PREVALENCE AND THE EFFECTS OF ANEMIA IN COPD PATIENTS, TERTIARY CARE HOSPITAL, INDIA

Mobina Dokhaei*1, S. Ramachandran2, Vida Bagheri3, Bita Bagheri4

Abstract

Background: Chronic obstructive pulmonary disease (COPD) is a typical preventable and treatable lifestyle-related disease with high global predominance. COPD is associated with significant morbidity and mortality worldwide. Comorbidities are important events in the natural history of the disease and adversely affect the morbidity and mortality of COPD patients. Cardiovascular diseases, lung malignant growth, osteoporosis, and wretchedness are normal comorbidities reported for COPD. Recently, anemia has been perceived as a frequent comorbidity in COPD patients.

Objectives: is to find the presence of anemia in COPD patients and its relationship with disease severity. Tertiary Care Hospital, India.

Method: It was a prospective observational study conducted in intensive care unit (ICU), medical wards, surgical wards and highly intensive care unit (HICU) of tertiary care hospital, conducted for 6 months. All patients diagnosed with Asthma and COPD in medical, surgery, and HICU and ICU wards included. The patient data collection form was used to collect all the details like inpatient, age, sex, social history, past history, laboratory data, diagnosis, therapeutic management. The second step was identification of anemic patients with COPD and Asthma or both, and analyzing the important laboratory data to find out the effect of anemia on disease and therapeutic managements for the same. The drug interaction from collected data was compare with guidelines. After complication analysis of prescription was completed then all the data was entered to the appropriate software and the results were obtained

Results: The result of this study showed male patients were listed more (66%) than female (34%). The majority members of patients were in 50-79 years' age group, also we found out that the percentage of anemic female (35.2%) is more than anemic male (30. 3%). In this study we found that out of 300 patient's anemia was confirmed in 96 patients. The clinical parameters as cough, expectoration, breathlessness, number of hospitalization and etc. were listed more in anemic patients compared to non-anemic. With the help of this study, it was understood that anemia is being more prevalent in most of the sufferers in from COPD. The result of this study provide evidence that variable of inflammatory biomarkers, including blood eosinophil and neutrophil were found to the higher them the normal level in COPD-ASTHMA patients.

Conclusion: The result of this study provide evidence that variable of inflammatory biomarkers, including blood eosinophil and neutrophil were increased in COPD-ASTHMA patients, that also can be used to support the diagnosis of ASTHMA-COPD.

Keywords: Anemia, disease severity, COPD and ASTHMA patients

[1,3,4] Doctor of Pharmacy Student, Department of Pharmacy Practice, GIET School of Pharmacy, Andhra University, India

[2] Professor and Head, Department of Pharmacology, GIET School of Pharmacy, Andhra University, India

[1*]Email: Mobina.do1998@gmail.com

2 Email: ramachandran@giet.ac.in

3 Email: vida.bagheri18@gmail.com

4 Email: Bitabagheri37@yahoo.com

https://orcid.org/0000-0002-4474-8964
https://orcid.org/my-orcid?orcid=0009-0004-4116-3436
https://orcid.org/my-orcid?orcid=0009-0004-9014-1989
https://orcid.org/my-orcid?orcid=0009-0001-8524-5511

Introduction

The global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (COPD) [1] defines COPD as a typical preventable and treatable disease. Described by a diligent wind current limit is typically progressive and associated with an improved chronic provocative reaction, in the airways and the lung, to harmful particles or gases. Intensifications and comorbidities add to the general severity in individual patients [2]. Systemic effects and/or comorbidities are significant occasions in the regular history of the disease and have an ability to increase the dismalness, financial weight, and mortality of COPD. Comorbidity is a disease interaction coexisting with COPD and is likely because of normal gamble factors. While coexisting illnesses are a direct result of the patient's basic COPD, it is known as a systemic impact. [1,3] Therefore, the systemic effects of COPD are direct consequences of the disease with a cause-and-impact relationship [4]. Screening of the comorbidities ought to be a significant component in the management of a COPD patient.

The factors that have been linked to systemic consequence and comorbidities in COPD patients are systemic inflammation and shared risk factors, smoking and actual inactivity/deconditioning.[3] Systemic inflammation is a generally concentrated on subject in COPD and has been possibly linked to comorbidities. Systemic inflammation in COPD might be the direct consequence of a systemic 'spill-over' of the ongoing pulmonary inflammation. Second, COPD is a piece of the chronic systemic inflammatory condition [5] and pulmonary indications are one piece of the numerous organs split the difference, because of the consequences of systemic inflammation. Systemic appearances and comorbidities regularly detailed in COPD include cardiovascular disease, hunger, osteoporosis, gastroesophageal reflux, and clinical despondency and anxiety.[6] lately, anemia has turned into another comorbidity that has gained significance in patients with COPD [7]. Traditional teaching in clinical medicine believes polycythemia to be a typical unfriendly occasion of hypoxemia in COPD. Notwithstanding, these days this happens less habitually because of more thorough revision of hypoxemia by domiciliary long haul oxygen therapy.[8] On the other hand, anemia has been accounted for all the more regularly in relationship with COPD lately with an effect on the personal satisfaction (QOL), healthcare use, and survival. [9,10] This survey will zero in on different causes of anemia, its pathogenesis, and its effect on patients with COPD.

Iron is a pivotal micronutrient as it is involved in several metabolic processes, for example, DNA synthesis, oxygen transport, cellular metabolism, and mitochondrial respiration [11, 12]. Then again, environmental sources of iron and other particles can upset and interfere with nearby iron-homeostasis in the lung [13]. Qualities connected with iron-metabolism are associated with COPD, and openness to tobacco smoking, air contamination, and other destructive substances influence on administrative instruments, possibly driving the pathogenesis of COPD [13-15]. In any case, these processes are not restricted to the lung, as inflammatory cytokines that are induced and delivered throughout COPD [16, 17] can likewise affect iron homeostasis. Thereby, inflammatory cytokines and the increased articulation of the expert controller of iron homeostasis hepcidin result in increased acquisition and storage of iron within cells of the reticuloendothelial framework. This results in functional iron deficiency (FID) and anemia of inflammation (man-made intelligence), reflected by low circulating iron levels and hence decreased accessibility of the metal for erythropoietic cells, while levels of the iron storage protein ferritin are typical or increased as a consequence of reticuloendothelial iron retention. [17]

MATERIALS AND METHODS

the study was conducted in intensive care unit (ICU), medical wards, surgical wards and highly intensive care unit (HICU) of Tertiary Care Hospital, India, for a period of 6 months from October 2021 march 2022. The first step was to design a data collection form. the patient data collection was used to collect all the details like

inpatient number, age, sex, social history, past history, laboratory data, diagnosis, therapeutic management. The second step was finding of anemic patients with COPD and Asthma or both, and analyzing of important laboratory data to find the effect of anemia on disease and therapeutic managements.

The diagnosis of COPD depended on pulmonary function test which was done in all patients. According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, COPD was defined based on the post bronchodilator forced expiratory volume in 1 s (FEV1)/forced vital capacity (FVC) ratio of <0.70 and reversibility to an inhaled bronchodilator in FEV1 <12% or <200 ml after administration of 200 μg salbutamol (2 puffs) using a compressed metered-portion inhaler with a spacer.[18]

Chart Cushion Crystal variant 6.01 (Diagram Cushion software Inc.; La, Jolla, CA, USA). was utilized for the analysis of data. All demographic and clinical data were communicated as a mean ± standard deviation or percentage. The Chi-square test was utilized for categorical data and gatherings were looked at by unpaired t-test or one-way analysis of variance. $P < 0.05$ was considered statistically significant. Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2016.

RESULT AND DISCUSION

Out of 100 patients 36 of them are female (2 of them are between 40-49 years old ,9 of them are between 50-59 years , 9 of them are between 60-69 years, 8 of them are between 70-79 and 8 of them are >79 years, all are married ,17 of them is educated and 17 of them are non-educated) and 66 of them are male (2 of them is between 30-39 years , one is between 40-49 years , 14 of them are between 50-59 years , 24 of them are between 60-69 years ,17 of them are between70-79 years and 8of them are >79 years old ,all are married ,55 of them are educated and 11 of them is non-educated). Table 1

Table 1: Demography details

	GENDER							
AGE	**MALE**				**FEMALE**			
Marital Status	**Single**		**Married**		**Single**		**Married**	
Educated	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**	**Yes**	**No**
1)20-29YRS	0	0	0	0	0	0	0	0
2)30-39 YRS	0	0	2	0	0	0	0	0
3)40-49 YRS	0	0	1	0	0	0	2	0
4)50-59 YRS	0	0	12	2	0	0	3	6
5)60-69 YRS	0	0	18	6	0	0	4	5
6)70-79 YRS	0	0	16	1	0	0	5	3
7) >79YRS	0	0	6	2	0	0	3	3
Presence Of Anemia	**Yes**		**No**		**Yes**		**No**	
	20		46		12		22	

Out of 100 patients, 8 of them have medical history of COPD, 4 of them has asthma, 10 of them has asthma-COPD, 47 with COPD-other, 28 with asthma- other and 3 with other medical history.

Out of the drugs used in treatment of patients 134 of them were anti-asthmatic /bronchodilator, 133 were antibiotics, 114 of them were anti-inflammatory, 2 of them were adrenal glucocorticoid and one of them was expectorant. Table 2

Table 2: Drugs used in patient

DRUG CLASS	DRUG NAME	NUMBER
Bronchodilator	AMINOPHYLLINE/ THEOPHYLINE/DOXOPHYLLINE/SALBUTAMOL-IPRATROPIUM BROMIDE INHALER/	134
Antibiotics	AZITHROMYCINE/PIPERACILIN-TAZOBACTAM/CEFTRIAXONE/AMOXICILLIN/ CLARITHROMYCIN/CIPROFLOXACIN	133
Anti-Inflammatory	BUDESONIDE INHALER/ HYDROCORTISONE/ MONTELUKAST	114
Adrenal Glucocorticoid	DEFLAZACORT	2
Expectorant	MUCOLYTE	1

Out of 100 patient's lab data result shows 56 of them have high level of neutrophil, 41 of them have low level of eosinophil and 46 of them have low level of hemoglobin. Table 3

Table 3: Lab Data for Asthmatic Patients

LAB DATA FOR ASTHMA PATIENTS		
Name	**Level (%)**	**Number**
Neutrophils count	NORMAL (45-75%)	13
	HIGH (>75%)	20
	LOW (<45%)	0
Eosinophil count	NORMAL (1-6%)	19
	HIGH (>6%)	1
	LOW (<1%)	13
Hemoglobin	NORMAL (13.5-17.5%)	17
	HIGH (>18%)	0
	LOW (<13%)	16

Table 4: lab data for COPD patient

LAB DATA FOR COPD PATIENTS		
Name	**Level (%)**	**Number**
Neutrophils Count	NORMAL (45-75%)	22
	HIGH (>75%)	35
	LOW (<45%)	0

Eosinophil Count	NORMAL (1-6%)	31
	HIGH (>6%)	2
	LOW (<1%)	24
Hemoglobin Count	NORMAL (13.5-17.5%)	26
	HIGH (>18%)	1
	LOW (<13%)	29

In our study from 11 COPD-Asthma patients 7 of them had elevated degree of neutrophil and low degree of eosinophil, additionally from 32 Asthmatic patients 20 of them had elevated degree of neutrophil and 16 of them had low degree of eosinophil and from 57 COPD patients, elevated degree of neutrophil and low degree of eosinophil with 35, 29 respectively. table 4

Our result has been contrasted and JING GAO et al, in their study result the degree of neutrophil significantly increased in COPD-Asthma (64%) when contrasted and asthma and COPD gatherings. Likewise, low eosinophil level was more in COPD-Asthma bunch (62%) when contrasted and the Asthma and COPD groups.[19]

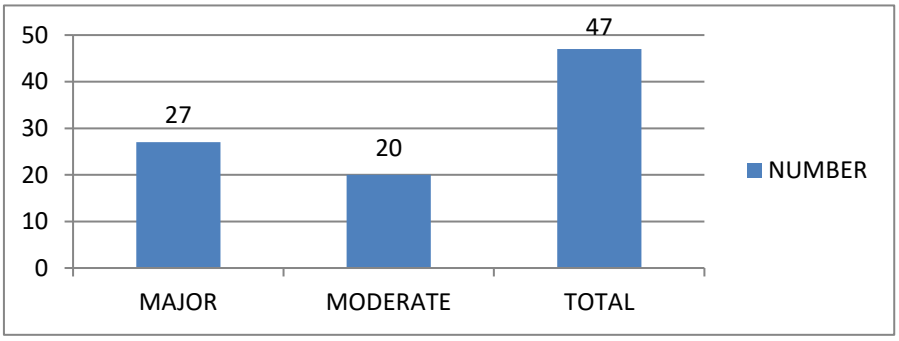

Figure 1: Number of Severity of drug interaction

In this study we found that these are some drug-drug interactions between drugs with each other. We found that from total 27 major interactions, interaction between ASPIRIN and CLOPIDOGREL was the most major drug-drug interaction, which caused increased risk of bleeding, so monitoring of blood counts may be warranted.

This result was same with the result which found by STOCKLY'S drug interaction edited by Williams D, [20] in their study also the concomitant use of ASPIRIN and CLOPIDOGREL may increase risk of bleeding so if co-administration is required, monitoring of blood counts may be warranted. [21]

Table 5: Clinical profile and morbidity associated with the COPD patients under study.

PARAMETER	ANEMIC	NON-ANEMIC	TOTAL NUMBER	P value
Cough	**18**	**52**	**70**	**0.065**
Expectoration	**15**	**47**	**62**	**0.066**
Breathlessness	**19**	**47**	**66**	**0.053**

Duration of Breathlessness	**(>5yrs) 3**	**18**	**21**	**0.063**
	(<5YRS)20	**45**	**65**	**0.063**
No. of Exacerbations	**(>5TIME) 2**	**5**	**7**	**0.074**
	(<5TIME) 24	**45**	**69**	**0.074**
No of Hospital Admissions	**(>2TIME) 12**	**19**	**31**	**0.053**
	(<2TIME) 18	**46**	**64**	**0.053**

we find out the clinical parameters as cough, expectoration, breathlessness, duration of breathlessness >5yrs, no of exacerbation >5time and no of hospital admission >2time, are listed more in anemic patients compared to non-anemic patients. Table 5

Prevalence and characterization of ID and Anaemia

In our study population, 139 patients (68.1%) had no ID, while 25 patients (12.3%) uncovered CID, 21 patients (10.3%) FID and 19 patients (9.3%) Help (Figure 2). The absolute number of patients with ID increased during follow-up; nonetheless, the noticed changes between the two time points were not significant ($p>0.05$) (Figure 2).

Iron-replete patients had a significantly higher DLCOc when contrasted with patients with ID (63.47 ± 21.64 versus 50.80 ± 19.25 %, $p<0.01$), while CRP (0.52 ± 0.68 versus 0.69 ± 0.82 mg/dl, $p=0.03$) values were significantly lower (Figure 3). There were no significant contrasts in age, FEV1, CAT-score and LVEF while comparing ID with iron-replete patients.

The mean hemoglobin levels at study inclusion were 142.80 ± 16.93 g/L and showed a slight yet not significant decline during follow up (139.44 ± 17.22g/L, $p=0.2$). Anemia was present in 29 patients (14.2%) at study inclusion, and the predominance increased to 20.8% during follow-up ($p=0.5$, Figure 4). Figure 4 shows the distribution of anemia types, IDA, IDA + artificial intelligence and anemia not related to ID at baseline and follow-up. Patients with anemia had a significantly lower FEV1 (43.19 ± 17.57 versus 51.49 ± 17.09%, $p=0.03$) and DLCOc (48.35 ± 17.74 versus 61.12 ± 21.78%, $p=0.01$), as well as higher CRP levels (0.77 ± 0.55 versus 0.54 ± 0.75 mg/dl, $p<0.01$) contrasted with subjects without anemia irrespective of the presence of ID. CRP levels correlated with ferritin ($r=0.02$, $p<0.01$), Tf ($r=-0.220$, $p<0.01$), and TSAT ($r=-0.281$, $p<0.001$).

A total of 116 patients (56.95 %) got an ACT. No significant contrasts in Hb, serum iron, ferritin, Tf and TSAT were seen between patients having ACT contrasted with patients without ACT, though sTfR (3.70 ± 2.58 versus 3.46 ± 0.95 mg/L, $p=0.02$) and ferritin-index (2.23 ± 2.52 versus 2.00 ± 0.94, $p<0.01$) were slightly, yet significantly higher in patients with ACT. Further, the presence of anemia didn't show a significant association with ACT ($p=0.42$) either. A total of 54 (26.5 %) of patients had a gastrointestinal comorbidity. No significant contrasts in Hb, serum iron, Tf, TSAT or sTfR were detected between patients with or without a gastrointestinal condition

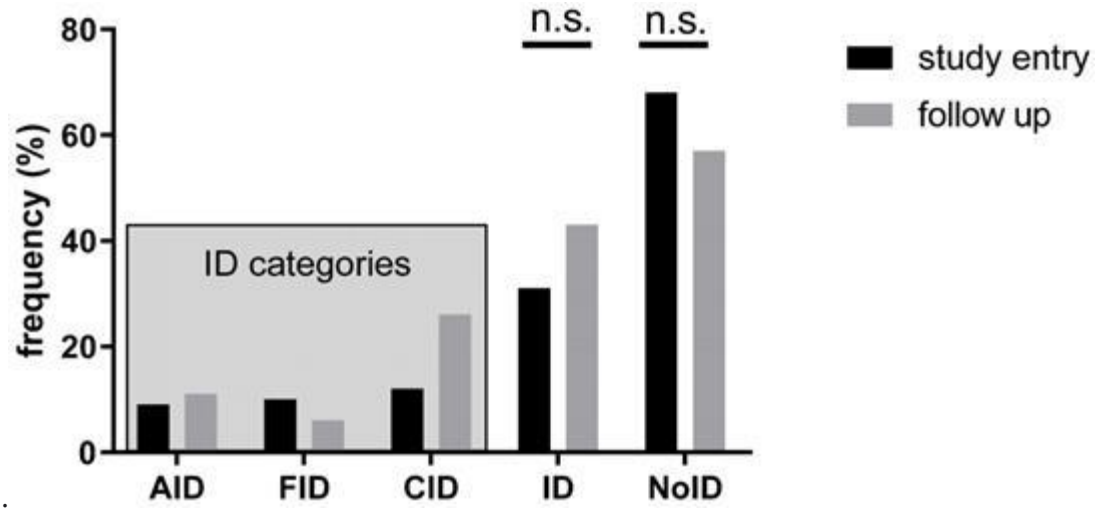

Figure 2 Prevalence of ID at study inclusion and follow-up. AID: absolute iron deficiency, FID: functional iron deficiency, CID: combined iron deficiency, ID: iron deficiency, NoID: no iron deficiency, n.s.: not significant at $p > 0.05$.

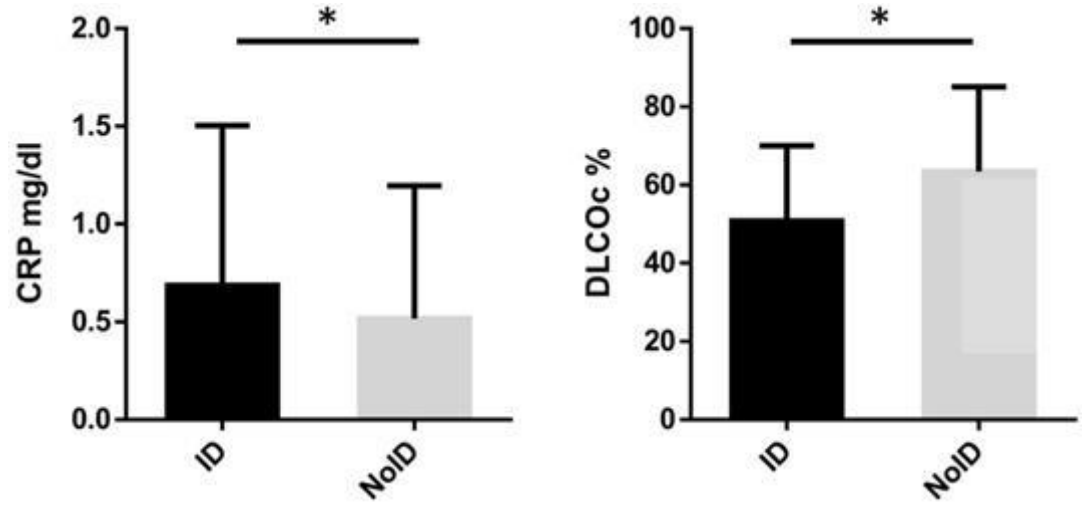

Figure 3 Diffusion capacity and CRP levels depending on iron status. * Indicates statistical significance at $p < 0.05$. ID: iron deficiency, NoID: no iron deficiency, DLCOc: diffusion capacity, CRP: C-reactive protein.

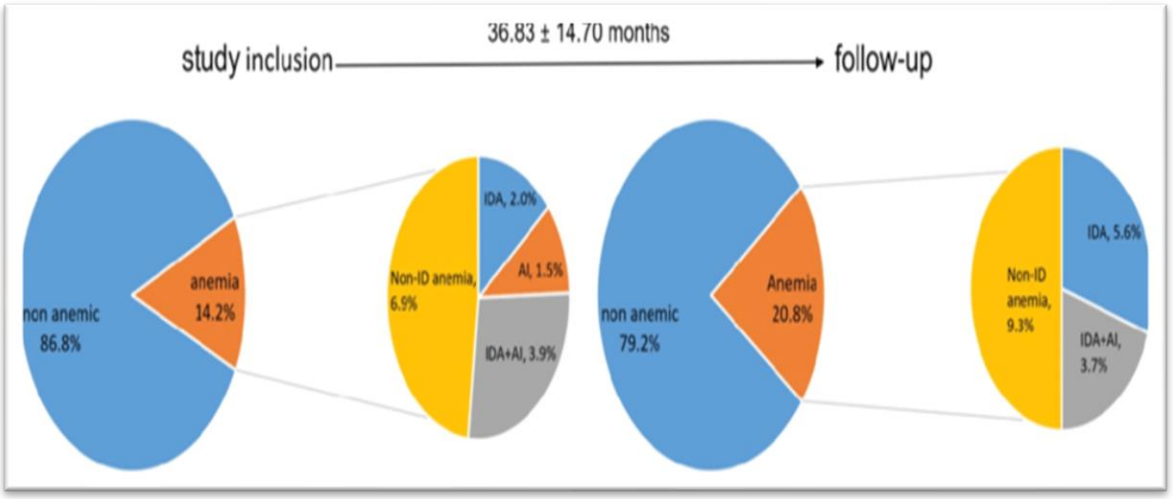

Figure 4 Distribution of anemia, IDA and ACD at study inclusion, and follow-up. IDA: iron deficient anemia, ACD: anemia of chronic disease, ID: iron deficiency.

Anemia was available in 14% of patients at concentrate on consideration, and the pervasiveness marginally increased during follow-up. Anemia was related with elevated CRP and a lower FEV1, parameters mirroring an all the more undeniable level illness, while ACT or gastrointestinal comorbidities didn't correspond with anemia. This underlines the ongoing verification that moreover anemia is significantly prevalent among COPD patients, going wherever somewhere in the range of 4.9 and 38.0% [22,23]. Anemia of persistent sickness is the most notable sort of anemia in COPD [24] depicted in the writing, equivalent to this study's discoveries. However, the little understanding numbers in the two studies limit the validity of these outcomes. Likewise, as ACT didn't influence hemoglobin count, its use may be viewed as safeguarded in this study accomplice. Differentiating, a multicenter investigation of patients with atrial fibrillation, of whom 70% got a Demonstration, contrasting clinical results in subgroups and without comorbid COPD uncovered a higher rate of hemorrhagic events in COPD patients [25]. Concerning the connection between iron parameters and COPD, just sTfR and ferritin-index were negatively connected with FEV1. Parameters like sTfR or ferritin-index permit more precise portrayal of ID as cell iron demand, iron capacity, and systemic aggravation are thought about. COPD stages, the repeat of severe intensifications, or side effects surveyed as Feline Score were not connected with systemic ID, which is amazing and questions the job of elevated ID power in the pathogenesis of COPD. In this specific circumstance, it is fundamental to recognize neighborhood and systemic iron dyshomeostasis. Past studies showed high iron substance in lung tissues of state of the art COPD patients stood out from sound controls, with a heterogeneous dissemination of iron at a cell level, including mitochondria [26]. Mitochondrial iron stacking has as of late been connected to COPD, as it is upregulated by iron-responsive component restricting protein 2, which is increased in COPD. Its deficiency seems to alleviate tobacco smoke prompted pulmonary aggravation [27] in light of the fact that mitochondrial iron stacking hinders mitochondrial capability and oxidative phosphorylation [28]. Moreover, Yoshida et al. showed that tobacco smoke receptiveness prompts ferroptosis, an iron-subordinate type of regulated cell demise, which could expect a section in COPD pathogenesis [29]. In this manner, fair-minded revision of ID of any reason could deal with systemic iron homeostasis yet could have undesired different insane regional impacts in the lung [30,31]. This study features that randomized prospective preliminaries investigating the advantage of iron supplementation in COPD are warranted to deal with the clinical administration of these patients.

Despite the fact that our information expand the ongoing information about ID in COPD patients, we really want to recognize a couple of limits, the significant one being the retrospective arrangement. In this manner, the observation time span was for the most part established on the availability of laboratory studies. Also, around 2/3 of the patients were lost during follow-up, biasing the outcomes, especially concerning anemia, given the low prevalence, especially in outright numbers. Further, the possible job of nutrition and pulmonary cachexia adding to ID

couldn't be tended to on account of the retrospective review plan. Further prospective studies, including organ-unequivocal iron appraisal as well as interventional studies investigating the advantage of iron supplementation, are warranted to certify the thus presented hypotheses.

CONCLUSION

The result of this study showed male patients is listed more (66%) than female (34%). the majority individual from patients was in 50-79 years' age bunch, additionally we figured out that the percentage of frail female (35.2%) is more than pale male (30.3%).

In this study we discovered that out of 100 patient's anemia was affirm in 32 patients. The clinical parameters as hack, expectoration, breathlessness, number of hospitalization and etc. are listed more in iron deficient patients contrasted with non-pallid. Likewise, we realize that anemia is being more prevalent in most of the victims of COPD.

The result of this study give proof that variable of inflammatory biomarkers, including blood eosinophil and neutrophil were more in COPD-ASTHMA patients, that additionally can be utilized to support the diagnosis of ASTHMA-COPD.

ID is normal among COPD patients, but the predominance exceptionally relies upon the definition applied, and a uniform definition for accurate diagnosis doesn't exist. ID is most frequently caused by a combination of absolute and functional ID, and commonness is increasing during the course of the disease. ID associates with FEV1 and DLCOc restriction, particularly while using more robust parameters like sTfR and ferritin-index, which account for inflammation. Respiratory doctors should know about the high commonness, as it might reflect a more severe COPD phenotype. Prior to iron supplementation, the underlying type of ID ought to be identified and particularly with the presence of Help extended screening to preclude occult blood misfortunes should be considered. Appropriate detection and treatment options of ID should be evaluated in future prospective studies.

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