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DISSERTATION

"IMPACT OF ANEMIA ON COMPLICATIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS-CASE-CONTROL STUDY"

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(M.D. GENERAL MEDICINE, 2019-20 BATCH)

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Dr. RAKESH KUMAR. G

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LIST OF ABBREVIATIONS

GLOSSARY	ABBREVIATIONS
ACD	Anemia of chronic disease
AECOPD	Acute exacerbation of COPD
AI	Anemia of inflammation
BMI	Body mass index
CAT	COPD assessment test
CBC	Complete blood count
CD4	Cluster of differentiation 4
CD8	Cluster of differentiation 8
CI	Confidence interval
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CPET	Cardiopulmonary exercise testing
CVS	Chorionic villus sampling
DALYs	Disability-adjusted life years
DBP	Diastolic blood pressure
DLCO	Diffusing capacity for carbon monoxide
ECG	Electrocardiogram
FEV1	Forced expiratory volume
FID	Functional iron deficiency
FVC	Forced vital capacity
GOLD	Global initiative for chronic obstructive lung disease
Hb	Hemoglobin
HCT	Hematocrit
HR	Hazard ratio
IC	Inspiratory capacity
ID	Iron deficiency
IL	Interleukin

IQR	Interquartile range
LMIC	Low- and middle-income countries
LTOT	Long-term oxygen treatment
MCH	Mean cell hemoglobin
MCHC	Mean cell hemoglobin concentration
MCV	Mean corpuscular volume
mMRC	Modified British medical research council
MRC	Medical research council
NICE	National Institute for clinical excellence
NIV	Non-invasive ventilation
PFT	Pulmonary function testing
RBC	Red blood cell
RV	Residual volume
SBP	Systolic blood pressure
SD	Standard deviation
SpO2	Oxygen saturation
TIBC	Total iron-binding capacity
TLC	Total lung capacity
TNF	Tumor necrosis factor
VAS	Visual analog scale
WHO	World health organization

ABSTRACT

Background: Anemia is a common comorbidity among COPD patients, and it has been associated to reduce functional ability, poor quality of life, increased COPD exacerbations, and early mortality. The study's goal is to compare the complications in COPD patients who have anaemia to those who don't.

Methods: This is a case-control study conducted in RL Jalappa Hospital on COPD patients with and without anemia during Jan- 2020 to Dec- 2021. CBC parameters, investigation parameters, vital signs parameters were considered as primary outcome variables. The study group (COPD with anemia Vs. COPD without anemia) was considered as a primary explanatory variable.

Results: The mean age in COPD with anemia group is 62.6 ± 9.43, and that in COPD without anemia is 61.4 ± 6.99. In our study, the mean Hb in COPD patients, both anaemic and non-anemic was 9.42 1.87 g/dL and 15.07 1.46 g/dL, respectively. Pulmonary function variables FVC, FEV1, FEV1/FVC, SpO2 (low), and respiratory rate between the study groups had no significant statistical difference (p-value >0.05).

Conclusions: Our study did not show any impact of anaemia on complications in chronic obstructive pulmonary disease**.**Complications like exacerbations of COPD, pleural effusion, pneumothorax, cardiac arrhythmias. Anemic COPD patients are found to have low body temperature, low hemoglobin, and relatively higher MCHC levels compared to non-anemic COPD patients.

Keywords: Anemia, chronic obstructive pulmonary disease, hemoglobin, Inflammation.

INTRODUCTION

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is a diversified, long-term inflammatory condition of the airways that frequently results in the loss of neighboring alveoli and vasculature. Symptoms range from a continual productive cough to incapacitating dyspnea. The. course of the disease ranges from years of. stability to fatal acute exacerbations and respiratory collapse. COPD continues to be a significant burden on patients, careers, and the healthcare system.[1] COPD is diagnosed by spirometry evidence of chronic airflow restriction, as defined by post-bronchodilator FEV1/FVC 70 percent, in individuals with relevant symptoms and a history of exposure to noxious stimuli.[2] The Global Initiative for Chronic Obstructive Lung Disease (GOLD) was established in 1997 with the goal of increasing global awareness of COPD and improving prevention and treatment.[3] The initial Executive Summary of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) was released in 2001[3], and since then, GOLD has updated the document annually and produced a significant report. COPD is distinguished by an increase in neutrophils, macrophages, and T lymphocytes (CD8 greater than CD4) in the lungs. In general, the severity of the inflammation is proportional to the degree of airflow restriction. These inflammatory cells produce a number of cytokines and mediators that contribute to the illness process. Nonsmokers may be at risk for COPD due to genetic factors, long-standing asthma, ambient tobacco smoke, outdoor air pollution (from traffic and other sources), biomass smoke, occupational exposure, recurrent respiratory tract infection in infancy, pulmonary TB, and poor socioeconomic status.[4] Chronic obstructive pulmonary disease (COPD) is the third leading cause of death worldwide, causing 3.23 million deaths in 2019. Over 80% of these deaths occurred in low- and middle-income countries (LMIC).[5] In India, three out of five leading causes of mortalities constitute non-communicable diseases, whereas COPD is the

second biggest cause of death. By 2016, the rate of Incidence had increased by 29.2 percent, posing a severe public health threat.[6]

Systemic effects and/or comorbidities are significant events in the natural history of COPD and have the potential to exacerbate morbidity, economic burden, and death.[7] Cardiovascular disease, malnutrition, osteoporosis, gastric reflux, and clinical anxiety, and depression are all prominent systemic symptoms and comorbidities in COPD.[8] Recently, anemia has become another comorbidity that has gained importance in patients. with COPD. Earlier in clinical medicine, polycythemia is known to be a common adverse event of hypoxemia in COPD; however, it has been occurring less frequently due to more rigorous correction of hypoxemia by domiciliary long-term oxygen therapy.[9] Several explanations have been offered for anemia in COPD patients, including the idea that the inflammatory load of COPD causes chronic anemia owing to the actions of IL-1 and TNF- (anemia in COPD), as well as CRP and IL-6.[10] Nutritional deficiencies in COPD patients, have been postulated as a cause of anemia.[11]

Anemia has been linked to decreased dyspnea and walking distance in people with COPD, as well as decreased circulatory efficiency (as measured by lower peak oxygen uptake and lower peak work rate), the need for home oxygen therapy, and lower mean peripheral oxygen levels both at rest and at the time of exercise.[12] In a retrospective investigation of stable COPD patients, Boutou et al.[13] found that the presence of anemia was significantly associated with survival, regardless of age or FEV1 percentage of expected. P = 0.035, the median survival rates in COPD patients, both anaemic and non-anemic were 68.7 (18.1 – 91.5) and 79.8 (57.5 – 98.4) months, respectively.

The prevalence of anemic COPD patients ranges from 7.5 percent to 33 percent. The most prominent kind of anemia connected with COPD is Anemia of chronic disease (ACD).[14] In a

hospital-based, cross-sectional investigation of 200 COPD patients, Parveen et al.[15] discovered anemia in 18% of the patients. Anemia has been linked to an increase in morbidity, as measured by the frequency of exacerbations and hospitalizations. A study by Silverberg et al.[12] 9 % of 107 consecutive patients hospitalized with an acute exacerbation of COPD (AECOPD) were found to be anemic on admission.

NEED OF THE STUDY:

Chronic obstructive pulmonary disease (COPD) is a long-term disorder in which the lungs' airways gradually become obstructed. Long-term exposure to irritants that damage the lungs and airways is the most common cause of COPD. Individuals with COPD have a life expectancy that ranges from good to poor, depending on their COPD stage, with the disease progressing toward stage IV, often known as "end-stage" chronic obstructive pulmonary disease. COPD, like other chronic diseases, has been linked to an increase in the number and severity of comorbidities as people get older. The most prevalent type of anaemia linked with COPD is anemia of chronic disease (ACD). The exact mechanism of anemia in COPD remains elusive. But its concomitant occurrence in COPD negatively influences the disease outcome. Anemia in COPD is associated with greater healthcare resource utilization, impaired quality of life, decreased survival, and a greater likelihood of hospitalization. It influences not only the treatment, management, and prognosis but also alters the quality of life. Thus, it is important that assessment of anemia should be done routinely in COPD patients attending clinics. There is a dearth of studies on the occurrence of anemia in COPD and its complication. There are not many studies done on the Indian population. The current study is carried out to study the impact of anemia on complications of COPD patients as compared to non-anemic patients.

AIMS & OBJECTIVES

AIMS & OBJECTIVES:

The objective of the study:

1. To evaluate the complications in COPD patients at RL Jalappa Hospital.

2. To compare the complications in COPD patients with and without anemia at RL Jalappa Hospital.

REVIEW OF

LITERATURE

REVIEW OF LITERATURE:

COPD:

COPD is a prevalent, preventable, and curable condition defined by respiratory symptoms and airflow restriction caused by airway and/or alveolar abnormalities, which are mainly induced by prolonged exposure to harmful gases or particles. COPD is characterized by chronic airflow restriction caused by a combination of small airway illness (e.g., obstructive bronchiolitis) and parenchymal damage (emphysema), the proportional contributions of which vary from person to person. Chronic inflammation causes structural changes, constriction of tiny airways, and loss of lung tissue. The loss of tiny airways may cause the disease's airflow constriction and muco-ciliary dysfunction.[16]

Among the criteria that are needed for making the diagnosis of chronic obstructive pulmonary disease (COPD) are deficits in the rate at which one can forcefully exhale. Most experts consider a low ratio (<0.70) of the forced expiratory volume in 1 second (FEV1) to the forced vital capacity (FVC) after bronchodilator use to be a key diagnostic criterion.[17] Once the diagnosis of COPD has been established, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) nomenclature grades severity according to the degree to which the measured FEV1 is lower than the patient's predicted value. GOLD stage 1, indicating mild disease, is defined as an FEV1 that is greater than or equal to 80% of the predicted value; GOLD stage 2, indicating moderate disease, as an FEV1 that is greater than or equal to 50% and less than 80% of the predicted value; GOLD stage 3, indicating severe disease, as an FEV1 that is greater than or equal to 30% and less than 50% of the predicted value; and GOLD stage 4, indicating very severe disease, as an FEV1 that is less than 30% of the predicted value.[18]

The National Institute for Clinical Excellence (NICE) published an update to its guidance on the diagnosis and management of COPD (NICE Guideline 115) in July 2019,[19], but many clinicians and formularies rely on the management recommendations produced by the GOLD, which are more regularly updated and more easily applied in practice than the NICE recommendations. The NICE guidelines recommend the Medical Research Council (MRC) dyspnea scale to grade the breathlessness according to the level of exertion required to elicit it.

Classification:

COPD has been classified, in most literatures, by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, that first was launched in 1997 and has been regularly updated to the current version in 2017.[16] In GOLD Version 2007, airflow restriction as evaluated by spirometry was used to standardize the severity of COPD (Grades I–IV).[20] GOLD Version 2011, followed by a revision in 2013, introduced the combined COPD assessment to recognize the consensus that factors other than airflow limitation alone should be considered for optimal COPD assessment, including symptoms, measured either by the modified Medical Research Council (mMRC) dyspnea score or by the COPD Assessment Test (CAT), and the risk of exacerbations based on the history of exacerbations and the grade of spirometric obstruction.[17] GOLD 2017, the fourth document in the GOLD report, was recently released, describing a refined composite classification that includes the components of the GOLD 2007 and GOLD 2013 parameters, as well as the severity of airflow limitation (spirometry Grades 1–4) and combined symptoms/exacerbation risk (Groups A–D), resulting in 16 subgroups. GOLD 2017 classification also recommends a pharmacologic treatment protocol by GOLD "A/B/C/D" group, based only on symptoms and exacerbations among participants recognized as having COPD based on the FEV1/FVC- 0.7 threshold.[16]

Epidemiology:

A systematic literature search of Medline, EMBASE (*via* Ovid) and Google Scholar, from January 1995 to March 2019 showed the estimated worldwide COPD mean prevalence (95% CI) was 13.1% (10.2–15.6%), with the following distribution by continents: Europe, 12.4% (8.8–16.0%); Africa, 13.9% (12.0–15.9%); America, 13.2% (10.5–15.9%); Asia, 13.5% (10.0–16.0%); and Oceania, 11.6% (9.8–13.1%).[21] The burden of chronic diseases, such as COPD, poses a special challenge in low-income countries, where healthcare resources are traditionally designed to respond episodically to acute disease, especially infectious diseases, and are not adapted to treating chronic diseases.[22] The contribution of chronic respiratory diseases to the total DALYs in India increased from 4·5% (95% UI 4·0–4·9) in 1990 to 6·4% (5·8–7·0) in 2016. Of the total global DALYs due to chronic respiratory diseases in 2016, 32% occurred in India. COPD was responsible for 75·6% of the chronic respiratory disease DALYs in India in 2016. The number of cases of COPD in India increased from 28·1 million (27·0–29·2) in 1990 to 55·3 million (53·1–57·6) in 2016, an increase in prevalence from 3·3% (3·1–3·4) to 4·2% (4·0–4·4).[23]

COPD causes chronic airflow restriction due to a combination of small airway illness (obstructive bronchiolitis) and parenchymal damage (emphysema).[24] Many individuals will have exacerbations or comorbidities, resulting in a deterioration of their overall health.[25] This deterioration might be attributed to the patient's continued exposure to established COPD risk factors, such as smoking cigarettes, or to the patient's failure to comply to the prescribed medical therapy. COPD patients will have symptoms such as dyspnea, persistent cough with or without sputum production, and maybe a history of exposure to risk factors for the ailment.[24]

Etiology and risk factors:

Chronic obstructive pulmonary disease (COPD) is distinguished by a lack of reversible airflow restriction and an inappropriate inflammatory response in the lungs. The latter represents the innate and adaptive immunological responses to long-term unpleasant aerosol and gas exposure, notably cigarette smoke. All cigarette smokers have some pulmonary inflammation, but those who develop COPD have an increased or aberrant response to hazardous substances inhalation. This heightened reaction can cause mucus hypersecretion (chronic bronchitis), tissue death (emphysema), and interferes with normal repair and defense systems, resulting in small airway inflammation and fibrosis (bronchiolitis).[26] Despite the fact that cigarette smoking is the most widely recognized reason of COPD, there is considerable evidence that hereditary factors impact the occurrence of COPD in response to smoking.[27]

COPD Etiology:

Table 1: Development of COPD. The factors shown contribute to the development of airflow limitation and eventual to clinical manifestations of COPD.[24]

Exposure to tobacco smoke	Poor lung growth and development	Outdoor pollution
Indoor air pollution from indoor fire pits and stoves	Alpha-1 antitrypsin deficiency	Occupational pollution
Lower socioeconomic status	Female gender	Aging
Respiratory infections	Asthma and hyper-reactivity of airway	

Epidemiological studies have evaluated various causes which can produce haze, for example, traffic-related air pollution, household air pollution, occupational exposure, and so on.Gan et al.[28] investigated the associations of long-term exposure to elevated traffic-related air pollution and wood smoke pollution and reported that an interquartile range (IQR) elevation in black carbon concentrations (0.97×10−5/m3, equivalent to 0.78 μg/m3 elemental carbon) was connected to a 6% [95% confidence interval (CI): 2–10%] increase in COPD

hospitalizations and a 7% (0–13%) increase in COPD mortality after adjustment for covariates. Exposure to higher levels of wood smoke pollution was connected to a 15% (2–29%) increase in COPD hospitalizations. Occupational risk factors are one of the leading causes of respiratory illnesses, accounting for 13% of all COPD causes. A cross-sectional assessment of brick kiln employees utilizing a questionnaire revealed that 22.4 % had a chronic cough, 21.2 % had chronic phlegm, 13.8 % had two or more incidents of breathing problems with wheeze, and 17.1 % had Chronic Bronchitis. 8.9 % of designated smoking workers had chronic bronchitis. According to a multivariate analysis, brick baking employees were more prone to develop chronic bronchitis.[29]

Pathophysiology:

The pathophysiology of chronic obstructive pulmonary disease (COPD) is complex which and can be attributed to multiple components: muco-ciliary dysfunction, airway inflammation, and structural changes, all contributing towards the development of airflow limitation, as well as an important systemic component.[30] It is characterised by increasing, non-reversible airflow limitation produced by two pathologic processes resulting from chronic inflammation: (1) narrowing of the smaller airways and [2] emphysematous destruction of lung parenchyma. Lung inflammation associated with an imbalance of proteinases and anti-proteinases and oxidative stress induced by noxious particles and gases contributes to the pathologic changes of COPD. The physiologic changes of COPD are associated with mucus hypersecretion, ciliary dysfunction, airflow limitation, pulmonary hyperinflation, gas exchange abnormalities, pulmonary hypertension, and cor pulmonale. However, the pathophysiology of COPD is complicated and largely undiscovered. This is complicated by the fact that there is heterogeneity of the disease, with some patients showing a predominant emphysema pattern,

whereas, in others, small airway disease predominates, although many patients have a mixed pattern.[31]

Clinical presentation:

The clinical manifestations of COPD include dyspnea, chronic cough (productive or non-productive), low exercise capacity, audible wheezing, and more frequent or longer-lasting bronchial infections; a further manifestation of advanced COPD is weight loss. The appearance of at least one of these manifestations associated with the risk factors (usually cigarette smoking) should arouse the suspicion of COPD.[32]

Diagnosis:

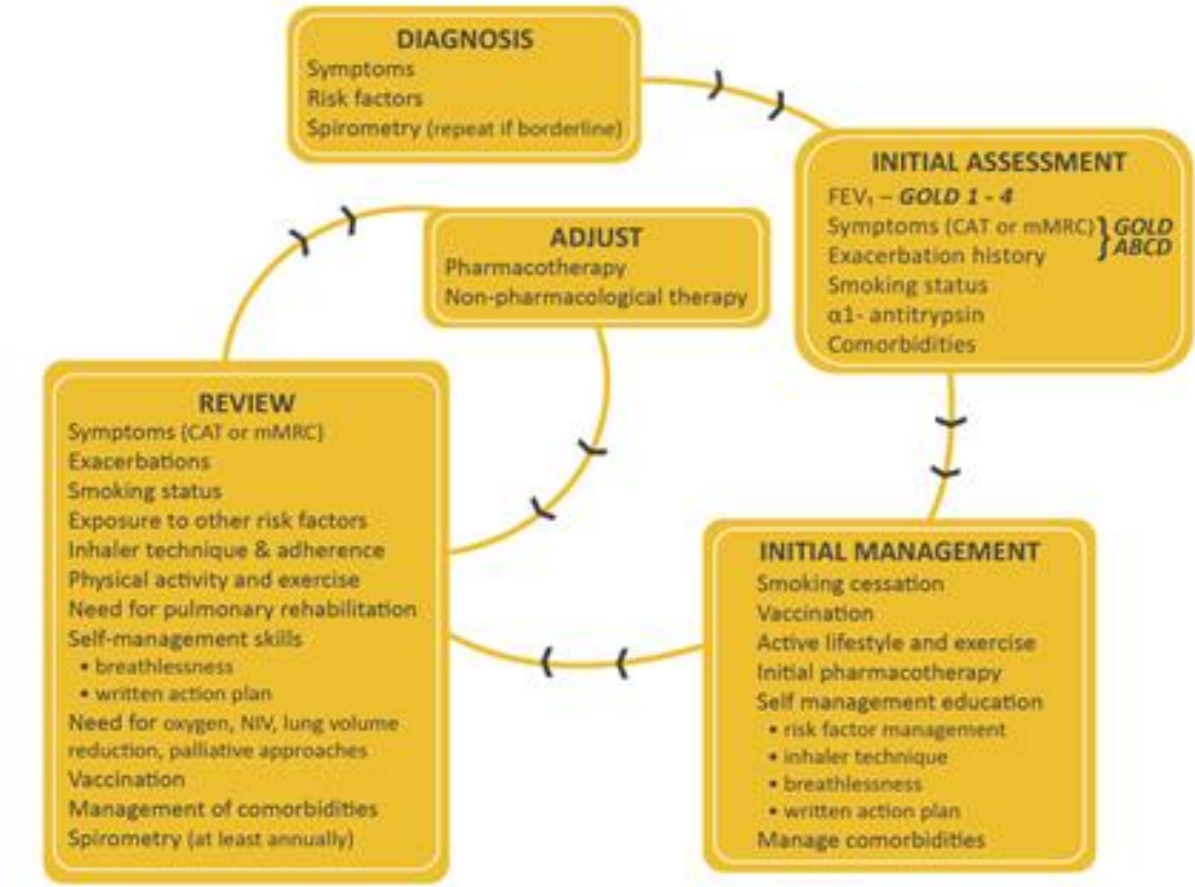
The current GOLD document recommends evaluating symptom burden (primarily dyspnea) and exacerbation history separately from airflow limitation. While spirometric measurements are required to make a diagnosis of COPD, the evaluation of respiratory symptoms is crucial for the therapeutic decision. The report also acknowledges that the most common respiratory symptoms, including dyspnea, cough, and/or sputum production, may be under-reported by patients.[2] The Improvement in health status in patients with chronic obstructive pulmonary disease (COPD) is one of the treatment objectives as recommended by the Global initiative for chronic Obstructive Lung Disease (GOLD) committee.[2] Health status can easily be measured in patients with COPD using the COPD Assessment Test (CAT). The COPD Assessment Test (CAT) contains eight items (cough, phlegm, chest tightness, breathlessness, limited activities, confidence leaving home, sleeplessness, and energy).[33] The GOLD 2018 report recommends a CAT score of 10 points or higher to classify patients with COPD as highly symptomatic.[2]

Complications:

Airflow obstruction has profound effects on cardiac function and gas exchange with systemic consequences. In addition, as COPD results from inflammation and/or alterations in repair mechanisms, the "spill-over" of inflammatory mediators into the circulation may result in important systemic manifestations of the disease, such as skeletal muscle wasting and cachexia. Systemic inflammation may also initiate or worsen comorbid diseases, such as ischemic heart disease, heart failure, osteoporosis, normocytic anemia, lung cancer, depression, and diabetes. Comorbid diseases potentiate the morbidity of COPD, leading to increased hospitalizations, mortality, and healthcare costs.[8]

Management:

Figure 1: Management of chronic obstructive pulmonary disease.[2]



FEV1 =forced expiratory volume in 1 second; CAT™=COPD Assessment Test™; mMRC=modified British Medical Research Council; GOLD=Global Initiative for Chronic Obstructive Lung Disease; NIV=non-invasive ventilation.

Association between anemia and COPD:

Anemia is defined by the World Health Organization (WHO) as hemoglobin (Hb) values of 12.0 g/dL in women and 13.0 g/dL in men. Normal Hb distribution, on the other hand, differs not just by gender but also by ethnicity and physiological health. Anemia is typically complex and is not a self-contained condition. The hematologic parameters, the underlying disease cause, and the patient history should all be addressed when classifying and diagnosing.[34] Anemia of chronic disease (ACD) is an immune-driven anomaly distinguished by continuously very low levels of circulating hemoglobin that has been observed in a variety of inflammatory disorders. COPD's systemic inflammation, which is now acknowledged as a characteristic, makes it a potential cause of ACD. Anemia, if prevalent in COPD, may exacerbate dyspnea and restrict exercise tolerance.[35]

Prevalence /incidence of anemia in COPD:

The prevalence of anemia in people with COPD is unknown, and it varies widely. This varies according to the way of analyzing (stable COPD or patients hospitalized for acute exacerbation), the tools used it to identify anemic subjects, and the definitions of anemia used. For the first time, John et al. revealed anemia prevalence in a steady COPD group. They discovered that 13 of 101 severe COPD patients (forced expiratory volume in one second [FEV1]37 2 percent expected) were anemic, indicating a 13 percent prevalence.[10] Anemia was shown to be prevalent in 31.6 percent of COPD patients in a case-control study. The proportion of patients with anemia was greater in COPD GOLD Stage 3 and 4 (82 percent),

with a substantial number of anemic patients aged 61–70 years, followed by 51–60 years.[36] According to the WHO criteria, the prevalence COPD patients diagnosed to have was 27 % in a cross-sectional study of 760 COPD patients.

A cohort of COPD exacerbation patients admitted to the intensive care unit with the diagnosis of early respiratory failure and requiring either invasive or noninvasive ventilation (NIV) disclosed anemia in 50 % of patients and no difference between sexes (49.4 percent of male and 52.2 percent of female patients were anemic; P=1.00). NIV failure was more common in anemic patients than in non-anemic patients (49 percent vs. 22.6 percent, respectively; P=0.001).[37]

A cohort of stable COPD patients reported just over 15% were anemic, and it was present in 12.6% males and 8.2% females.[13] In a retrospective cohort of adults with acute exacerbations of COPD admitted to the hospital, 9.8% had a diagnosis of anemia.[38] Anemia was present in 6.6% of the COPD patients, and while gender distribution was similar between anemia and non-anemia groups, elderly patients were more frequent in the anemic group.[39] The prevalence of anemia was 18.5% and was not influenced by the GOLD stage in a retrospective study from France.[40]

A retrospective study investigating the prevalence of hemoglobin disorders in a cohort of 100 patients with stable, moderate to severe COPD (II to IV GOLD classification) identified 31 % patients with anemia while only 15 % had polycythemia. Anemia was more frequent in male patients.[41]

The study of the prevalence of anemic patients with acute syndromes may overstate the true number of cases; yet, the frequency of anemia during AECOPD is also an important problem, as it indicates a state of heightened systemic inflammation, which may alter hemoglobin levels in COPD. In a study of 107 consecutive AECOPD patients, 43.9 percent were found to be anemic on admission.[12] The overall frequency of anemia in the community was 30.9 percent in a study sample of 6,969 AECOPD patients. Anemia was seen in 39.1 percent of hospitalized men and 23.8 percent of admitted females, respectively.[42]

Risk factors for the development of anemia in COPD:

It must be noted that factors other than inflammation can be responsible for anemia in COPD patients. Besides the obvious comorbidities (e.g., gastrointestinal bleeding or folate deficiency), malnutrition can play a role and implement a vicious circle of inflammation. Tobacco smoking itself, probably through the associated oxidative stress, interferes with red cell production and with the effects of long-term oxygen therapy on this production.[43]

Renal impairment, which is highly prevalent in COPD, can lead to anemia by two different—and complementary—mechanisms. EPO is produced in the kidney, and impaired renal flow leads to disruption in EPO production in response to hypoxia.[44] Additionally, reduced renal clearance of hepcidin seen in patients with renal impairment leads to increased serum hepcidin levels, which limits iron availability for erythropoiesis.[45] Theophylline treatment was associated with decreased hematocrit in COPD patients, as compared to untreated controls with similar oxygen saturation.[46]

Pathophysiology:

COPD's main pathogenetic traits are oxidative stress and protease/antiprotease imbalance, which cause local airway inflammation and reorganization as well as chronic systemic inflammation.[47] Fiber is an essential micronutrient because it is involved in several aerobic metabolisms, including DNA synthesis, oxygen transport, cellular metabolism, and mitochondrial respiration.[48,49] Environmental sources of iron and other particles, on the other hand, can disturb and interfere with local iron homeostasis in the lung.[50] COPD is connected with genes related to iron metabolism, and exposure to cigarette smoking, air pollution, and other toxic chemicals have an influence on regulatory processes, potentially driving the pathogenesis of COPD.[50–52] These processes, however, are not restricted to the lung since inflammatory cytokines are produced and released during the course of COPD. Iron homeostasis can also be affected by them.[53,54]

As a result, inflammatory cytokines and increased expression of the master regulator of iron homeostasis, hepcidin, result in enhanced iron uptake and storage inside reticuloendothelial system cells. This causes functional iron deficiency (FID) and anemia of inflammation (AI), which are characterized by low circulation iron levels and consequently reduced metal availability for erythropoietic cells, but ferritin levels are normal or raised as a result of reticuloendothelial iron retention.[54]

Disease mechanisms which can potentially explain the increased occurrence of anemia in COPD patients:

Iron deficiency and inflammatory processes are two disease pathways that might explain the increased prevalence of anemia in COPD patients.[44] Several ideas were offered, for example, that the inflammatory load of COPD induced chronic disorder anemia owing to the actions of

IL-1 and TNF- (anemia in COPD), as well as CRP and IL-6.[10] This could be due to decreased RBC survival, dysregulation of iron homeostasis, and poor bone marrow erythropoietic response.[55] Nutritional deficiencies in COPD patients have been considered as a cause of anemia.[11] Tobacco use and its impact in oxidative stress also play a role in RBC synthesis.[43] Furthermore, the significance of comorbidities such as upper GI hemorrhage and folate insufficiency in COPD patients was hypothesized; however, these were significantly associated to smoking.[56]

Impact/consequences of Anemia on COPD:

In COPD, iron deficiency could be particularly deleterious since hypoxemia is common, is a marker of disease severity, and is important in the pathophysiology and extrapulmonary manifestations of the condition.[57] Pulmonary hypertension is considered one of the strongest predictors of decreased survival in COPD and is significantly driven by hypoxia[58]; it may also be augmented by iron deficiency.

Patients with iron deficiency are more hypoxemic even though they dint have significantly worse airflow limitation. This unexpected daytime and nocturnal hypoxemia are due to reduced iron levels as iron is a cofactor in a key cellular pathway that senses hypoxia and modulates levels of the hypoxia-inducible factor family of transcription factors.[59] In COPD, hypoxemia is most commonly caused by a ventilation/perfusion (V/Q) mismatch. Aside from a V/Q mismatch, low oxygen content owing to anemia may play a role in COPD progression, and oxygenation and compensatory mechanisms may not be enough to offset the consequences. As a result, anemic COPD patients may have greater indications for long-term oxygen treatment (LTOT) than those who do not have anemia.[60]

Anemia was shown to be one of the most important independent variables connected to an elevated risk of readmission in people with COPD; anaemic patients had a 25% higher risk of readmission than non-anemic patients..[38] Anemia has been correlated with poor functional outcomes, higher healthcare utilization, and expenses, and increased mortality in COPD patients, according to a review of the research publications.[61]

Management of Anemia in COPD:

Currently, data are limited on the effects of either treating anemia or utilizing iron supplementation in COPD patients having anemia. If iron supplementation might therefore reverse some of the declines that patients experience, then routine screening and treatment may turn out to be an effective, simple, and inexpensive intervention.[61] Randomized trials targeted at both identifying and treating anemia would be required to provide further insight into the importance of anemia and whether improving hemoglobin would impact these outcomes. Until such trials are conducted, it is difficult to know whether screening for or treating anemia would be of value to patients with COPD and should be incorporated in clinical practice guidelines. Anemia is a treatable disorder, and treating anemia in chronic diseases other than COPD has been linked to improved health. There are presently no clinical trials on the treatment of anemia in COPD patients; however, it has been shown in research papers that blood transfusion assisted in weaning off mechanical ventilation and improved both ventilation rate and effort of breathing. Intravenous iron and erythropoiesis-stimulating medications were used to improve hemoglobin and dyspnea. The etiological therapy of anemia is prescribed in COPD patients.[62]

Complications in COPD subjects with Anemia vs. COPD subjects without anemia:

In a cross-sectional study, the RBC count of anemic patients was significantly lower than non-anemic group (4.3 ± 0.5 vs. 5.02± 0.8 ×106/µL; p < 0.001). Erythropoietin levels in the anemic group were significantly higher than in the non-anemic group (16.33±2.43 vs. 10.22 ± 2.67 mu/ml; p < 0.001), and there was a important inverse correlation of hemoglobin vs. erythropoietin (r= −0.8).[63] Hospital mortality in the patient having anemic group was 52.8 percent, while it was 20.8 percent in the non-anemic group (P=0.001). In a logistic regression investigation of hospital mortality, anaemia and NIV failure were revealed to be independent predictors of death..[37]

Anemia (Hb 13 g/dl) and past exacerbations (3.5 exacerbations) were found to be independent predictors of death after the 1st year in patients hospitalized for AECOPD, according to a study of 117 AECOPD patients.[64] Anemia was substantially related to increased dyspnea, and there was a link between breathlessness worsening (as measured by the mMRC score) and anemia, with 45 percent of anemic patients having mMRC breathlessness Grade 3 or 4. In a case-control study, only 27% of non-anemic patients had mMRC dyspnea Grade 3 or 4.[36]

CRP levels in anemic patients were greater than in non-anemic patients, and serum CRP concentrations were negatively associated to hemoglobin levels (r = 0349, p 0.0001). In comparison to non-anemic individuals, anemic patients experienced more severe airflow blockage.[63] Although the correlantion was not statistically significant, pulmonary function measures (FEV1, FVC, and FEV1/FVC) were lower in COPD patients having anemia compared to COPD patients not having anemia and patients with anemia had more severe COPD in terms of post-bronchodilator FEV1 percent.[36] Anemic individuals had a higher

hospital admission rate, a longer hospital stay, and a higher death rate than non-anemic patients, according to a study of stable COPD patients.[13]

Anemic people were found to be older, more likely to be women, and had a higher comorbidity load than non-anemic people. Numerous regression modeling found that multiple independent variables were linked to an increased probability of readmission in COPD patients. Anemia was one of the most serious hazards, with anemic patients having a 25% greater risk of readmission than non-anemic patients (odds ratio [OR], 1.25; 95 percent confidence interval [CI], 1.21–1.29).[38] Patients who were anemic had a higher Charlson comorbidity score and a lower body mass index. The total mortality rate in the anemia group was 46.5 percent, while it was 32.1 percent in the non-anemia group. The average period of follow-up was 100.036.5 months (87.739.9 in anemia vs. 100.836.1 in non-anemia).[39]

SOD, Catalase, and GPx levels were considerably lower in the anemic COPD group compared to the non-anemic COPD group. MDA (an indirect measure of free radicals) levels were substantially greater in the anemic COPD group than in the non-anemic COPD group. Anemic COPD patients exhibit abnormal Hemoglobin, MCV, and MCHC values.[65] In a study to investigate the effect of anemia on dyspnea and exercise capacity in COPD patients using the cardiopulmonary exercise test (CPET), anemic COPD patients had higher dyspnea scores and lower peak oxygen uptake (Vo2), lower work rate, and peak Vo2/heart rate compared to COPD patients without having anemia . There was also a tendency toward a lower anaerobic threshold in impoverished COPD patients.[35]

For anemic individuals, oxygen-carrying capacity may be affected by hemoglobin levels, and oxygen delivery is critical for the maintenance of oxidative metabolism. Anemia had a deleterious influence on gas exchange and exercise tolerance in individuals with severe

COPD. The diffusing capacity of the lungs for carbon monoxide adjusted by Hb was considerably lower in anemia patients compared to non-anemic individuals. Overall, anemia had a detrimental influence on exercise capacity.[66] Anemia does not produce more pronounced hypoxemia following exercise in COPD patients, according to prospective research involving a control group. However, in anemic COPD patients, the observed Spo2 level was considerably lower than the Sao2 level after exercise.[60]

Anemic COPD patients were older, had a lower BMI (P0.001), lower blood cholesterol level (P=0.001), lower serum albumin level (P0.001), and a shorter 6-minute walking distance (P=0.046) than non-anemic COPD patients.[67] The anemic COPD group had a Charlson score of 5.42 against 4.11.5 (p0.01) when compared to the non-anemic COPD group. At 3 years, mortality in COPD patients having anemia was 36% versus 7% in non-anemic patients presenting (p0.05). The existence of logistic regression anemia was found to be the most crucial predictor of death after three years.[40] When looked with those with anemia, critically sick COPD patients who required intrusive mechanical ventilation for acute respiratory failure but did not have anemia on admission had a greater overall survival.[68]

MOST RELEVANT STUDIES:

Gadre et al.[68] **(2020**) examined the association of anemia (hemoglobin <12 g/dL) and 90-day and overall mortality in patients with COPD having acute respiratory failure requiring invasive mechanical ventilation in a retrospective study. The 90-day mortality, though lower in the non-anemic patients compared to the patients with anemia, was not statistically significant (35.6% vs 44.9%; hazard ratio [HR] [95% confidence interval; CI] = 1.16 [0.91 - 1.48], P = .22). The overall mortality was lower in the non-anemic patients compared to patients with anemia (HR [95% CI] = 0.68 [0.55-0.83], P < .001). There was a 5% decrease in

risk of death for every unit increase in hemoglobin (P = .01). There was no correlation in terms of both 90-day and overall mortality in patients who received blood transfusions compared to patients who dint receive any transfusion.

Miranda Machado et al.[69] **(2019)** conducted research to determine the correlation between anemia and the occurrence of outcomes associated to chronic obstructive pulmonary disease exacerbations. At the outset of the study, 43.9 percent of the participants were anemic. Relapses occurred at the rate of 63 percent in group of anemic vs. 55.5 percent in the non-anemic group. The cumulative incidence of exacerbation recurrence was 30.4 percent in group of anemic vs. 38.8 percent in the non-anemic group. Hospitalizations for exacerbations were 30.4 percent in the anemic group and 33.3 percent in the non-anemic group. The study concluded that there is no significant correlation between anemia and the incidence of chronic obstructive pulmonary disease exacerbations, the incidence of recurrence of the first exacerbation, the rate of hospitalizations for chronic obstructive pulmonary disease exacerbations, and the recurrence time of the first exacerbation of chronic obstructive pulmonary disease exacerbation.

Pandey et al.[36] **(2018)** Case-control study of 150 COPD patients was conducted to determine the prevalence of anemia and its relationship with various other parameters. Anemia was seen in 31.6 percent of COPD patients. The mean hemoglobin level in group of anemic was 11.04 1.1 g/dl, while it was 13.9 0.8 g/dl in the non-anemic group. Anemia was shown to be substantially linked with greater dyspnea as measured by the modified Medical Research Council grade (P = 0.04). The study revealed that anemia is a comorbidity in COPD patients and is related with a poor quality of life and high mortality in the form of exacerbations and hospitalizations.

Park et al.[39] **(2018)** Using a large population-based database, researchers investigated whether anemia is associated with long-term mortality in COPD patients. A number of 7,114 COPD patients were identified. The average age was 65.09.3 years, and 62.9 percent of the population was male. Anemia was found in 469 of the 469 individuals (6.6 percent). The total mortality rate in the anemia groups was 46.5 percent, compared to 32.1 percent in non-anemia groups (p0.001). Anemia had a hazard ratio of 1.31 (95 percent CI, 1.11–1.54) for death. The hemoglobin level is associated strongly with death in anemic individuals. They determined that anemia was linked to an elevated risk of long-term COPD mortality and that even moderate anemia was associated with a dramatically higher risk.

Copur et al.[60] **(2018**) demanded to discover if anemia caused more evident hypoxia by lowering total oxygen content after exercise in COPD patients having anemia. After exercise, the oxygen content in the group of anemic was lower (15.22 1.28 versus 15.07 1.22) but not significantly lower. There was no reduction in oxygen content following exercise in the non-anemic group (18.83 1.41 vs. 18.9 1.37). Interestingly, in anemic individuals with COPD, the Spo2, but not the Sao2, was considerably reduced after exercise (93.46 percent 5.06 percent versus 88.20 percent 6.35 percent before and after exercise, respectively). The analysis revealed that anemia did not result in more pronounced hypoxemia following exercise in COPD patients. However, following activity, the measured Spo2 levels in COPD patients having anemia were considerably lower.

Waseem et al.[65] **(2017)** evaluated oxidant-antioxidant imbalance in anemic and non-anemic COPD patients. There was a substantial difference in Hb in the mild, moderate, and severe/very severe COPD groups based on disease severity in the anemic COPD group. In the

same group, there were no significant differences in MCV and MCHC. The findings were similar in the non-anemic mild, moderate, severe/very severe COPD groups. In both the anemic and non-anemic COPD groups, substantial differences in Hb and MCHC were identified in both males and females. The study found that anemic COPD patients had an oxidant-antioxidant imbalance. Anemia is a co-morbidity in COPD, and it is likely to impact the disease's treatment outcome. The presence of anemia has a detrimental impact on patients' quality of life. As a result, it is critical to detect anemia in COPD patients.

Oh, et al.[67] **(2017)** tried to determine the predictive impact of anemia in the clinical course of COPD and to study the parameters associated with serum hemoglobin levels in COPD. Anemic COPD patients were older, had a lower BMI (P0.001), lower blood cholesterol level (P=0.001), lower serum albumin level (P0.001), and a shorter 6-minute walking distance (P=0.046) than non-anemic COPD patients. Anemia was shown to be an independent risk factor for mortality in COPD, while age, lower serum albumin level, and lower BMI were found to be independent variables related with lower serum hemoglobin levels.

Ergan et al.[37] **(2016)** undertook research to see if the presence of anemia increased the risk of mortality in patients suffering from acute respiratory failure owing to severe COPD exacerbations. Anemia was found in 50% of the patients, and 36.8 percent died during their hospital stay. When compared to non-anemic patients, inpatient mortality in the group of anemic was considerably greater (20.8 percent vs. 52.8 percent, respectively; P=0.001). In this group, anemia was not related with long-term survival. According to the findings of the study, anemia may be a risk factor for hospital mortality in severe COPD exacerbations needing mechanical ventilation.

AMenou et al.[40] **(2016)** The researchers evaluated 151 COPD patients retrospectively and discovered that the frequency of anemia was 18.5 percent, regardless of the GOLD stage. Anemia in COPD patients is easy to detect, is frequently related with co-morbidities, notably cardiovascular, and is a significant predictor of death at three years. A non-significant tendency toward increased expenditures, particularly through hospitalizations, was detected, but this has to be validated by a larger medico economic investigation.

Pirotte et al.[41] **(2016**) A retrospective research looked at the incidence of hemoglobin abnormalities in a group of 100 people with stable, mild to severe COPD (II to IV GOLD classification). They discovered that 31% of the participants had anemia, but only 15% had polycythemia. Male patients had a higher incidence of anemia. Hemoglobin and CRP levels had a negative connection (R=-0.56, p less than 0.0001). COPD patients with anemia had a greater risk of exacerbation hospitalizations in the preceding year than those with polycythemia (p inferior to 0.05). Anemia is a common comorbidity in COPD; it is linked to systemic inflammation and an increased risk of hospitalization for exacerbation.

Toft-Petersen et al.[42] **(2016)** A register-based cohort of patients hospitalized to Danish hospitals for the first time for acute COPD exacerbations was investigated. Hemoglobin levels were less than 130 g/L in 39% of males and less than 120 g/L in 24% of females. In-hospital death rates were 11.6 percent and 5.4 percent for individuals with hemoglobin levels below or beyond these thresholds, respectively. After discharge, the hazard ratio (HR) for men with hemoglobin 120 g/L was 1.45 (95 percent confidence interval [CI] 1.22–1.73), adjusted HR 1.37 (95 percent CI 1.15–1.64), compared to hemoglobin 130 g/L. Females with hemoglobin 110 g/L had an HR of 1.4 (95 percent CI 1.17–1.68) compared to hemoglobin 120 g/L, with an adjusted HR of 1.28 (95 percent CI 1.06–1.53). In conclusion, low hemoglobin

concentrations are frequent in COPD patients with acute exacerbations and predict long-term mortality.

Nickol et al.[59] **(2015**) conducted observational research to investigate the frequency of iron deficiency in COPD and its relationships with clinical phenotypic differences. When compared to controls, individuals with COPD had a higher rate of iron insufficiency (18%). According to the findings, the non-anemic iron shortage is frequent in COPD and appears to be caused by inflammation. Iron deficiency is associated with hypoxemia, an increase in exacerbations, and perhaps decreased exercise tolerance, all of which are indicators of a bad prognosis. Given its efficacy in other chronic illnesses, intravenous iron treatment should be investigated as a potential therapeutic option for COPD.

Guo et al.[66] **(2015)** this study was done to look at the possible links between anemia in patients with severe COPD (GOLD stage III) and pulmonary function at rest, exercise capacity, and ventilatory efficiency is utilizing pulmonary function testing (PFT) and cardiopulmonary exercise testing (CPET). The diffusing capacity for carbon monoxide (DLCO) adjusted by Hb was substantially lower in the anemia group (15.31.9) mL/min/mm Hg) than in the non-anemia group (17.21.1) mL/min/mm Hg) (p0.05). In patients having severe COPD, anemia has a deleterious influence on gas exchange and exercise tolerance. The quantity of oxygen intake is connected to the decrease in the amplitude of Hb levels.

Parveen et al.[15] **(2014)** conducted a cross-sectional investigation for the determination of prevalence of COPD patients having anemia and its possible influence on COPD morbidity. A sum of 36 cases (20 men and 16 females) with anemia were found, yielding an 18% prevalence. The normocytic normochromic form of anemia was seen in 32 (88.89%) of the

patients, whereas the rest exhibited normocytic hypochromic anemia. Most of the patients were in GOLD stage 11 with low serum iron, transferrin saturation, and TIBC. Erythropoietin levels in COPD patients having anemia were substantially higher than in COPD patients not having anemia. The following parameters were substantially linked with anemia: number of COPD exacerbations, frequency of hospital admissions, BMI, and erythropoietin levels. The research demonstrates that anemia is occurring frequently in COPD patients and was related with greater morbidity in the form of acut exacerbations and hospitalizations. Correcting anemia in those patients may benefit their clinical outcomes.

Silverberg et al.[12] **(2014)** conducted a study to determine the prevalence and treatment of anemia and iron deficiency (ID) in patients hospitalized for COPD exacerbation, as well as to investigate the hematological responses and degree of dyspnea before and after anemia correction with subcutaneous Erythropoiesis Stimulating Agents (ESAs) and intravenous (IV) iron therapy, in ambulatory anemic patients with both COPD and chronic kidney disease. On admission, 43.9 percent of patients hospitalized with AECOPD were determined to be anemic. ID was discovered in 91.7 percent of anemic ambulatory individuals. The ESAs and IV-iron therapy significantly enhanced hemoglobin (Hb), hematocrit (Hct), and VAS scale ratings. According to the research, correcting ID in COPD patients with ESAs and IV iron can help with anaemic ID and breathlessness.

Comeche Casanova et al.[70] **(2013)** Anemia prevalence was reported to be 6.2 percent in research to assess the prevalence of anemia in individuals with stable COPD. The study found that COPD associated with anemia was less common in their study group than in previous studies and that it was linked to specific clinical and inflammatory variables.

Boutou et al.[13] **(2013)** The researchers looked at the potential link between anemia and survival in a group of stable COPD outpatients. With Hb 13 g/dl, 15.6 percent were anemic. The median survival duration differed considerably between anemic [68.7 (18.1–91.5) months] and non-anemic patients [79.8 (57.5–98.4) months, p = 0.035]. Anemia [hazard ratio (HR) 1.87, 95 percent confidence interval (CI) 1.06–3.29], age (HR 1.08, 95 percent CI 1.04–1.12), and FEV 1 percent expected (HR 0.94, 95 percent CI 0.92–0.97) were independent predictors of death in the overall population. The study found that anemia is independently related to survival in stable COPD outpatients and proposed that it be treated as a categorical feature in future scoring systems.

Zavarreh et al.[63] **(2013)** In a cross-sectional investigation, researchers looked at the correlation between anemia and the severity of COPD. The overall frequency of anemia was 27%, and there was no relationship between the severity of COPD and anemia. COPD patients had a significant rate of anemia. Anemia can exacerbate the symptoms of COPD. Thus, treating anemia may enhance these individuals' quality of life. Further research is needed to determine the actual incidence of anemia and its physiologic implications in COPD patients.

Ozyilmaz et al.[71] **(2013)** conducted a study to assess the possibly modifiable triggering variables of frequent severe exacerbations necessitating hospitalization in COPD Hematocrit 41 percent, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker use, positive gastro-oesophageal reflux disease symptoms, poor adherence to inhaled therapy/regular outpatient follow-up visits, and FEV1 50 percent were independent predictors of frequent severe exacerbations, according to multivariate analysis. The risk of readmission within two months after hospital release was 39.3 percent. Poor adherence to inhaled

therapy/regular outpatient follow-up visits, serum hematocrit 41%, and FEV1 50% were independent risk factors for readmission. The study suggested that COPD patients with frequent exacerbations should be thoroughly examined for modifiable confounding risk factors, independent of low lung function, in order to reduce exacerbation frequency and the associated poor prognosis.

AK et al.[35] **(2011)** Using cardiopulmonary exercise testing, researchers evaluated the incidence of chronic disease anemia (ACD) in COPD patients and its influence on dyspnea and exercise capacity (CPET). ACD was detected in 29 individuals, representing a 10.24 percent frequency; the degree of anemia was typically modest (mean Hb: 12.19 0.66 g/dl). According to the study, ACD affects around 10% of stable COPD patients and has a deleterious influence on dyspnea and circulatory efficiency during exercise.

LACUNAE IN LITERATURE:

Anemia is a common comorbidity in COPD patients, worsening their outcome in terms of acute exacerbations and hospitalizations. There haven't been many studies on the occurrence of anemia and its impact on the complications of COPD. Anemia is frequently seen in developing countries such as India; however, there has been relatively few research on its frequency in COPD patients. This study is an attempt to find the occurrence of anemia and its impact on the complications of COPD patients in the Indian context.

MATERIALS & METHODS

MATERIALS & METHODS:

Study site: This study was conducted in the Department of General Medicine at Sri Devaraj Urs Academy of Higher Education and Research, Tamaka, Kolar- 563101.

Study population: All the eligible patients of COPD undergone in the Department of General Medicine at Sri Devaraj Urs Academy of Higher Education and Research College were considered as the study population.

Study design: The current study was a Case-Control study.

Sample size: The sample size calculated using the below formula came to 36 in each group.

The formula used is:

$$n = \frac{\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)^2}{[FZ(\rho_1) - FZ(\rho_0)]^2} + 3$$

$$FZ(\rho_1) = \frac{1}{2}\ln\left[\frac{1+\rho_1}{1-\rho_1}\right] \qquad FZ(\rho_0) = \frac{1}{2}\ln\left[\frac{1+\rho_0}{1-\rho_0}\right]$$

Where,

ρ_0 : Population correlation coefficient

ρ_1 : Sample correlation coefficient

$Z_{1-\alpha/2}$: Desired confidence level

$1-\beta$: Power

Sampling method: All the eligible subjects were recruited into the study consecutively by convenient sampling until the sample size was reached.

Study duration: The data collection for the study was conducted between January 2020 to December 2021.

Inclusion Criteria:

GROUP A: - COPD WITH ANEMIA

1. Age above 18 years.
2. All patients diagnosed with COPD.
3. COPD diagnosis was diagnosed, according to the GOLD criteria, by the presence of a ratio of forced expiratory volume in 1 s (FEV1) to the forced vital capacity of <0.7.
4. Anemia (hemoglobin levels <13g% in males and <12g% in females).

GROUP B: - COPD WITHOUT ANEMIA

1. Age above 18 years.
2. All patients diagnosed with COPD.
3. COPD diagnosis was diagnosed, according to the GOLD criteria, by the presence of a ratio of forced expiratory volume in 1 s (FEV1) to the forced vital capacity of <0.7.
4. Hemoglobin levels >13g% in males and >12g% in females).

Exclusion criteria: Patients with

- MALIGNANCY
- DIABETES MELLITUS
- HIV
- LONG TERM IMMUNOSUPPRESSIVE DRUGS USAGE
- ACUTE BLOOD LOSS
- CHRONIC ALCOHOL ABUSE
- PRIMARY CAUSES OF HEART FAILURE
- RENAL IMPAIRMENT.

Ethical considerations: The study was approved by the institutional human ethics committee. The informed consent was taken from all the participants, and only those participants willing to sign the informed consent were included in the study. The risks and benefits involved in the study and the voluntary nature of participation were explained to the participants before obtaining consent. The confidentiality of the study participants was maintained.

Data collection tools: All the relevant parameters were documented in a structured study proforma.

Methodology:

All the eligible patients of COPD visiting the Department of General Medicine and the Department of Pulmonology at Sri Devaraj Urs Academy of Higher Education and Research College will be considered as the study population. After taking informed consent, a thorough history is taken, physical examination and investigations will be done to rule out exclusion criteria and detect other comorbidities. Then, the selected patients who satisfy inclusion criteria will be divided into two groups. Group A: COPD with anemia and group B: COPD without anemia. Later patient will undergo Pulmonary function test (spirometry) will be done and FEV1/FVC ratio was taken. FEV1/FVC < 0.7 is required to make a diagnosis of COPD, and patients are classified according to GOLD 2018 criteria. Evaluation of right ventricle will be done by 2D-ECHO. Other complication like pneumothorax, pleural effusion, cardiac complication, acute infective exacerbation will be looked for.

Our study requires investigations such as following investigations will be done on all the patients in the study group.

- CBC WITH PERIPHERAL SMEAR
- PFT
- RFT

- HIV
- RBS
- ECG
- CHEST XRAY
- 2D-ECHO
- OTHER INVESTIGATIONS WHERE CLINICALLY WARRANTED.

STATISTICAL METHODS:

CBC parameters, investigation parameters, vital signs parameters were considered as primary outcome variables. The study group (COPD with anemia Vs. COPD without anemia) was considered as a primary explanatory variable. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Non-normally distributed quantitative variables were summarized by the median and interquartile range (IQR). Data was also represented using appropriate diagrams like bar diagrams, pie diagrams. All Quantitative variables were checked for normal distribution within each category of an explanatory variable by using visual inspection of histograms and normality Q-Q plots. Shapiro-Wilk test was also conducted to assess normal distribution. Shapiro Wilk test p-value of >0.05 was considered as a normal distribution. For normally distributed Quantitative parameters, the mean values were compared between study groups using an independent sample t-test (2 groups). Categorical outcomes were compared between study groups using the Chi-square test /Fisher's Exact test (If the overall sample size was < 20 or if the expected number in any one of the cells is < 5, Fisher's exact test was used). P-value < 0.05 was considered statistically significant. Data were analyzed by using co-Guide software, V.1.03.[72]

OBSERVATIONS AND RESULTS

Results:

A total of 80 subjects were included in the final analysis.

Table 2: Descriptive analysis of study group in the study population (N=80)

Study Group	Frequency	Percentages
COPD with anemia	40	50.00%
COPD without anemia	40	50.00%

Among the study population, 40(50%) participants were COPD with anemia group, and 40(50%) participants were COPD without anemia group. (Table 2)

Table 3: Comparison of mean of baseline characteristics between study group (N=80)

Parameter	Study group (Mean± SD)		P-value
	COPD with anemia (N=40)	COPD without anemia (N=40)	
Age (in years)	62.6 ± 9.43	61.4 ± 6.99	0.520
Height (in cm)	171.63 ± 5.51	172.58 ± 5.24	0.432
Weight (in kg)	65.28 ± 6.03	65.08 ± 5.92	0.881
BMI (kg/m2)	22.16 ± 1.8	21.86 ± 1.82	0.454
SBP (mmHg)	128.15 ± 5.86	131.08 ± 8.56	0.078
DBP (mmHg)	77.63 ± 6.36	77.93 ± 7.67	0.850
Pulse rate	79.2 ± 7.63	81.38 ± 6.74	0.181

There was statistically not significant difference in baseline characters like, age (p value 0.520), height (in cm) (p value 0.432), weight (in kg) (p value 0.881), BMI (in kg/m2) (p value 0.464), systolic blood pressure (in mmHg) (p value 0.078), diastolic blood pressure (in mmHg) (p value 0.850) and pulse rate (p value 0.181) between the study group. (Table 3)

Table 4: Comparison of gender between study groups (N=80)

Gender	Study Group		Fisher exact P-value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)	
Male	37 (92.5%)	38 (95%)	1.000
Female	3 (7.5%)	2 (5%)	

In COPD with anemia group, 37 (92.5%) were male participants, and 3 (7.5%) were female participants. In COPD without anemia group, 38 (95%) were male participants, and 2 (5%) were female participants. The association between gender and study group was statistically not significant (P-value 1.000). (Table 4 & Figure 2)

Figure 2: Stacked bar chart of comparison of gender between study group (N=80)

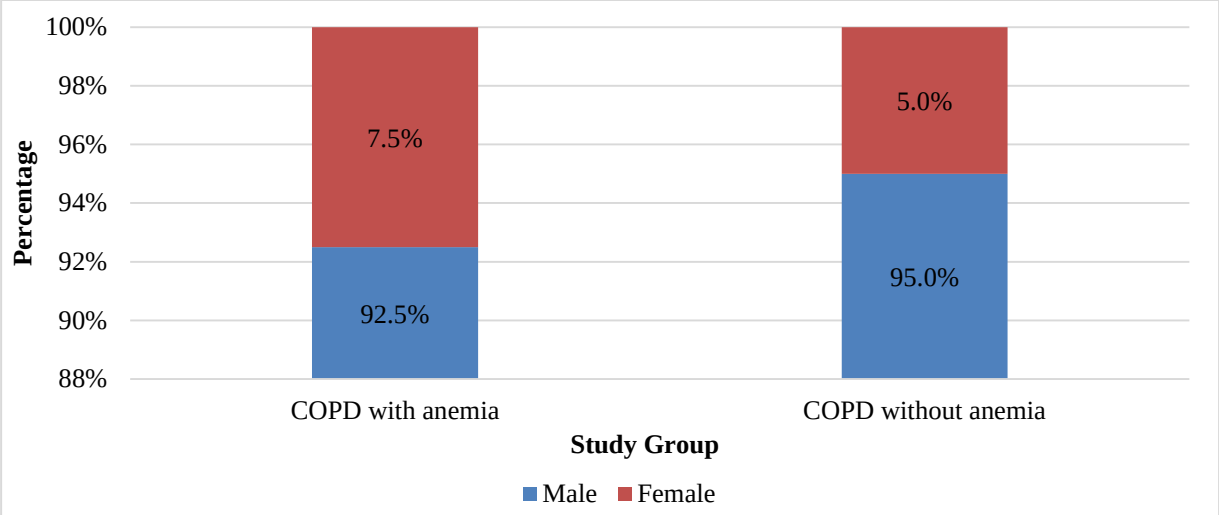


Table 5: Comparison of RS between study group (N=80)

RS	Study Group		Chi square	P-value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)		
Bilateral Rhonchi	23 (57.5%)	17 (42.5%)	3.684	0.298
Left Sided Absent Breath Sounds	8 (20%)	9 (22.5%)		
Right Sided Absent Breath Sounds	8 (20%)	9 (22.5%)		
Bilateral Crackles Present	1 (2.5%)	5 (12.5%)		

Out of 40 participants in COPD with anemia group, 23 (57.5%) had bilateral rhonchi, 8 (20%) had left and right-sided absent breath sounds for each, and 1 (2.5%) had bilateral crackles present. Out of 40 participants in COPD without anemia group, 17 (42.5%) had bilateral rhonchi, 9 (22.5%) had left and right-sided absent breath sounds for each, and 5 (12.5%) had bilateral crackles present. The association between RS and the study group was statistically not significant (P-value 0.298). (Table 5)

Table 6: Comparison of mean of CBC parameters between study group (N=80)

Parameter	Study group (Mean± SD)		P-value
	COPD with anemia (N=40)	COPD without anemia (N=40)	
Total Cell Count (/µL)	8785.43 ± 1994.65	8416.3 ± 2345.03	0.451
Polymorphs / Neutrophils (%)	60.45 ± 9.27	59.05 ± 9.88	0.515
Lymphocytes (%)	34.23 ± 6.42	33.03 ± 7.22	0.434
Eosinophils (%)	4.13 ± 1.54	3.83 ± 1.69	0.409
Monocytes (%)	6.25 ± 2.83	6.13 ± 2.67	0.839
Basophils (%)	0.7 ± 0.46	0.63 ± 0.49	0.484
Hemoglobin (g/dl)	9.42 ± 1.87	15.07 ± 1.46	<0.001
Red blood cells (x106/µL)	3.53 ± 0.85	4.15 ± 0.83	0.001
Packed Cell Volume (%)	44.45 ± 4.14	42.58 ± 4.24	0.049
Platelet Count (µL)	265856.4 ± 81565.03	256655.73 ± 71381.35	0.593
MCV (fl)	90.65 ± 6.08	91.9 ± 5.19	0.326
MCH (pg)	30.27 ± 3.26	31.17 ± 3.23	0.220
MCHC (%)	33.73 ± 1.58	31.98 ± 1.12	<0.001
Erythrocyte sedimentation rate (mm)	4.04 ± 0.5	4.27 ± 0.52	0.048

There was statistically not a significant difference in CBC parameters (like total Cell Count (/µL), Polymorphs / Neutrophils (%), Lymphocytes (%), Eosinophils (%), Monocytes (%), Basophils (%), Platelet Count (µL), MCV (fl) and MCH (pg)) between the study group. (p-

value >0.05). The mean hemoglobin of COPD with anemia group was 9.42 ± 1.87 g/dl, and COPD without anemia group was 15.07 ± 1.46 g/dl, the mean red blood cells of COPD with anemia group was 3.53 ± 0.85 (x106/µL) and COPD without anemia group was 4.15 ± 0.83(x106/µL), the mean Packed Cell Volume of COPD with anemia group was 44.45 ± 4.14 (%) and COPD without anemia group was 4.15 ± 0.83(%), the mean MCHC of COPD with anemia group was 33.73 ± 1.58 (%) and COPD without anemia group was 31.98 ± 1.12 (%), and the mean Erythrocyte sedimentation rate of COPD with anemia group was 4.04 ± 0.5 (mm), and COPD without anemia group was 4.27 ± 0.52 (mm), and the mean difference of CBC parameters between two groups was statistically significant (P-value <0.05). (Table 6)

Table 7: Comparison of mean various investigation parameters between study group (N=80)

Parameter	Study group (Mean± SD)		P-value
	COPD with anemia (N=40)	COPD without anemia (N=40)	
Urea (mg/dl)	26.53 ± 11.36	25 ± 9.22	0.512
Creatinine (mg/dl)	1 ± 0.46	1.07 ± 0.47	0.522
Uric Acid (mg/dl)	5.43 ± 1.51	5.87 ± 1.59	0.205
Blood Urea Nitrogen (mg/dl)	13.25 ± 4.19	12.58 ± 3.41	0.432
FVC	65.08 ± 4.2	66.63 ± 4.55	0.118
FEV1	37.93 ± 4.42	37.88 ± 4.15	0.959
FEV1/FVC	0.58 ± 0.07	0.57 ± 0.06	0.277
SpO2 (low)	97.05 ± 1.71	97.45 ± 1.58	0.281
Temperature	98.65 ± 2.36	99.85 ± 1.92	0.015
Respiratory Rate	21.6 ± 3.99	20.23 ± 4.7	0.163

There was statistically not a significant difference in investigations like Urea (mg/dl), Creatinine (mg/dl), Uric Acid (mg/dl), Blood Urea Nitrogen (mg/dl), FVC, FEV1,

FEV1/FVC, SpO2 (low) and Respiratory Rate between the study group. (p-value >0.05). The mean temperature of COPD with the anemia group was 98.65 ± 2.36, and COPD without anemia group was 99.85 ± 1.92; the mean difference of temperature between the two groups was statistically significant (P-value 0.015). (Table 7)

Table 8: ECG between study group (N=80)

ECG	Study Group	
	COPD With Anemia (N=40)	**COPD Without Anemia (N=40)**
Atrial Fibrillation	4 (10%)	5 (12.5%)
Multi Focal Atrial Tachycardia	5 (12.5%)	6 (15%)
Sinus Rhythm	30 (75%)	29 (72.5%)
Ventricular Premature Complex	1 (2.5%)	0 (0%)

No statistical test was applied- due to 0 subjects in the cells

In COPD with anemia group, 4 (10%) participants were of atrial fibrillation, 5 (12.5%) were Multi focal atrial tachycardia, 30 (75%) were Sinus Rhythm, and 1 (2.5%) were ventricular premature Complex. In COPD without anemia group, 5 (12.5%) participants were atrial fibrillation, 6 (15%) were Multi focal atrial tachycardia, and 29 (72.5%) were Sinus Rhythm. (Table 8)

Table 9: Comparison of chest x-ray between study group (N=80)

Chest X-Ray	Study Group	
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)
B/L Non-Homogenous Opacities	2 (5%)	5 (12.5%)
Emphysema	22 (55%)	16 (40%)
Left Sided Homogenous Opacities	4 (10%)	8 (20%)
Left Sided Non-Homogenous Opacity	0 (0%)	1 (2.5%)
Left Sided Pneumothorax	4 (10%)	0 (0%)
Right Sided Homogenous Opacity	5 (12.5%)	9 (22.5%)
Right Sided Non-Homogenous Opacity	0 (0%)	1 (2.5%)
Right Sided Pneumothorax	3 (7.5%)	0 (0%)

No statistical test was applied- due to 0 subjects in the cells

Out of 40 participants in COPD with anemia, 2 (5%) were bilateral non-homogenous opacities, 22 (55%) were emphysema, 4 (10%) were left sided homogenous opacities, 4 (10%) were left sided pneumothorax, 5 (12.5%) were right sided homogenous opacity and 3 (7.5%) were right sided pneumothorax. Out of 40 participants in COPD without anemia, 5 (12.5%) were bilateral non-homogenous opacities, 16 (40%) were emphysema, 8 (20%) were left sided homogenous opacities, 1 (2.5%) were left sided non-homogenous opacity, 9 (22.5%) were right sided homogenous opacity and 1 (2.5%) were right sided non-homogenous opacity. (Table 9)

Table 10: Comparison of acute exacerbation of COPD between study group (N=80)

Acute Exacerbation of COPD	Study Group		Chi-square	P-value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)		
Yes	17 (42.5%)	14 (35%)	0.474	0.491
No	23 (57.5%)	26 (65%)		

The difference in acute exacerbation of COPD between study groups was found to be insignificant, with a P-value of 0.491. (Table 10)

Table 11: Comparison of lung malignancy between study group (N=80)

Lung Malignancy	Study Group		Chi-square	P-value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)		
Yes	7 (17.5%)	7 (17.5%)	0.000	1.000
No	33 (82.5%)	33 (82.5%)		

The difference in lung malignancy between study groups was found to be insignificant, with a P-value of 1.000. (Table 11)

Table 12: Comparison of pleural effusion between study group (N=80)

Pleural Effusion	Study Group		Chi-square	P value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)		
Yes	9 (22.5%)	10 (25%)	0.069	0.793
No	31 (77.5%)	30 (75%)		

The difference in pleural effusion between study groups was found to be insignificant, with a P-value of 0.793. (Table 12)

Table 13: Comparison of pneumothorax between study group (N=80)

Pneumothorax	Study Group		Chi-square	P value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)		
Yes	7 (17.5%)	7 (17.5%)	0.000	1.000
No	33 (82.5%)	33 (82.5%)		

The difference in pneumothorax between study groups was found to be insignificant, with a P-value of 1.000. (Table 13)

Table 14: Comparison of COR pulmonale between study group (N=80)

Cor Pulmonale	Study Group		Chi-square	P-value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)		
Yes	13 (32.5%)	8 (20%)	1.614	0.204
No	27 (67.5%)	32 (80%)		

The difference in cor pulmonale between study groups was found to be insignificant, with a P-value of 0.204. (Table 14)

Table 15: Comparison of cardiac arrhythmias between study group (N=80)

Cardiac Arrhythmias	Study Group		Chi-square	P-value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)		
Yes	10 (25%)	11 (27.5%)	0.065	0.799
No	30 (75%)	29 (72.5%)		

The difference in cardiac arrhythmias between study groups was found to be insignificant, with a P-value of 0.799. (Table 15)

Table 16: Comparison of 2D echo between study group (N=48)

2D Echo	Study Group		Chi-square	P-value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)		
Normal	27 (67.5%)	32 (80%)	1.614	0.204
Ra RV Dilated	13 (32.5%)	8 (20%)		

In COPD with anemia group, 27 (67.5%) were normal 2D echo, and 13 (32.5%) were RA R V dilated. In COPD without anemia, 32 (80%) were normal 2D echo, and 8 (20%) were RA R V dilated. The association between 2D echo and the study group was statistically not significant (P-value 0.204). (Table 16 & Figure 3)

Figure 3: Cluster bar chart of comparison of 2d echo between study group (N=80)

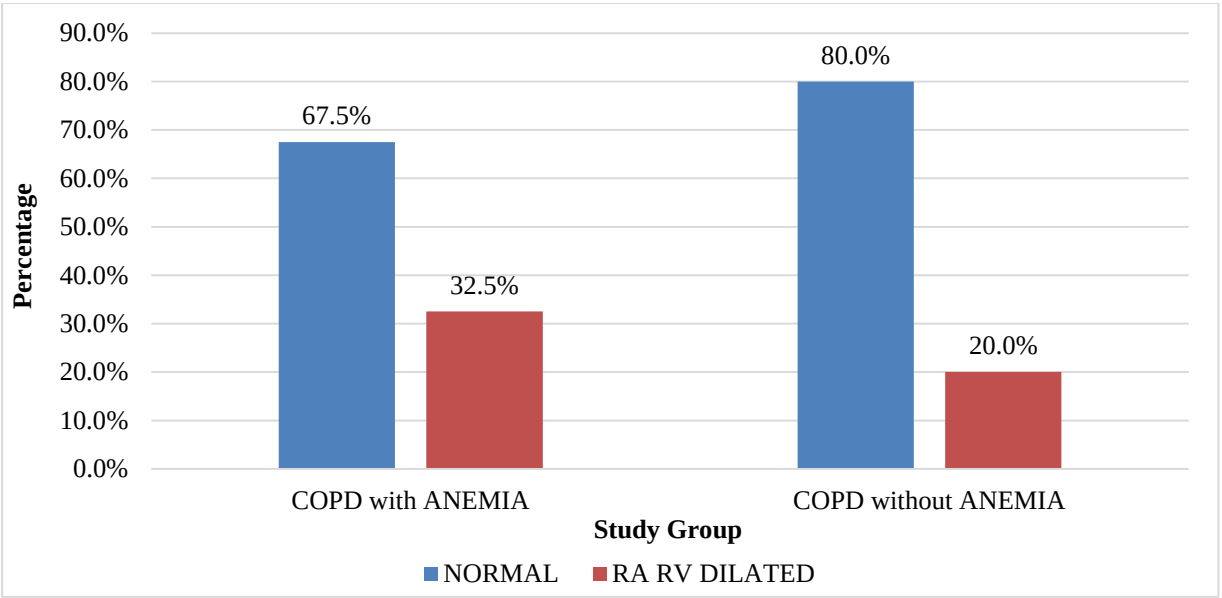
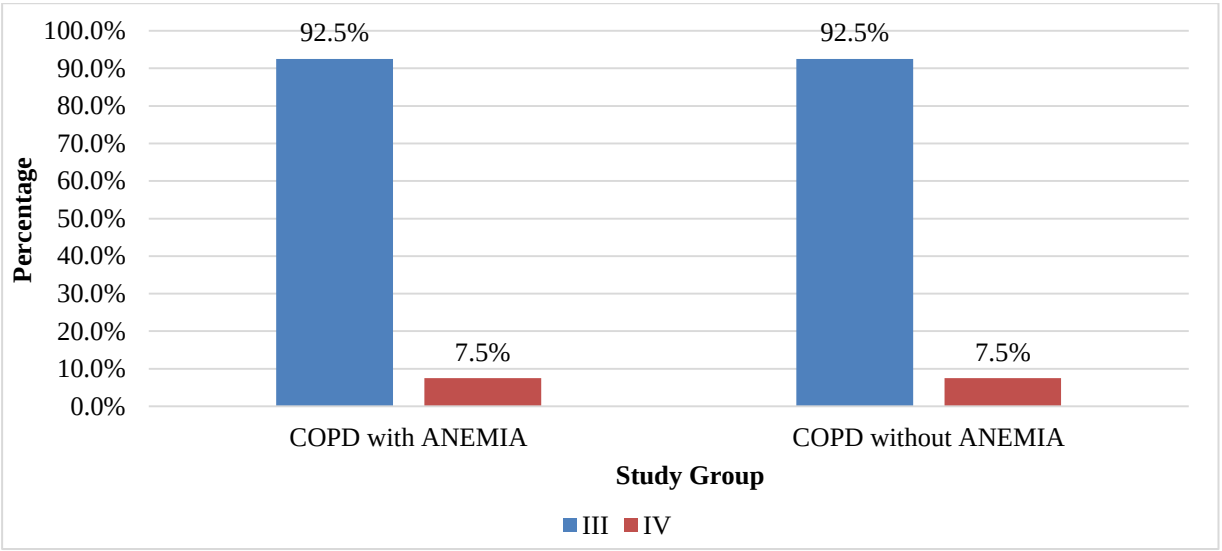


Table 17: Comparison of stages of COPD between study group (N=80)

Stages of COPD	Study Group		Fisher exact P-value
	COPD With Anemia (N=40)	COPD Without Anemia (N=40)	
III	37 (92.5%)	37 (92.5%)	1.000
IV	3 (7.5%)	3 (7.5%)	

In COPD with anemia group, 37 (92.5%) had COPD stage III, and 3 (7.5%) had COPD stage IV. In COPD without anemia group, 37 (92.5%) had COPD stage III, and 3 (7.5%) had COPD stage IV. The association between stages of COPD and the study group was statistically not significant (P-value 0.204). (Table 17 & Figure 4)

Figure 4: Cluster bar chart of comparison of stages of COPD between study group (N=80)



DISCUSSION

DISCUSSION:

COPD is a chronic inflammatory illness characterized by persistent airflow restriction, which is generally progressive and is accompanied by an enhanced chronic inflammatory response to toxic substances or gases in the airways and lungs. Exacerbations and comorbidities have an impact on the overall severity of COPD. Systemic effects and/or comorbidities are important events in the natural history of the disease because they have the potential to increase morbidity, economic burden and death.[17] Anemia is a condition that has recently acquired significance among persons with COPD. Two potential disease pathways that might explain the higher occurrence of COPD patients having anemia are iron deficiency and inflammatory mechanisms. Nonetheless, little is known about the significance of anemia, iron deficiency, and iron deficiency anemia in COPD patients, and as a result, these illnesses are undervalued in most COPD healthcare situations.

Patients attending RL Jalappa Hospital who meet the inclusion criteria were separated into two equal groups of 40 each, COPD with anemia and COPD without anemia. CBC parameters, investigation parameters, vital signs parameters were considered as primary outcome variables. COPD staging is done according to GOLD criteria. Anemia is defined as hemoglobin levels <13g% in males and <12g% in females. There are no statistically significant differences in the baseline characteristics between the study groups with regards to age, height, weight, BMI, systolic blood pressure, diastolic blood pressure, and pulse rate. The mean age in COPD with anemia group is 62.6 ± 9.43, and that in COPD without anemia is 61.4 ± 6.99. Oh, et al.[67] had an older age group in their cohort, with the mean age in the anemic group being 73.1±6.9 and the mean age in the non-anemic group 66.5±7.4. Compared to the non-anemic COPD group, the patients of the anemic COPD group were significantly older (P<0.001) and had lower BMI (P=0.005) in their study. A similar trend was noted in

Waseem et al.[65] study with the mean age of anemic, and non-anemic COPD group was 46.63±14.26 and 40.89±13.38 years, respectively (p<0.001). Their study had a much younger population compared to ours. The mean age of COPD patients having anemia was slightly more than COPD patients without anemia in Pandey et al.[36] studies, with a mean age in the anemic group being 57.2± 9.5 and in the non-anemic group 56.7 ± 9.33. Guo et al.[66] had a similar distribution to our study group, with a mean age in the anemic group at 61.32±6.03 and the non-anemic group at 60.82±7.13. COPD is a chronic condition that worsens over time. COPD is linked to advancing age, which is a well-known risk factor.[73] Inflammation is thought to have an effect on the pathogenesis of COPD, and there is a link between anemia and inflammation in chronic diseases.[74] Anemic patients were significantly older than non-anemic patients; mean (SD) age was 64.47±7.97 and 60.71±8.85 years in anemic and non-anemic patients, respectively in Parveen et al.[15] study.

There is a preponderance of male gender in both groups with 92.5% males in COPD with anemia group and 95% in COPD without anemia group. Overall, in the Anemic COPD group, 53.57% and 46.43% were male and female, respectively. In the non-anemic group, males and females were 71.43% and 28.57%, respectively, in Waseem et al.[65] studies. Similar to our study group, Oh et al.[67] and Guo et al.[66] studies also had a preponderance of males in both groups with 96.6% in the anemia group and 84.4% in the non-anemic group and 94% in the anemic group, and 91% in the non-anemic group respectively. There is no statistically significant difference in BMI (in kg/m2) (p-value 0.464) between the two groups in our study as was observed in Pandey et al.[36] study, although the mean BMI of anemic patients was lower than non-anemic patients. In Oh et al.[67] study, the patients of the anemic COPD group had lower BMI (P=0.005)' but again, Guo et al.[66] observations were similar to our study with 21.72±2.93 BMI in the anemic group and 22.18±2.15 in the non-anemic group.

Table 18: Mean age and BMI in anemic COPD and non-anemic COPD patients across studies.

Study	Anemic COPD group		Non-anemic COPD group	
	Mean age (years)	BMI (kg/m2)	Mean age (years)	BMI (kg/m2)
Current study	62.6 ± 9.43	22.16 ± 1.8	61.4 ± 6.99	21.86 ± 1.82
Pandey et al.[36]	57.2± 9.5	19.99±3.87	56.7±9.33	20.9±4.23
Oh et al.[67]	73.1±6.9	21.4±2.9	66.5±7.4	23.1±3.2
Waseem et al.[65]	46.63±14.26	19.37±2.18	40.89±13.38	21.97±2.94
Guo et al.[66]	61.32±6.03	21.72±2.93	60.82±7.13	22.18±2.15

As expected, there is a statistically significant difference in the CBC parameters, namely hemoglobin (g/dl), Red blood cells (x106/µL), Packed Cell Volume (%), MCHC (%), and Erythrocyte sedimentation rate (mm) between the two study groups. Similar to our observation, a significant difference was found between mean Hb, MCV, and MCHC between two groups in the Waseem et al.[65] studies. MCHC is within normal limits in the anemic COPD group in our study, as is in Waseem et al.[65] study, implying anemia of chronic disease is present in the patients. Normocytic normochromic anemia has been reported in COPD illnesses.[14] Parveen et al.[15] reported that the majority of the patients having anemia had decreased serum iron levels, transferrin saturation, and TIBC in their study.

The mean Hb in anemic and non-anemic COPD groups in our study is 9.42 ± 1.87 and 15.07 ± 1.46 g/dL, respectively. The mean Hb in the anemic group in Pandey et al.[36] study is higher at 11.04 ± 1.1, while it was lower in the non-anemic group at 13.9 ± 0.8 g/dL compared to our study. Park et al.[39] studies also had higher levels of mean hemoglobin level in the anemic group at 11.5±1.1 g/dL and lower in the non-anemic group at 14.2±1.2 g/dL compared to ours. These variations can be attributed to a variety of factors, including the anemia cut-off levels employed, sample size, and COPD severity. With the severity of the disease, it is

expected that erythropoietin will increase, but at the same time, there is resistance to erythropoietin.[56] The mean Hb in COPD groups having anemia and not having anemia was found to be 11.01± 4.67 and 14.03 ±1.51gm/dl, respectively, in Waseem et al.[65] studies. Erythropoietin levels were significantly raised in anemic COPD patients compared to non-anemic COPD patients in the Parveen et al.[15] study.

With p <0.05, there was no statistically significant difference in urine markers such as urea, creatinine, uric acid, and Blood Urea Nitrogen between the research groups. In the Oh, et al.[67] study, patients in the COPD group having anemia had decreased serum albumin levels (P0.001) compared to the non-anemic COPD group, but inflammatory indicators such as leukocyte count and high-sensitivity C-reactive protein (hs-CRP) level were not different between the two groups. Pirotte et al.[41] discovered a negative relationship between hemoglobin and CRP levels (R=-0.56, p less than 0.001).

In our investigation, the mean difference in temperature between the two groups was statistically significant (p-value 0.015). Iron is essential not just for oxygen transport to tissues but also as a cofactor for various enzymes involved in energy metabolism and thermoregulation.[75] The pulmonary function variables FVC, FEV1, FEV1/FVC, SpO2 (low), and the respiratory rate did not change significantly across study groups (p-value >0.05). Pandey et al. found that pulmonary function measures (FEV1, FVC, and FEV1/FVC) were lower in COPD patients having anemia than in non-anemic COPD patients, albeit the difference was not statistically significant in their research. In terms of postbronchodilator FEV1 percent, they discovered that individuals with anemia had more severe COPD.[36] Similarly, Oh et al.[67] studies found no differences in radiographic examinations and pulmonary function tests such as FVC, FEV1, FEV1/FVC, DLCO/VA (alveolar volume),

DLCO, RV/TLC, and inspiratory capacity (IC)/TLC. According to Guo et al.[66] study, resting pulmonary ventilation performance was equivalent in both patient groups. DLCO adjusted by Hb, on the other hand, was substantially lower in subjects with anemia compared to those without anemia (p0.05). This suggests that a drop in Hb levels may impair the pace of oxygen absorption across the alveolo-capillary bed and diminish the diffusing capacity of the lungs while having no discernible effect on pulmonary ventilation performance. Ergan et al.[37] discovered a favorable correlation between hemoglobin levels and FEV1 percent predicted (r=0.388, P=0.011).

Multiple independent characteristics have been linked to an increased risk of readmission in people with COPD having anemia being the most serious hazards, according to Pandey et al.[36] In Pirotte et al.[41] study, COPD patients having anemia had a greater rate of hospitalization for exacerbation in the last year than those with polycythemia (p 0.05). In our study, like in Oh et al.[67] the difference in acute exacerbation of COPD across study groups was found to be negligible (p 0.491). (p 0.313). Anemia was shown to have a significant connection with COPD exacerbations (p 0,004) and hospital admissions in the study by Parveen et al.[15] (p 0.001). In our study, the most of patients (92.5 percent) in both groups had COPD GOLD criteria III, with 7.5 percent having grade IV illness. In the Menou et al.[40] study, anemia was not impacted by the GOLD stage, which is going with our findings. Pandey et al.[36] study had a higher proportion of anemic patients in Stage III and IV (82%) while proportions of nonanemic patients were (65%) (P = 0.03). Most of Parveen et al.[15] study population were in GOLD Stage II, and they also found no correlation between lung function tests and anemia.
In Parveen et al.[15] study, the number of COPD exacerbations, hospital admissions, BMI, and erythropoietin levels were all substantially linked with anemia. Oh, et al.[67] proposed that in COPD, anemia was an independent risk factor for death and that dietary parameters such as a

lower serum albumin level and a lower BMI were independent risk factors for a lower hemoglobin level. Guo et al.[66] found that anemia reduced both gas exchange function and exercise capacity in patients with severe COPD compared to individuals without anemia but had minimal effect on pulmonary ventilation function and ventilatory efficiency. In Parveen et al.[15] study, the number of COPD exacerbations, hospital admissions, BMI, and erythropoietin levels were all substantially linked with anemia.

Toft-Petersen et al.[42] reported that even concentrations of hemoglobin around the lower end of the normal range were predictive of mortality in COPD. Park et al.[39] showed that anemia was associated with increased long-term mortality of COPD, and even mild anemia was related to a significantly increased risk of death. Pirotte et al.[41] concluded that anemia is associated with systemic inflammation and a propensity to hospitalization for exacerbation from their study. Our study did now show any association with the number of exacerbations of COPD, pulmonary function parameters, pleural effusion, pneumothorax, cardiac arrhythmias, ECG, cardiac echo, with anemia in COPD patients. Anemic COPD patients are found to have low body temperature, low hemoglobin, and relatively higher MCHC levels compared to non-anemic COPD patients.

SUMMARY

SUMMARY:

This is a case-control study among patients attending RL Jalappa Hospital who fulfill the inclusion and exclusion criteria to compare the complications in COPD patients with and without anemia. CBC parameters, investigation parameters, vital signs parameters were considered as primary outcome variables. The study group (COPD with anemia vs. COPD without anemia) was considered as a primary explanatory variable. There are no statistically correlation between the baseline characteristics between the study groups with regards to age, height, weight, BMI, systolic blood pressure, diastolic blood pressure, and pulse rate. The mean age in COPD with anemia group is 62.6 ± 9.43, and that in COPD without anemia is 61.4 ± 6.99. A maximum number of patients in both groups in our study had COPD GOLD criteria III (92.5%), with 7.5% having grade IV disease. Our study did now show any association with xacerbations of COPD, pulmonary function parameters, pleural effusion, pneumothorax, cardiac arrhythmias, ECG, cardiac echo, with anemia in COPD patients. Anemic COPD patients are found to have low body temperature, low hemoglobin, and relatively higher MCHC levels compared to COPD patients not having anemia .

CONCLUSION

CONCLUSION:

The baseline characteristics between the study groups with regards to age, height, weight, BMI, systolic blood pressure, diastolic blood pressure, and pulse rate were matched. Our study did now show any association with exacerbations of COPD, pulmonary function parameters, pleural effusion, pneumothorax, cardiac arrhythmias with or without anemia in COPD. Anemic COPD patients are found to have low body temperature, low hemoglobin, and relatively higher MCHC levels compared to COPD patients not having anemia .

LIMITATIONS AND RECOMMENDATIONS:

The sample size in our study is small, hence it cannot to generalized to all the patients with COPD. The present data is derived from patients with GOLD stage III and IV COPD and thus cannot be applied to the overall population of COPD patients.

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ANNEXURES

IMPACT OF ANEMIA ON COMPLICATIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS-CASE-CONTROL STUDY

PROFORMA

Name:

Age / Sex:

Residential Address:

Mobile No:

Case History:

Other known Illness:

BP: Pulse rate:

CVS-
RS-
P/A-
CNS-

Outcome Measures:

Complete blood count	
Pulmonary function test	
Renal function test	
HIV Serology	
RBS	
ECG	
CHEST X-RAY	
2D-ECHO	

EXCLUSION CRITERIA:

HISTORY OF	YES	NO
1. MALIGNANCY		
2. DIABETES MELLITUS		
3. HIV		
4. LONG TERM IMMUNOSUPPRESSIVE USAGE		
5. ACUTE BLOOD LOSS		
6. PRIMARY CAUSES OF HEART FAILURE		
7. RENAL IMPAIRMENT		

Signature

PATIENT INFORMATION SHEET

Study Title: IMPACT OF ANEMIA ON COMPLICATIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS-CASE-CONTROL STUDY

Study site: R.L Jalappa hospital, Tamaka, Kolar.

Aim: To compare the complications involved in COPD patients with and without anemia.

Chronic obstructive pulmonary disease (COPD) is a leading respiratory disease affecting the length and quality of lives around the globe.

In India, three out of five leading causes of mortalities constitute non-communicable diseases, whereas COPD is the second biggest cause of death.

The prevalence of anemia in patients with COPD varies from 7.5% to 33%. Anemia in COPD is associated with greater healthcare resource utilization, impaired quality of life, decreased survival, and a greater likelihood of hospitalization, increased morbidity and mortality, higher costs of care, increased risk of heart failure, increased risk of acute exacerbation of COPD. So, we aim at studying the complications of COPD and to compare them with anemia and without anemia.

Pulmonary function tests and complete blood count will be done for patients, and patients will be divided into two groups, and other relevant investigations will be done. The information is intended to give you the general background of the study. Please read the following information and discuss it with your family members. You can ask any questions regarding the study. If you agree to participate in the study, we will collect information (as per proforma) from you or a person responsible for you or both. Relevant history will be taken. This information collected will be used only for publication. The principal investigation will be paying for the investigations.

All information collected from you will be kept confidential and will not be disclosed to any outsider. Your identity will not be revealed. This study has been reviewed by the Institutional

Ethics Committee, and you are free to contact the member of the Institutional Ethics Committee. There is no compulsion to agree to this study. The care you will get will not change if you don't wish to participate. You are required to sign/ provide a thumb impression only if you voluntarily agree to participate in this study.

For any further clarification, you can contact the study investigator:

Dr. RAKESH KUMAR G

Mobile no: 9901917979

Email: rakeshkumarvinay@gmail.com

INFORMED CONSENT FORM

I ---------- participant, hereby give consent to participate in the study entitled "IMPACT OF ANEMIA ON COMPLICATIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE PATIENTS-CASE-CONTROL STUDY."

I have been explained that;

1. I would have to provide a blood sample for the study purpose.
2. I have to answer the questionnaires related to the project.
3. I do not have to incur any additional expenditure on my inclusion into the study.
4. The data generated from my clinical examination and laboratory tests, and other reports will be used in the study (which may be subsequently published) without revealing my identity in any manner.

I affirm that I have been given full information about the purpose of the study and the procedures involved and have been given ample opportunity to clarify my doubts in my mother tongue. In giving my consent, I have not faced any coercion. I have been informed that, notwithstanding this consent given, I can withdraw from the study at any stage.

For any further clarification, you can contact the study investigator:

Dr. Rakesh Kumar G

Mobile no: 9901917979

Email: rakeshkumarvinay@gmail.com

Signature of participant: Place:

Name of participant: Date:

ರೋಗಿಯಮಾಹಿತಿಹಾಳೆ

ಅಧ್ಯಯನದಶೀರ್ಷಿಕೆ:ದೀರ್ಘಕಾಲದಅಬ್ಸ್ಟ್ರಕ್ಟಿವ್ಪಲ್ಮನರಿಕಾಯಿಲೆರೋಗಿಗಳ-ಕೇಸ್-
ಕಂಟ್ರೋಲ್ಅಧ್ಯಯನದಲ್ಲಿನತೊಡಕುಗಳಮೇಲೆರಕ್ತಹೀನತೆಯಪರಿಣಾಮ

ಅಧ್ಯಯನಸ್ಥಳ: ಆರ್.ಎಲ್ಜಲಪ್ಪಆಸ್ಪತ್ರೆ, ತಮಾಕಾ, ಕೋಲಾರ.

ಗುರಿ: ರಕ್ತಹೀನತೆಯೊಂದಿಗೆಮತ್ತುಇಲ್ಲದೆಸಿಒಪಿಡಿರೋಗಿಗಳಲ್ಲಿಉಂಟಾಗುವತೊಂದರೆಗಳನ್ನುಹೋಲಿಕೆಮಾಡುವುದು.

ದೀರ್ಘಕಾಲದಪ್ರತಿರೋಧಕಶ್ವಾಸಕೋಶದಕಾಯಿಲೆ (ಸಿಒಪಿಡಿ)
ಎಂಬುದುವಿಶ್ವದಾದ್ಯಂತದಜೀವನದಉದ್ದಮತ್ತುಗುಣಮಟ್ಟದಮೇಲೆಪರಿಣಾಮಬೀರುವಪ್ರಮುಖಉಸಿರಾಟದಕಾಯಿಲೆಯಾಗಿದೆ
.

ಭಾರತದಲ್ಲಿ, ಸಾವಿನಐದುಪ್ರಮುಖಕಾರಣಗಳಲ್ಲಿಮೂರುಸಾಂಕ್ರಾಮಿಕವಲ್ಲದಕಾಯಿಲೆಗಳಾಗಿವೆ,
ಆದರೆಸಿಒಪಿಡಿಸಾವಿಗೆಎರಡನೇದೊಡ್ಡಕಾರಣವಾಗಿದೆ.

ಸಿಒಪಿಡಿರೋಗಿಗಳಲ್ಲಿರಕ್ತಹೀನತೆಯಹರಡುವಿಕೆಯು 7.5% ರಿಂದ 33% ವರೆಗೆಬದಲಾಗುತ್ತದೆ.
ಸಿಒಪಿಡಿಯಲ್ಲಿನರಕ್ತಹೀನತೆಯುಹೆಚ್ಚಿನಆರೋಗ್ಯಸಂಪನ್ಮೂಲಬಳಕೆ, ಜೀವನದಗುಣಮಟ್ಟ,
ದುರ್ಬಲಗೊಂಡಬದುಕುಳಿಯುವಿಕೆಮತ್ತುಆಸ್ಪತ್ರೆಗೆದಾಖಲುಮಾಡುವಹೆಚ್ಚಿನಸಂಭವನೀಯತೆ,
ಹೆಚ್ಚಿದಕಾಯಿಲೆಮತ್ತುಮರಣಪ್ರಮಾಣ, ಹೆಚ್ಚಿನಆರೈಕೆಯವೆಚ್ಚಗಳು, ಹೃದಯವೈಫಲ್ಯದಅಪಾಯ,
ಸಿಒಪಿಡಿಯತೀವ್ರಉಲ್ಬಣಗೊಳ್ಳುವಿಕೆಯಅಪಾಯದೊಂದಿಗೆಸಂಬಂಧಿಸಿದೆ.
ಆದ್ದರಿಂದನಾವುಸಿಒಪಿಡಿಯತೊಡಕುಗಳನ್ನುಅಧ್ಯಯನಮಾಡುವುದುಮತ್ತುಅವುಗಳನ್ನುರಕ್ತಹೀನತೆಮತ್ತುರಕ್ತಹೀನತೆಇಲ್ಲದೆ
ಹೋಲಿಸುವಗುರಿಹೊಂದಿದ್ದೇವೆ.

ರೋಗಿಗಳಿಗೆಶ್ವಾಸಕೋಶದಕಾರ್ಯಪರೀಕ್ಷೆಮತ್ತುಸಂಪೂರ್ಣರಕ್ತದಎಣಿಕೆಮಾಡಲಾಗುವುದುಮತ್ತುರೋಗಿಗಳನ್ನುಎರಡುಗುಂಪು
ಗಳಾಗಿವಿಂಗಡಿಸಲಾಗುವುದುಮತ್ತುಇತರಸಂಬಂಧಿತತನಿಖೆಗಳನ್ನುಮಾಡಲಾಗುತ್ತದೆ.
ಮಾಹಿತಿಯುನಿಮಗೆಅಧ್ಯಯನದಸಾಮಾನ್ಯಹಿನ್ನೆಲೆಯನ್ನುನೀಡಲುಉದ್ದೇಶಿಸಿದೆ.
ದಯವಿಟ್ಟುಈಕೆಳಗಿನಮಾಹಿತಿಯನ್ನುಓದಿಮತ್ತುನಿಮ್ಮಕುಟುಂಬಸದಸ್ಯರೊಂದಿಗೆಚರ್ಚಿಸಿ.
ಅಧ್ಯಯನಕ್ಕೆಸಂಬಂಧಿಸಿದಂತೆನೀವುಯಾವುದೇಪ್ರಶ್ನೆಗಳನ್ನುಕೇಳಬಹುದು.
ಅಧ್ಯಯನದಲ್ಲಿಭಾಗವಹಿಸಲುನೀವುಒಪ್ಪಿದರೆನಾವುನಿಮ್ಮಿಂದಅಥವಾನಿಮ್ಮಿಂದಅಥವಾಇಬ್ಬರಿಗೂಜವಾಬ್ದಾರರಾಗಿರುವವ್ಯಕ್ತಿ
ಯಿಂದಮಾಹಿತಿಯನ್ನು (ಪ್ರೊಫಾರ್ಮಾದಪ್ರಕಾರ) ಸಂಗ್ರಹಿಸುತ್ತೇವೆ. ಸಂಬಂಧಿತಇತಿಹಾಸವನ್ನುತೆಗೆದುಕೊಳ್ಳಲಾಗುವುದು.
ಸಂಗ್ರಹಿಸಿದಈಮಾಹಿತಿಯನ್ನುಪ್ರಕಟಣೆಗೆಮಾತ್ರಬಳಸಲಾಗುತ್ತದೆ. ಪ್ರಧಾನತನಿಖೆಯುತನಿಖೆಗೆಪಾವತಿಸಲಿದೆ.

ನಿಮ್ಮಿಂದಸಂಗ್ರಹಿಸಲಾದಎಲ್ಲಾಮಾಹಿತಿಯನ್ನುಗೌಪ್ಯವಾಗಿಡಲಾಗುತ್ತದೆಮತ್ತುಯಾವುದೇಹೊರಗಿನವರಿಗೆಬಹಿರಂಗಪಡಿಸುವುದಿಲ್ಲ. ನಿಮ್ಮಗುರುತುಬಹಿರಂಗಗೊಳ್ಳುವುದಿಲ್ಲ.

ಈಅಧ್ಯಯನವನ್ನುಸಾಂಸ್ಥಿಕನೈತಿಕಸಮಿತಿಯುಪರಿಶೀಲಿಸಿದೆಮತ್ತುನೀವುಸಾಂಸ್ಥಿಕನೈತಿಕಸಮಿತಿಯಸದಸ್ಯರನ್ನುಸಂಪರ್ಕಿಸಲುಮುಕ್ತರಾಗಿದ್ದೀರಿ. ಈಅಧ್ಯಯನವನ್ನುಒಪ್ಪಿಕೊಳ್ಳಲುಯಾವುದೇಬಲವಂತವಿಲ್ಲ.

ನೀವುಭಾಗವಹಿಸಲುಬಯಸದಿದ್ದರೆನೀವುಪಡೆಯುವಕಾಳಜಿಬದಲಾಗುವುದಿಲ್ಲ.

ಈಅಧ್ಯಯನದಲ್ಲಿಭಾಗವಹಿಸಲುನೀವುಸ್ವಯಂಪ್ರೇರಣೆಯಿಂದಒಪ್ಪಿಕೊಂಡರೆಮಾತ್ರನೀವುಹೆಬ್ಬೆರಳುಅನಿಸಿಕೆಗೆಸಹಿ / ಒದಗಿಸುವಅಗತ್ಯವಿದೆ.

ಯಾವುದೇಹೆಚ್ಚಿನಸ್ಪಷ್ಟೀಕರಣಕ್ಕಾಗಿನೀವುಅಧ್ಯಯನತನಿಖಾಧಿಕಾರಿಯನ್ನುಸಂಪರ್ಕಿಸಬಹುದು:

ಡಾ.ರಾಕೇಶ್ಕುಮಾರ್ಜಿ

ಮೊಬೈಲ್ಸಂಖ್ಯೆ: 9901917979

ಇಮೇಲ್: rakeshkumarvinay@gmail.com

MASTER SHEET

COPD with anemia:

S. No	Study group	Age (in years)	Gender	Height (in cm)	Weight (in kg)	BMI	SBP	DBP	Pulse rate	CVS	RS	P/A	CNS	Total Cell Count	Polymorphs / Neutrophils	Lymphocytes	Eosinophils	Monocytes	Basophils	Hemoglobin	Red blood cells	Packed Cell Volume	Platelet Count	MCV	MCH	MCHC
1	902859	60	Male	181	77	23.50	130	90	88	normal	b/l rhonchi	normal	normal	9259	48	35	4	7	1	8.60	4.74	45	376432	87	26.74	31
2	883026	65	Male	176	70	22.60	126	80	72	normal	b/l rhonchi	normal	normal	4641	61	40	3	6	1	6.60	4.72	46	166080	99	34.72	31
3	863153	70	Male	170	60	20.76	140	82	76	normal	b/l rhonchi	normal	normal	10779	71	29	6	4	1	9.30	3.57	43	189653	92	30.57	34
4	900204	65	Male	178	70	22.09	136	82	84	normal	b/l rhonchi	normal	normal	4524	50	30	6	10	0	8.00	4.71	42	161780	97	26.71	36
5	902629	50	Male	168	74	26.22	130	86	96	normal	b/l rhonchi	normal	normal	7606	51	41	3	3	1	10.00	2.69	50	385694	96	28.69	36
6	846060	71	Male	174	69	22.79	130	88	76	normal	right sided absent breath sounds	normal	normal	8685	47	42	1	3	1	12.50	4.61	36	330557	92	31.61	35
7	846420	68	Male	165	66	24.24	126	80	76	normal	b/l rhonchi	normal	normal	6988	40	32	4	6	1	8.60	2.68	40	197611	81	28.68	34
8	846898	68	Male	169	72	25.21	130	86	78	normal	b/l rhonchi	normal	normal	7685	41	33	3	2	1	7.50	2.50	44	225067	95	34.5	34
9	850085	60	Male	165	60	22.04	120	84	98	normal	left sided absent breath sounds	normal	normal	10883	70	43	4	7	1	11.90	4.60	36	338989	83	31.6	34
10	894749	46	Male	170	70	24.22	130	78	80	normal	left sided absent breath sounds	normal	normal	10505	49	36	5	2	0	11.90	3.59	48	180236	87	34.59	32
11	898108	55	Male	179	70	21.85	128	70	72	normal	right sided absent breath sounds	normal	normal	8261	71	24	3	10	1	10.00	3.77	39	303420	92	34.77	31
12	883669	70	Male	178	68	21.46	136	76	78	normal	left sided absent breath sounds	normal	normal	8824	65	22	4	8	1	6.90	2.65	41	394998	91	26.65	34
13	903021	60	Male	173	73	24.39	130	76	73	normal	b/l rhonchi	normal	normal	9383	70	38	2	4	0	7.30	2.68	48	230326	83	28.68	34
14	839553	70	Male	176	68	21.95	126	82	78	normal	right sided absent breath sounds	normal	normal	10976	65	36	4	4	0	9.70	2.53	46	397459	95	25.53	35
15	838126	72	Male	174	64	21.14	110	72	76	normal	b/l rhonchi	normal	normal	8773	59	40	6	2	1	6.20	3.79	46	270981	99	29.79	32
16	841647	56	Male	173	74	24.73	130	84	86	normal	right sided absent breath sounds	normal	normal	9922	74	28	3	8	1	9.20	3.77	48	399267	84	34.77	33
17	841661	70	Male	168	60	21.26	146	74	71	normal	b/l rhonchi	normal	normal	8211	70	31	4	3	1	9.90	3.57	39	212301	95	30.57	36
18	842158	42	Male	160	60	23.44	120	68	72	normal	left sided absent breath sounds	normal	normal	10768	66	42	4	6	0	11.10	2.70	45	192764	83	33.47	34

19	842963	70	Male	170	64	22.15	130	72	72	normal	b/l rhonchi	normal	normal	6721	55	38	5	7	1	11.70	3.56	49	289866	89	30.56	35
20	844038	45	Male	172	70	23.66	126	66	78	normal	b/l rhonchi	normal	normal	9209	74	43	4	3	0	8.25	2.64	50	375554	98	29.64	33
21	845191	70	Male	169	58	20.31	126	70	76	normal	b/l rhonchi	normal	normal	8624	66	33	1	7	1	12.00	4.61	45	221942	81	33.61	34
22	863572	50	Male	168	72	25.51	130	75	78	normal	b/l crackles present	normal	normal	11039	62	36	6	9	0	7.90	2.51	49	188916	100	25.51	31
23	887357	72	Male	172	58	19.61	130	76	70	normal	right sided absent breath sounds	normal	normal	6487	62	32	4	10	1	11.10	4.71	49	274333	89	26.71	35
24	642281	70	Female	174	63	20.81	126	72	82	normal	b/l rhonchi	normal	normal	9181	55	38	5	4	0	12.50	4.60	38	165319	96	31.6	33
25	889910	65	Male	174	68	22.46	127	84	78	normal	b/l rhonchi	normal	normal	10507	59	42	6	9	1	7.40	3.58	45	162991	95	32.58	31
26	892738	40	Male	175	70	22.86	127	64	74	normal	left sided absent breath sounds	normal	normal	10929	67	23	4	10	1	7.70	3.56	45	218647	94	30.56	35
27	892671	71	Male	180	60	18.52	126	72	74	normal	b/l rhonchi	normal	normal	10847	64	33	6	9	1	8.60	4.61	49	209097	89	33.61	35
28	898108	60	Male	178	70	22.09	126	76	92	normal	b/l rhonchi	normal	normal	5744	59	43	5	9	1	10.70	4.76	46	254524	90	27.76	31
29	757495	58	Male	172	69	23.32	126	78	86	normal	left sided absent breath sounds	normal	normal	10986	67	37	6	2	0	9.00	2.55	45	198145	92	25.55	34
30	901526	65	Female	160	60	23.44	126	70	80	normal	right sided absent breath sounds	normal	normal	7449	70	33	3	8	1	11.90	2.52	46	190828	89	29.52	35
31	763626	49	Male	165	60	22.04	126	70	82	normal	b/l rhonchi	normal	normal	6356	65	32	1	7	1	7.00	2.52	46	353411	85	25.52	34
32	763635	67	Male	168	61	21.61	126	86	72	normal	right sided absent breath sounds	normal	normal	9346	57	45	5	10	0	12.90	3.57	39	231783	93	30.57	35
33	764124	69	Male	161	55	21.22	125	84	70	normal	b/l rhonchi	normal	normal	7759	64	37	3	5	1	7.20	2.48	36	200163	83	24.48	31
34	764699	72	Male	167	57	20.44	125	76	92	normal	left sided absent breath sounds	normal	normal	11038	53	40	4	4	1	10.20	3.59	48	253375	98	34.59	35
35	764279	65	Male	172	57	19.27	125	76	80	normal	left sided absent breath sounds	normal	normal	5833	49	26	6	7	1	9.20	3.77	45	362362	97	34.77	34
36	766534	75	Male	174	56	18.50	125	80	76	normal	b/l rhonchi	normal	normal	11040	63	24	6	10	0	9.10	4.60	46	342266	80	31.6	34
37	766753	60	Male	179	68	21.22	125	76	80	normal	b/l rhonchi	normal	normal	4970	49	28	4	3	1	10.20	2.50	47	151523	97	32.5	34
38	767919	75	Male	174	64	21.14	140	84	70	normal	b/l rhonchi	normal	normal	10111	75	32	6	9	0	7.20	3.83	38	302117	81	29.83	33
39	767615	56	Male	179	70	21.85	130	82	98	normal	b/l rhonchi	normal	normal	9329	63	29	5	10	1	10.90	2.50	49	376307	96	24.5	36
40	762023	62	Female	165	56	20.57	130	78	78	normal	right sided absent breath sounds	normal	normal	11239	52	23	1	3	1	8.90	3.58	46	357172	83	32.58	35

S. No	Erythrocyte sedimentation rate	Red cell distribution width	Urea (mg/dl)	Creatinine (mg/dl)	Uric Acid (mg/dl)	Blood Urea Nitrogen (mg/dl)	FVC	FEV1	FEV1/FVC	HIV Serology	ECG	Chest x-ray	Acute exacerbation of COPD	Lung malignancy	Pleural effusion	Pneumothorax	Cor pulmonale	Cardiac arrhythmias	SpO2 (low)	Temperature	Respiratory Rate	2D ECHO	STAGES OF COPD
1	3.52		25	0.74	4.74	8	67	38	0.57	negative	multi focal atrial tachycardia	EMHYSEMA	No	No	No	No	Yes	Yes	100	95	19	RA RV DILATED	III
2	3.57		37	0.72	4.72	7	63	40	0.63	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	97	96	23	NORMAL	III
3	4.48		37	0.57	3.57	20	67	36	0.54	negative	sinus rhythm	B/L non-homogenous opacities	Yes	No	no	no	No	No	95	101	25	NORMAL	III
4	3.59		39	0.71	7.71	12	62	41	0.66	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	95	95	22	NORMAL	III
5	3.77		38	1.69	7.69	8	64	36	0.56	negative	atrial fibrillation	EMHYSEMA	No	No	No	No	No	Yes	99	96	17	NORMAL	III
6	4.6		13	0.61	4.61	14	65	40	0.62	negative	sinus rhythm	right sided homogenous opacities	No	Yes	Yes	No	No	No	95	97	17	NORMAL	III
7	3.5		12	1.68	7.68	17	64	42	0.66	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	100	98	25	NORMAL	III
8	3.83		17	1.5	5.5	13	60	35	0.58	negative	sinus rhythm	EMHYSEMA	No	No	No	No	Yes	No	96	98	20	RA RV DILATED	III
9	4.5		37	0.6	6.6	13	62	43	0.69	negative	atrial fibrilation	left sided homogenous opacities	Yes	Yes	Yes	No	No	Yes	99	102	22	NORMAL	III
10	3.58		29	0.59	3.59	10	73	46	0.63	negative	atrial fibrilation	left sided pneumothorax	Yes	No	No	Yes	Yes	Yes	98	100	25	RA RV DILATED	III
11	3.58		34	0.77	3.77	8	61	38	0.62	negative	sinus rhythm	right sided homogenous opacities	No	No	Yes	No	Yes	No	95	98	16	RA RV DILATED	III
12	3.64		20	1.65	7.65	19	63	37	0.59	negative	sinus rhythm	left sided homogenous opacities	No	No	Yes	No	Yes	No	99	97	25	RA RV DILATED	III
13	4.52		36	1.68	7.68	11	65	38	0.58	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	97	97	14	NORMAL	III
14	4.72		24	1.53	4.53	16	61	30	0.49	negative	multi focal atrial tachycardia	right sided homogenous opacities	Yes	No	Yes	No	No	Yes	95	102	21	NORMAL	III
15	3.51		44	0.79	6.79	9	67	46	0.69	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	98	95	17	NORMAL	III
16	4.62		9	0.77	6.77	10	65	39	0.60	negative	sinus rhythm	right sided pneumothorax	No	Yes	No	Yes	No	No	97	99	25	NORMAL	III
17	4.74		17	0.57	3.57	15	72	37	0.51	negative	sinus rhythm	EMHYSEMA	Yes	No	No	No	No	No	100	96	13	NORMAL	III
18	4.72		42	1.7	7.7	20	64	29	0.45	negative	multi focal atrial tachycardia	left sided homogenous opacities	Yes	Yes	Yes	No	No	Yes	98	101	24	NORMAL	IV
19	3.57		38	0.56	3.56	9	60	34	0.57	negative	sinus rhythm	EMHYSEMA	Yes	No	No	No	No	No	97	96	25	NORMAL	III
20	4.71		17	1.64	4.64	16	61	29	0.48	negative	sinus rhythm	EMHYSEMA	No	No	No	No	Yes	No	99	97	21	RA RV DILATED	IV
21	4.69		36	0.61	4.61	11	68	44	0.65	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	97	100	20	NORMAL	III
22	4.61		30	1.51	5.51	15	60	35	0.58	negative	multi focal atrial tachycardia	B/L non homogenous opacities	Yes	Yes	No	No	No	Yes	98	100	25	NORMAL	III
23	3.68		32	0.71	7.71	17	63	39	0.62	negative	sinus rhythm	right sided pneumothorax	No	No	no	Yes	No	No	96	98	12	NORMAL	III
24	3.5		40	0.6	6.6	17	72	33	0.46	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	99	96	22	NORMAL	III
25	4.6		19	0.58	3.58	11	62	41	0.66	negative	sinus rhythm	EMHYSEMA	Yes	No	No	No	Yes	No	96	102	26	RA RV DILATED	III
26	3.59		18	0.56	3.56	8	60	36	0.60	negative	multi focal atrial tachycardia	left sided pneumothorax	Yes	no	no	Yes	No	Yes	99	101	26	NORMAL	III
27	3.77		17	0.61	4.61	12	73	47	0.64	negative	sinus rhythm	EMHYSEMA	Yes	No	No	No	Yes	No	96	100	25	RA RV DILATED	III
28	3.65		27	0.76	4.76	8	60	38	0.63	negative	sinus rhythm	EMHYSEMA	No	No	No	No	Yes	No	96	97	23	RA RV DILATED	III

29	4.68		22	1.55	4.55	20	71	37	0.52	negative	sinus rhythm	left sided homogenous opacities	Yes	No	Yes	No	Yes	No	95	101	26	RA RV DILATED	III
30	3.53		33	1.52	6.52	9	60	40	0.67	negative	sinus rhythm	right sided pneumothorax	No	Yes	No	Yes	No	No	100	100	25	NORMAL	III
31	3.79		27	1.52	4.52	8	65	34	0.52	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	95	97	20	NORMAL	III
32	3.77		12	0.57	3.57	13	64	43	0.67	negative	sinus rhythm	right sided homogenous opacities	No	No	Yes	No	No	No	98	98	17	NORMAL	III
33	4.59		22	1.48	5.48	17	70	36	0.51	negative	sinus rhythm	EMHYSEMA	No	No	No	No	Yes	No	96	100	23	RA RV DILATED	III
34	3.77		7	0.59	3.59	20	69	41	0.59	negative	atrial fibrilation	left sided pneumothorax	Yes	No	No	Yes	No	Yes	95	102	26	NORMAL	III
35	4.65		13	0.77	6.77	18	67	37	0.55	negative	sinus rhythm	left sided pneumothorax	No	no	no	Yes	Yes	No	97	95	20	RA RV DILATED	III
36	4.68		45	0.6	6.6	10	63	29	0.46	negative	sinus rhythm	EMHYSEMA	Yes	No	No	No	No	No	95	101	26	NORMAL	IV
37	3.53		43	1.5	5.5	20	74	39	0.53	negative	sinus rhythm	EMHYSEMA	Yes	Yes	No	No	No	No	96	98	17	NORMAL	III
38	3.79		32	0.83	6.83	14	64	37	0.58	negative	sinus rhythm	EMHYSEMA	Yes	No	No	No	Yes	No	98	103	25	RA RV DILATED	III
39	3.77		8	1.5	5.5	11	70	40	0.57	negative	ventricular permature complex	EMHYSEMA	No	No	No	No	No	Yes	95	100	19	NORMAL	III
40	3.57		13	0.58	3.58	16	62	37	0.60	negative	sinus rhythm	right sided homogenous opacities	Yes	No	Yes	No	No	No	96	101	25	NORMAL	III

COPD without anemia:

S. No	Study group	Age (in years)	Gender	Height (in cm)	Weight (in kg)	BMI	SBP	DBP	Pulse rate	CVS	RS	P/A	CNS	Total Cell Count	Polymorphs / Neutrophils	Lymphocytes	Eosinophils	Monocytes	Basophils	Hemoglobin	Red blood cells	Packed Cell Volume	Platelet Count	MCV	MCH	MCHC
1	888601	62	Male	176	70	22.60	134	76	77	normal	b/l rhonchi present	normal	normal	5272	53	21	6	3	0	16.96	3.58	50	205661	87	32.58	33
2	886936	70	Female	160	60	23.44	140	84	90	normal	b/l rhonchi present	normal	normal	7206	66	28	2	5	1	13.50	4.64	38	210391	92	26.64	31
3	889880	60	Male	178	70	22.09	130	74	88	normal	left sided absent breath sounds	normal	normal	11075	60	29	1	10	1	15.30	3.52	45	246561	97	25.52	34
4	889876	64	Male	170	70	24.22	120	76	73	normal	b/l rhonchi present	normal	normal	5696	75	36	6	9	1	14.30	4.72	39	188105	89	26.72	33
5	870347	64	Male	179	70	21.85	130	86	82	normal	b/l rhonchi present	normal	normal	8661	48	40	3	5	1	14.20	5.51	42	178975	92	25.51	32
6	891489	60	Male	169	58	20.31	150	75	80	normal	b/l crackles present	normal	normal	10275	50	32	6	10	1	15.30	4.62	37	268297	85	33.62	31
7	652845	58	Male	174	68	22.46	134	76	74	normal	b/l rhonchi present	normal	normal	7688	43	28	4	7	1	17.80	2.64	38	349299	84	26.64	32
8	897483	60	Male	170	73	25.26	130	74	72	normal	right sided absent breath sounds	normal	normal	10695	66	45	2	4	1	16.70	4.54	47	228215	89	34.54	31
9	841361	55	Male	178	70	22.09	126	70	82	normal	b/l rhonchi present	normal	normal	11085	64	41	5	7	1	13.56	2.70	37	387415	100	28.7	32
10	841585	67	Male	181	70	21.37	136	70	76	normal	left sided absent breath sounds	normal	normal	7766	53	41	2	6	1	13.80	3.41	49	208008	100	34.41	31
11	797085	63	Male	174	68	22.46	130	88	98	normal	left sided absent breath sounds	normal	normal	10980	62	34	4	3	1	17.15	4.62	37	185456	91	33.62	35
12	844873	51	Male	175	70	22.86	126	66	78	normal	right sided absent breath sounds	normal	normal	6994	73	23	5	10	0	15.53	5.70	36	322262	84	33.7	31
13	845344	58	Male	180	60	18.52	120	70	88	normal	left sided absent breath sounds	normal	normal	9739	43	24	3	10	0	13.48	4.71	40	381475	86	33.71	34
14	945459	69	Male	178	70	22.09	130	84	86	normal	b/l rhonchi present	normal	normal	11086	70	26	3	8	0	14.50	2.67	37	267117	93	33.67	31
15	503028	70	Male	172	57	19.27	130	88	76	normal	right sided absent breath sounds	normal	normal	5588	54	25	6	4	1	13.50	4.68	50	376670	86	34.68	33
16	845275	65	Male	170	60	20.76	140	82	76	normal	b/l rhonchi present	normal	normal	9482	54	24	6	8	1	17.40	3.50	45	385321	97	34.5	32
17	537610	75	Male	173	73	24.39	130	84	78	normal	b/l rhonchi present	normal	normal	10649	43	23	4	4	1	13.10	4.60	44	196985	85	31.6	31
18	369488	65	Male	176	68	21.95	126	66	88	normal	right sided absent breath sounds	normal	normal	10923	50	32	6	3	0	16.90	4.59	37	333241	93	31.59	31
19	895762	51	Male	174	64	21.14	130	84	80	normal	right sided absent breath sounds	normal	normal	8162	63	33	3	6	1	14.63	3.77	43	216137	98	34.77	33
20	897483	68	Male	165	60	22.04	130	84	78	normal	b/l rhonchi present	normal	normal	8378	60	35	4	9	0	15.83	2.65	44	154577	97	33.65	31
21	900377	53	Male	168	61	21.61	120	76	98	normal	b/l rhonchi present	normal	normal	4192	75	37	1	8	1	16.20	4.68	38	390306	89	28.68	32

22	898593	65	Male	180	60	18.52	130	88	86	normal	b/l crackles present	normal	normal	10829	60	45	2	9	1	15.10	4.53	46	207490	95	25.53	32
23	900455	55	Male	167	57	20.44	126	66	88	normal	right sided absent breath sounds	normal	normal	5867	66	36	1	3	1	14.90	3.79	47	245026	97	32.79	31
24	902928	53	Male	172	57	19.27	128	66	82	normal	b/l rhonchi present	normal	normal	6435	50	37	4	10	1	13.90	4.77	44	178950	91	34.77	32
25	903261	45	Male	170	64	22.15	124	76	78	normal	b/l crackles present	normal	normal	11064	70	42	5	4	0	15.90	3.57	48	357510	92	32.57	31
26	852580	57	Male	172	70	23.66	126	68	82	normal	left sided absent breath sounds	normal	normal	4979	52	37	3	2	0	14.80	4.70	40	324250	90	33.7	32
27	899370	62	Male	169	58	20.31	130	84	74	normal	b/l rhonchi present	normal	normal	5464	73	38	2	5	1	16.85	3.56	49	323522	86	30.56	31
28	886621	70	Male	170	60	20.76	134	76	92	normal	b/l rhonchi present	normal	normal	5483	60	37	5	5	0	15.80	2.64	38	181650	98	26.64	32
29	850698	65	Male	172	58	19.61	146	74	76	normal	left sided absent breath sounds	normal	normal	11003	59	35	4	2	1	12.00	4.61	42	236588	100	33.61	31
30	812974	63	Male	173	74	24.73	140	84	94	normal	right sided absent breath sounds	normal	normal	8868	53	35	5	8	0	17.50	3.51	46	255282	96	25.51	32
31	780337	44	Male	168	60	21.26	110	76	78	normal	b/l rhonchi present	normal	normal	7070	43	25	5	10	1	13.10	4.71	47	193411	91	26.71	31
32	780783	60	Male	160	60	23.44	126	66	82	normal	b/l crackles present	normal	normal	10412	74	34	4	4	1	14.40	4.60	42	201580	94	31.6	32
33	781280	56	Male	170	64	22.15	130	84	78	normal	left sided absent breath sounds	normal	normal	4500	55	25	4	5	0	15.44	3.58	40	275124	95	32.58	33
34	781810	69	Male	180	60	18.52	130	88	79	normal	right sided absent breath sounds	normal	normal	10933	71	41	4	3	1	13.70	3.56	41	207019	91	30.56	31
35	782321	58	Male	181	77	23.50	146	74	78	normal	left sided absent breath sounds	normal	normal	8897	55	29	1	5	0	16.60	4.61	41	159221	91	33.61	33
36	783209	64	Female	168	60	21.26	134	84	84	normal	right sided absent breath sounds	normal	normal	6491	67	42	6	10	0	13.20	4.76	46	227819	100	27.76	31
37	785079	65	Male	170	60	20.76	146	74	78	normal	b/l rhonchi present	normal	normal	9189	50	38	1	2	1	16.00	5.55	41	309517	80	32.55	31
38	785853	60	Male	178	70	22.09	134	76	72	normal	b/l crackles present	normal	normal	11092	55	44	3	5	0	14.50	4.92	41	233926	88	29.52	34
39	786083	71	Male	168	74	26.22	115	96	74	normal	b/l rhonchi present	normal	normal	5278	50	21	6	7	1	15.86	4.52	42	248732	97	34.52	31
40	790377	66	Male	175	70	22.86	146	84	82	normal	left sided absent breath sounds	normal	normal	11206	74	23	6	7	0	13.70	3.57	49	219138	90	32.57	34

S. No	Erythrocyte sedimentation rate	Red cell distribution width	Urea (mg/dl)	Creatinine (mg/dl)	Uric Acid (mg/dl)	Blood Urea Nitrogen (mg/dl)	FVC	FEV1	FEV1/FVC	HIV Serology	ECG	Chest x-ray	Acute exacerbation of COPD	Lung malignancy	Pleural effusion	Pneumothorax	Cor pulmonale	Cardiac arrhythmias	SpO2	Temperature	Respiratory Rate	2D ECHO	STAGES OF COPD
1	3.79		39	0.58	3.58	11	61	37	0.61	negative	Multi focal atrial tachycardia	EMHYSEMA	No	No	No	No	Yes	Yes	95	99	22	RA RV DILATED	III
2	4.56		40	1.64	7.64	12	63	36	0.57	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	98	99	15	NORMAL	III
3	3.64		22	1.52	4.52	13	65	40	0.62	negative	sinus rhythm	left sided homogenous opacity	Yes	No	Yes	no	No	No	99	102	25	NORMAL	III
4	4.61		14	0.72	4.72	8	62	38	0.61	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	96	101	13	NORMAL	III
5	3.51		34	1.51	5.51	12	66	41	0.62	negative	atrial fibrillation	EMHYSEMA	No	No	No	No	No	Yes	98	99	24	NORMAL	III
6	4.71		27	0.62	7.62	7	69	36	0.52	negative	sinus rhythm	b/l non-homogenous opacities	Yes	No	no	no	No	No	97	101	23	NORMAL	III
7	4.6		8	1.64	7.64	14	63	29	0.46	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	98	101	13	NORMAL	IV
8	3.58		27	1.54	4.54	9	70	40	0.57	negative	sinus rhythm	right sided homogenous opacity	No	No	Yes	No	No	No	95	101	22	NORMAL	III
9	4.5		23	1.7	7.7	9	64	37	0.58	negative	atrial fibrillation	right sided non-homogenous opacity	Yes	Yes	No	No	Yes	Yes	96	102	24	RA RV DILATED	III
10	4.6		29	1.41	5.41	15	72	40	0.56	negative	sinus rhythm	left sided homogenous opacity	No	No	No	Yes	No	No	98	96	23	NORMAL	III
11	4.59		30	0.62	7.62	15	72	42	0.58	negative	sinus rhythm	left sided homogenous opacity	Yes	No	Yes	No	No	No	97	101	23	NORMAL	III
12	3.77		15	0.7	7.7	10	63	38	0.60	negative	sinus rhythm	righ sided homogenous opacity	No	Yes	Yes	No	No	No	98	100	16	NORMAL	III
13	4.65		28	0.71	4.71	16	62	40	0.65	negative	Multi focal atrial tachycardia	left sided homogenous opacity	No	No	No	Yes	Yes	Yes	99	98	19	RA RV DILATED	III
14	4.68		12	1.67	7.67	19	65	41	0.63	negative	sinus rhythm	EMHYSEMA	Yes	No	No	No	No	No	95	103	22	NORMAL	III
15	3.53		8	1.68	7.68	16	70	37	0.53	negative	sinus rhythm	right sided homogenous opacity	No	No	Yes	No	No	No	100	97	20	NORMAL	III
16	3.79		30	1.5	5.5	19	62	37	0.60	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	96	100	14	NORMAL	III
17	4.77		21	0.6	6.6	8	60	38	0.63	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	99	99	12	NORMAL	III
18	3.57		22	0.59	6.59	9	68	43	0.63	negative	Multi focal atrial tachycardia	right sided homogenous opacity	Yes	Yes	Yes	No	No	Yes	95	101	20	NORMAL	III
19	4.7		33	0.77	6.77	17	60	30	0.50	negative	sinus rhythm	right sided homogenous opacity	No	No	No	Yes	No	No	95	96	23	NORMAL	III
20	4.66		22	1.65	7.65	16	64	36	0.56	negative	sinus rhythm	EMHYSEMA	No	No	No	No	Yes	No	96	95	17	RA RV DILATED	III
21	4.64		24	1.68	7.68	19	73	37	0.51	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	98	101	14	NORMAL	III
22	4.61		25	1.53	4.53	12	74	41	0.55	negative	multi focal atrial tachycardia	b/l non-homogenous opacities	Yes	No	No	No	No	Yes	97	102	25	NORMAL	III

23	3.51		14	0.79	6.79	12	71	37	0.52	negative	sinus rhythm	right sided homogenous opacity	No	No	Yes	No	No	No	100	98	22	NORMAL	III
24	4.71		16	0.77	6.77	12	60	29	0.48	negative	atrial fibrillation	EMHYSEMA	No	Yes	No	No	No	Yes	99	97	25	NORMAL	IV
25	4.6		11	0.57	3.57	10	70	41	0.59	negative	sinus rhythm	b/l non-homogenous opacities	Yes	No	No	No	No	No	97	101	24	NORMAL	III
26	4.55		17	0.7	7.7	15	73	37	0.51	negative	sinus rhythm	left sided homogenous opacity	No	No	No	Yes	Yes	No	98	98	15	RA RV DILATED	III
27	4.83		28	0.56	3.56	16	68	44	0.65	negative	sinus rhythm	EMHYSEMA	Yes	No	No	No	No	No	99	100	24	NORMAL	III
28	3.5		13	1.64	7.64	14	72	42	0.58	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	98	101	12	NORMAL	III
29	3.58		22	0.61	7.61	14	67	35	0.52	negative	Multi focal atrial tachycardia	left sided homogenous opacity	Yes	No	Yes	No	No	Yes	97	101	26	NORMAL	III
30	4.58		29	1.51	5.51	9	71	37	0.52	negative	sinus rhythm	right sided homogenous opacity	No	Yes	No	Yes	No	No	99	98	19	NORMAL	III
31	3.64		38	0.71	4.71	14	64	41	0.64	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	95	101	14	NORMAL	III
32	4.83		21	0.6	4.6	11	62	35	0.56	negative	atrial fibrillation	b/l non-homogenous opacities	Yes	No	No	No	No	Yes	99	101	25	NORMAL	III
33	4.72		32	0.58	3.58	7	68	47	0.69	negative	sinus rhythm	left sided non-homogenous opacity	No	Yes	No	No	Yes	No	100	98	24	RA RV DILATED	III
34	3.51		35	0.56	3.56	15	73	39	0.53	negative	sinus rhythm	right sided homogenous opacity	Yes	No	No	Yes	No	No	96	102	26	NORMAL	III
35	4.62		23	0.61	7.61	16	70	43	0.61	negative	atrial fibrillation	left sided homogenous opacity	No	No	Yes	No	No	Yes	96	99	22	NORMAL	III
36	3.64		20	0.76	4.76	11	60	30	0.50	negative	sinus rhythm	right sided homogenous opacity	No	Yes	No	Yes	No	No	99	101	14	NORMAL	III
37	4.54		40	1.55	4.55	8	70	37	0.53	negative	Multi focal atrial tachycardia	EMHYSEMA	No	No	No	No	Yes	Yes	99	100	20	RA RV DILATED	III
38	3.7		41	1.52	4.52	14	73	39	0.53	negative	sinus rhythm	b/l non-homogenous opacities	Yes	No	No	No	No	No	99	101	27	NORMAL	III
39	4.89		37	1.52	4.52	10	64	39	0.61	negative	sinus rhythm	EMHYSEMA	No	No	No	No	No	No	97	101	15	NORMAL	III
40	4.62		30	0.57	3.57	9	61	29	0.48	negative	sinus rhythm	left sided homogenous opacity	Yes	No	Yes	No	Yes	No	96	102	26	RA RV DILATED	IV