅಧ್ಯಯನದ ಶೀರ್ಷಿಕೆ: ದೀರ್ಘಕಾಲದ ಪ್ರತಿರೋಧಕ ಶ್ವಾಸಕೋಶದ ಕಾಯಿಲೆ ಪ್ರಕರಣ ನಿಯಂತ್ರಣ ಅಧ್ಯಯನದ ತೀವ್ರ ಉಲ್ಬಣದಲ್ಲಿ ಸೀರಮ್ ಮೆಗ್ನೀಸಿಯಮ್ ಮಟ್ಟವನ್ನು ಅಧ್ಯಯನ ಮಾಡಲು.

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿ: ಡಾ.ಮನೋಹರಗೌಡ ಬಿ ಜಿ / ಡಾ.ರವೀಶಾ ಎ

ಶ್ರೀ ದೇವರಾಜ್ ಉರ್ಸ್ ಮೆಡಿಕಲ್ ಕಾಲೇಜಿನಲ್ಲಿ ಸಾಮಾನ್ಯ ಔಷಧಿ ವಿಭಾಗದಲ್ಲಿ ಸ್ನಾತಕೋತ್ತರ ವಿದ್ಯಾರ್ಥಿ ಡಾ.ಮನೋಹರ ಗೌಡ ಬಿ ಜಿ, ''ದೀರ್ಘಕಾಲದ ಪ್ರತಿರೋಧಕ ಶ್ವಾಸಕೋಶದ ಕಾಯಿಲೆ ಪ್ರಕರಣ ನಿಯಂತ್ರಣ ಅಧ್ಯಯನದ ತೀವ್ರ ಉಲ್ಬಣದಲ್ಲಿ ಸೀರಮ್ ಮೆಗ್ನೀಸಿಯಮ್ ಮಟ್ಟವನ್ನು ಅಧ್ಯಯನ ಮಾಡಲು'' ಎಂಬ ಅಧ್ಯಯನವನ್ನು ನಡೆಸಲಿದ್ದೇನೆ. ಮುಂದಿನ ದಿನಗಳಲ್ಲಿ ಸಿಒಪಿಡಿಯ ತೀವ್ರ ಉಲ್ಬಣಗೊಳ್ಳುವಿಕೆಯ ಮತ್ತಷ್ಟು ನಿರ್ವಹಣೆಗೆ ಉಪಯುಕ್ತವಾಗಿದೆ. ಶ್ವಾಸಕೋಶದ ಕಾರ್ಯ ಪರೀಕ್ಷೆಗಳು ಮತ್ತು ಸೀರಮ್ ಮೆಗ್ನೀಸಿಯಮ್ ಮಟ್ಟಗಳಿಗೆ ಅಗತ್ಯವಾದ ಹಣವನ್ನು ನನ್ನ ಸ್ವಂತ ವೆಚ್ಚದಲ್ಲಿ ಮಾಡಲಾಗುತ್ತದೆ ಈ ಅಧ್ಯಯನದಲ್ಲಿ ಭಾಗವಹಿಸುವ ಪ್ರತಿಯೊಬ್ಬ ರೋಗಿಗಳಿಂದ ಸೀರಮ್ ಮೆಗ್ನೀಸಿಯಮ್ ಮಟ್ಟವನ್ನು ಅಂದಾಜು ಮಾಡಲು 2 ಮಿಲಿ ರಕ್ತವನ್ನು ಎಳೆಯಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನವನ್ನು ಡಾ.ರವೀಶಾ ಎ, ಎಚ್ಒಡಿ ಮಾರ್ಗದರ್ಶನದಲ್ಲಿ ಮಾಡಲಾಗುವುದು

ಎಲ್ಲಾ ಡೇಟಾವನ್ನು ಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆ ಮತ್ತು ಸಂಸ್ಥೆಯು ನಿರ್ದಿಷ್ಟಪಡಿಸಿದ ಉದ್ದೇಶಕ್ಕಾಗಿ ಮಾತ್ರ ಬಳಸಲಾಗುತ್ತದೆ. ಈ ಅಧ್ಯಯನದಲ್ಲಿ ನಿಮ್ಮ ಭಾಗವಹಿಸುವಿಕೆಗೆ ನೀವು ಒಪ್ಪಿಗೆ ನೀಡಲು ಮುಕ್ತರಾಗಿದ್ದೀರಿ. ಯಾವುದೇ ಕಾರಣಗಳನ್ನು ನೀಡದೆ ನೀವು ಯಾವುದೇ ಸಮಯದಲ್ಲಿ ಅಧ್ಯಯನದಿಂದ ನಿಮ್ಮನ್ನು ಹಿಂತೆಗೆದುಕೊಳ್ಳಬಹುದು. ನೀವು ಭಾಗವಹಿಸಲು ನಿರಾಕರಿಸುವುದರಿಂದ ಈ ಸಂಸ್ಥೆಯಲ್ಲಿ ಯಾವುದೇ ಪ್ರಸ್ತುತ ಅಥವಾ ಭವಿಷ್ಯದ ಆರೈಕೆಗೆ ನೀವು ಪೂರ್ವಾಗ್ರಹ ಮಾಡುವುದಿಲ್ಲ.

ಯಾವುದೇ ಸ್ಪಷ್ಟೀಕರಣಗಳು ಅಗತ್ಯವಿದ್ದರೆ ನೀವು ನನ್ನನ್ನು ಈ ಮೊಬೈಲ್ ಸಂಖ್ಯೆಯಲ್ಲಿ ಸಂಪರ್ಕಿಸಲು ಮುಕ್ತರಾಗಿದ್ದೀರಿ - 9591147245

ಪ್ರಧಾನ ತನಿಖಾಧಿಕಾರಿಯ ಹೆಸರು ಮತ್ತು ಸಹಿ

ದಿನಾಂಕ-

ರೋಗಿಯ ಅಥವಾ ರೋಗಿಯ ವೀಕ್ಷಕರ ಸಹಿ

PROFORMA

To Study the Serum Magnesium Levels in Acute Exacerbation of Chronic Obstructive Pulmonary Disease A Case Control Study

NAME	
AGE	
GENDER	
DATE OF ADMISSION	
PRESENTING COMPLIANTS	a. Shortness of breath – b. Severe cough (with/without sputum) -
Risk factor : **1. SMOKER (Y/N)** **If Yes , number of pack years** **2. Tobacco chewing (Y/N)** **3. OCCUPATION :**	
Is the patient already a known case of COPD (Y/N)	
If Yes then details about treatment history	
Treatment history	• Inhaled steroids(Y/N) • Oral steroids at admission (Y/N) • Oral steroids(Y/N) • Antibiotics(Y/N) • Home oxygen(Y/N) • Vaccination status
CORMORDBIDITES	
DURATION OF STAY IN HOSPITAL	
TIMES OF READMSSION FOR THE SAME COMPLAINTS	
GOLD CRITERIA STAGING	

INVESTIGATIONS

1.COMPLETE HEMOGRAM

DATE	HB	RBC	PCV	MCV	WBC	PLATLETS

2. SERUM ELECTROLYTES AND RFT

DATE	UREA	CREAT	SODIUM	POTASSIUM	MAGNESIUM

3. CHEST XRAY

4 . PULMONARY FUNCTION TEST

Master Sheet:

Sr.No	Study group	Age (years)	Gender	Total duration of stay (in days)	Risk factor	Pack years	Occupation	Socioeconomic status	K/C/O COPD	Duration of diagnosis	Any treatment history	Pneumococcal vaccine taken	Any readmission for same complaints since the time of diagnosis of COPD	Number of readmissions	Gold's criteria staging	Haemoglobin (gm%)	Red Blood Cell Count(mil/cu.mm)	Packed Cell Volume (%)	Mean Corpuscular Volume(fl)	White Blood Cell Count(thousands/cu.mm)	Platelet count(thousands/cu.mm)	Blood Urea(mg/dL)	Serum Creatinine (mg/dL)	Serum Sodium (mEq/L)	Serum Potassium (mEq/L)	Serum Magnesium(mg/dL)	Pulmonary Function Test (Forced Expiratory Volume)	Chest Xray	Status
1	Cases	69	1	9	1	15	FARMER	3	1	10	2	2	1	10	3	12	3.9	35	78	10	192	33	0.8	137	5	1.5	36	2	2
2	Cases	60	1	7	1	20	CARPENTER	4	1	15	2	2	1	15	3	13.2	4	38	80	15	200	40	0.9	133	4.3	1.4	40	2	2
3	Cases	70	1	10	1	12	FARMER	3	1	12	2	2	1	9	3	9	3.7	36	77	12	227	36	0.6	140	4.4	1.3	45	2	1
4	Cases	72	1	8	1	15	FARMER	4	1	20	1	2	2	0	4	12	3.8	35	80	11	208	39	0.9	136	3.6	1.2	27	1	2
5	Cases	60	1	9	1	20	TRUCK DRIVER	3	1	15	2	2	1	10	3	15	3.9	38	80	15	230	36	0.8	135	3.9	1.2	36	2	2
6	Cases	56	2	6	2		House wife	2	1	16	2	1	1	15	2	17	4.2	40	82	16	260	40	0.9	136	4	1.5	60	1	1
7	Cases	63	1	10	1	18	CASHIER	3	1	9	1	2	2	0	3	9	3.6	35	70	10	298	36	0.7	133	3.6	2	40	2	2
8	Cases	70	2	9	2		SILK WEAVER	4	1	9	2	2	1	14	4	10	4	36	78	18	303	40	0.9	142	4	1.3	27	1	2
9	Cases	72	1	10	1	20	MECHANIC	4	1	10	2	2	1	12	4	14	3.8	32	70	21	400	33	0.8	140	4	1.2	25	2	2
10	Cases	68	2	9	2		House wife	3	1	12	2	2	1	10	3	17	4.1	36	84	14	309	40	1	136	3.9	1.4	50	2	1
11	Cases	58	1	8	1	15	FARMER	4	1	19	2	2	1	9	3	15	4.2	40	80	13	278	27	0.6	130	4	1.5	46	1	2
12	Cases	62	1	10	1	20	FARMER	3	1	19	2	2	1	10	3	10	3.8	36	76	11	356	20	0.5	139	5.1	1.5	54	2	2
13	Cases	58	1	6	1	15	ENGINEER	2	1	8	1	1	2	0	2	13	4.2	42	80	13	402	28	0.6	132	4.3	1.9	70	1	2
14	Cases	75	1	6	1	20	PAINTER	4	1	10	2	2	1	10	3	12	4.2	36	79	12	182	48	1	140	4.2	1.4	36	2	1
15	Cases	72	1	8	1	15	FARMER	3	1	15	1	2	1	14	3	14.2	4.5	40	80	14.7	308	45	1	136	4	1.8	40	1	2
16	Cases	78	1	7	1	14	FARMER	4	1	17	2	2	1	10	4	12	3.6	35	69	15	402	24	0.9	133	3.9	1.2	26	2	2
17	Cases	75	1	4	1	10	FARMER	3	1	14	2	2	1	13	3	11	4	40	86	18	382	21	0.8	142	4.1	1.3	40	1	2
18	Cases	60	2	7	2		SILK WEAVER	3	1	16	2	2	2	0	2	13	3.9	42	87	16	245	26	0.9	136	3.6	1.2	66	1	2

19	Cases	63	2	6	2		House wife	2	1	10	1	1	2	0	2	12	3.5	39	82	10	187	37	0.7	138	4.2	2.1	68	2	2
20	Cases	78	1	9	1	16	FARMER	3	1	8	2	2	1	10	3	13	4	42	84	14	287	42	0.9	130	3.8	1.3	40	2	2
21	Cases	66	1	10	1	20	SILK WEAVER	4	1	11	2	2	1	11	4	12	3.2	30	70	13	265	30	0.9	134	4	1.2	20	2	1
22	Cases	58	1	8	1	20	CONTTRACTER	2	1	14	2	1	2	0	2	12	3.9	36	79	18	389	27	0.8	138	3.9	1.9	68	1	2
23	Cases	50	1	10	1	25	FARMER	3	1	17	1	2	1	10	4	14	4.2	41	82	14	145	20	0.6	133	3.8	1.3	20	2	2
24	Cases	67	1	7	1	20	FARMER	3	1	13	2	2	1	9	3	11	3.9	38	76	18	129	23	0.8	130	4	1.4	40	1	2
25	Cases	60	1	10	1	16	Coolie	4	1	8	1	2	2	0	4	9.2	3.6	36	78	14	254	21	0.6	132	3.3	1.9	18	2	2
26	Cases	67	1	9	1	23	FARMER	3	1	9	2	2	1	10	3	10.4	3.9	39	80	14	300	18	0.5	140	3.5	1	44	2	2
27	Cases	60	2	7	2		House wife	3	1	10	2	2	1	10	4	16	4.2	42	82	19	201	22	0.8	139	4.3	1.2	19	2	2
28	Cases	57	1	10	1	10	RTO OFFICER	1	1	7	2	1	2	0	2	17	4.8	44	79	22	455	20	0.9	133	5	1.8	69	1	2
29	Cases	63	1	7	1	20	FARMER	3	1	8	2	2	1	12	3	13	4	40	80	16	293	23	0.8	130	4.5	1.2	45	2	2
30	Cases	70	1	10	1	20	FARMER	3	1	10	1	2	1	10	4	12	4.2	38	78	14	278	20	0.9	143	3.9	1.4	19	2	1
31	Controls	60	1	0	1	10	FARMER	3	1	10	1	2	2	0	2	14	4	39	80	14	202	29	0.8	140	3.9	2.3	70	1	3
32	Controls	50	1	0	1	10	FARMER	3	1	9	1	2	2	0	2	17	4	40	82	9	264	30	1	139	4	2.4	68	1	3
33	Controls	66	2	0	2	14	House wife	4	1	10	1	2	2	0	3	10.3	3.9	39	78	8.8	306	22	0.9	132	3.6	2.6	50	1	3
34	Controls	59	1	0	1	10	TRUCK DRIVER	4	1	5	2	2	2	0	2	12	3.8	42	76	7.7	434	36	0.8	135	4.5	2.2	58	1	3
35	Controls	55	2	0	2		Coolie	4	1	10	1	2	2	0	3	15	4	39	78	10	333	10	0.7	130	4.4	1.4	40	1	3
36	Controls	56	1	0	1	12	ENGINEER	2	1	10	2	1	2	0	2	17	4.2	50	82	13	213	12	0.6	133	4	2.4	70	1	3
37	Controls	50	1	0	1	10	FARMER	3	1	6	1	2	2	0	2	15	4.4	45	87	12	264	24	0.7	140	4.5	2.5	68	1	3
38	Controls	70	1	0	1	20	SILK WEAVER	3	1	15	2	2	2	0	2	10	4	40	85	13.6	303	22	0.8	133	3.9	2.9	70	1	3
39	Controls	65	1	0	1	10	Coolie	4	1	10	1	2	2	0	3	10	3.8	36	82	12	379	29	0.5	139	4.7	2.7	50	1	3
40	Controls	53	1	0	1	8	ENGINEER	2	1	9	2	1	2	0	2	13	4	34	80	10	376	39	0.9	130	4.3	1.5	69	1	3
41	Controls	54	2	0	2		House wife	3	1	5	1	2	2	0	2	12	3.9	37	78	9.8	202	30	0.9	134	4	2.9	60	1	3
42	Controls	59	1	0	1	10	FINANCIER	2	1	10	2	1	2	0	2	16	4.7	51	83	9	222	32	0.7	132	4.3	2	67	1	3
43	Controls	60	1	0	1	9	FARMER	3	1	9	1	1	2	0	2	16.2	4.9	55	80	10.5	422	30	0.5	132	4.5	2.1	70	1	3
44	Controls	64	1	0	1	10	Coolie	4	1	10	2	2	2	0	2	14	4.2	43	82	10	320	29	0.9	129	4	2.2	67	1	3
45	Controls	59	1	0	1	10	MECHANIC	4	1	10	1	2	2	0	3	18.6	4	51	88	8.1	182	31	1	138	3.3	2.1	48	1	3
46	Controls	65	1	0	1	15	FARMER	3	1	14	1	2	2	0	2	14	4.7	42	81	7.8	192	28	0.4	132	4.2	1.4	60	1	3
47	Controls	72	1	0	1	12	FARMER	3	1	8	1	2	2	0	3	11	4	41	78	9	204	20	0.9	130	3.9	2.2	50	1	3
48	Controls	68	1	0	1	10	ENGINEER	2	1	5	1	1	2	0	2	14	4.2	40	81	9.3	293	40	0.8	132	4	2.1	67	1	3

49	Controls	61	1	0	1	8	FARMER	3	1	10	1	1	2	0	2	15	4.4	45	89	9.4	329	24	0.8	130	4.4	2.2	70	1	3
50	Controls	59	1	0	1	10	FARMER	4	1	13	1	2	2	0	2	18.5	4.2	51	77	14	452	21	0.7	136	3.8	2.4	70	1	3
51	Controls	56	2	0	2		House wife	3	1	12	1	2	2	0	4	12	3.9	45	81	11	190	32	0.9	139	3.7	2.5	20	1	3
52	Controls	55	1	0	1	10	FARMER	3	1	15	1	1	2	0	3	14	3.8	44	85	10	182	37	0.7	141	3.3	1.4	50	1	3
53	Controls	50	1	0	1	20	FARMER	4	1	10	1	2	2	0	2	14	4	40	83	5.4	158	16	0.6	132	4.3	2.2	66	1	3
54	Controls	51	2	0	2		SILK WEAVER	3	1	9	2	2	2	0	2	12.1	4.2	42	73	6.7	203	19	0.7	140	4	2	67	1	3
55	Controls	60	1	0	1	15	FARMER	3	1	11	1	2	2	0	3	10.2	3.9	39	69	8.4	289	21	0.9	138	5	2.4	45	1	3
56	Controls	62	1	0	1	12	FARMER	3	1	12	1	2	2	0	2	12.2	3.9	48	70	8.9	302	39	1.1	132	5.1	1.5	63	1	3
57	Controls	57	1	0	1	10	PAINTER	4	1	16	1	2	2	0	2	17.5	4.3	52	81	10	300	31	0.6	136	4.7	3	70	1	3
58	Controls	58	1	0	1	9	CARPENTER	4	1	15	2	2	2	0	2	14	4	44	82	9	276	28	0.8	134	4.2	2.9	62	1	3
59	Controls	61	1	0	1	12	MECHANIC	4	1	13	1	2	2	0	3	13	4.2	42	78	6.2	401	22	0.9	142	3.8	1.2	45	1	3
60	Controls	72	1	0	1	15	MECHANIC	4	1	12	1	2	2	0	2	14.4	4	50	80	9.7	269	20	0.6	130	4.1	3.2	70	1	3

Key of the Master Sheet:

Variable Name	
Study group	1=Cases, 2=Controls
Gender	1=Male, 2= Female
Risk factor	1=Smoker, 2=Nil
Socioeconomic status	1= Class 1, 2=Class 2, 3=Class 3, 4=Class 4
K/C/O COPD	1=Yes
Any treatment history	1=Inhaled steroids, 2=No
Pneumococcal vaccine taken	1=Taken, 2=Not taken
Any readmission for same complaints since the time of diagnosis of COPD	1=Yes, 2=No
Chest Xray	1=Normal, 2=Non-Homogenous Opacities
Status	1=Dama, 2=Discharged, 3=Nil