

ASSOCIATION BETWEEN ANEMIA AND CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

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ABSTRACT:

Introduction: Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease. Systemic inflammation in (COPD) may initiate or worsen comorbidity of the disease. Anemia is one important comorbidity.

Aim: We aimed to analyze prevalence of anemia in patients with Chronic Obstructive Pulmonary Disease (COPD) and to correlate severity of anemia with severity of COPD with respect to: FEV1 values, mMRC grading and exacerbation.

Materials and Methods: This is a cross-sectional study conducted in Tishreen University Hospital, Lattakia, Syria during the period between July 2017 and July 2018. 107 COPD patients were recruited. CBC was determined and pulmonary function tests were performed for all patients. The symptoms of COPD in each patient were estimated by modified Medical Research Council (mMRC) dyspnea scale. The parameters of pulmonary function (FEV1 and FVC), history of exacerbation were also evaluated.

Results: Among 107 COPD patients there were 21 anemic patients (19.62%). Mean hemoglobin was (10.86±0.98) in anemic patients while was (14.11±1.2) in non-anemic ones. That was statistically significant with 'p' value of 0.0001.

Correlation was found with the following: number of acute exacerbations in the past year (P value=0.0001) (r = -0.5), British Medical Research Council dyspnea scale (P value=0.0001) (r = -0.4), while there was no correlation with forced expiratory volume in one second % predicted (FEV1%; (0.2).

Conclusion: Anemia may be found in patients with COPD because of the inflammatory process that occurs. Prevalence of anemia is unknown. It may be associated with poor clinical status.

Keywords: Anemia, COPD, FEV1, mMRC



INTRODUCTION:

Chronic obstructive pulmonary disease (COPD), a highly prevalent condition associated with increased morbidity and mortality, is basically characterized by the presence of expiratory flow limitation that is not fully reversible.^[1]

It is not possible to define COPD based solely on forced expiratory volume in the 1s (FEV1) so the Global Initiative for Chronic Obstructive Lung Disease (GOLD) has devised a multidimensional definition

to assess COPD. The new COPD assessment integrates a combined assessment of clinical symptoms (the COPD Assessment Test (CAT)), severity of airflow limitation, the previous history of exacerbations, the modified Medical Research Council (mMRC) and classifying patients into groups A-D.^[2]

Systemic inflammation in chronic obstructive pulmonary disease may also

initiate or worsen comorbid diseases. Anemia is one important comorbidity.^[3]

The anemia found in patients with chronic infectious, inflammatory and neoplastic disorders, known as ACD, is one of the most common syndromes in medicine. A characteristic finding of the disorders associated with ACD is increased production of cytokines that mediate the immune or inflammatory response, such as tumor necrosis factor, interleukin-1 and the interferons. All the processes involved in the development of ACD can be attributed to these cytokines, including shortened red cell survival, blunted erythropoietin response to anemia, impaired erythroid colony formation in response to erythropoietin and abnormal mobilization of reticuloendothelial iron stores.^[4]

There is limited information in the current literature describing the distribution of hemoglobin (Hb) and its impact on outcomes in the COPD population. Polycythemia, traditionally thought to be highly prevalent in COPD, occurs less frequently now with more rigorous correction of hypoxemia.^[5] Conversely, recent reports suggest that anemia in patients with COPD is highly prevalent and associated with increased mortality.^[6-7] Although the association between anemia and dyspnea is generally well established,^[8] the contribution of Hb to breathlessness and other clinical manifestations in patients with COPD is not known and may be of great interest as a potential target for directed

therapy.^[9] The purpose of this study was to determine the prevalence of anemia in patients with COPD attending a pulmonary clinic, as well as to explore the associations between severity of anemia and severity of COPD with respect to mMRC grading, exacerbations and FEV1 values.

MATERIALS AND METHODS:

A clinical diagnosis of COPD was considered in all patients above 40 years of age came to in pulmonology department at Tishreen University Hospitals, Lattakia, Syria, during the period between July 2017 and July 2018 and who had dyspnea, chronic cough or sputum production, and/or a history of exposure to risk factors like smoke, fumes etc. for the disease.

Inclusion criteria: Stable COPD patients meet Spirometry criteria (patients with post bronchodilator FEV1/FVC < 0,7), whose age is above 40 years.

Exclusion criteria:

- Bronchial asthma.
- History of malignancy or hematological disorder
- Autoimmune disorder
- Thyroid disease
- Liver cirrhosis
- Heart failure (ejection fraction <50%)
- History of gastrointestinal or other hemorrhage
- Renal failure
- Blood transfusion in the last 4 months

- Pregnancy
- Mental impairment

-All patients were subjected to physical examination , chest X- ray , respiratory function test , and routine blood analysis test and the data collected included age, gender, current medications and accompanying diseases.

COPD assessment : all patients enrolled were assessed by a detailed questionnaire .

The number of exacerbations in the previous year , Dyspnea was assessed by the mMRC dyspnea scale

Lung function in COPD was classified into four grades based on post-bronchodilator FEV1: GOLD1(FEV1 \geq 80% predicted), GOLD2 (50% \leq FEV1<80% predicted) , GOLD3 (30% \leq FEV1<50% predicted) , GOLD4 (FEV1 <30% predicted).

CBC test: Anemia was defined by hemoglobin level <13 mg/dl in male patients and <12 mg/dl in female patients.^[10] To differentiate between iron deficiency anemia and anemia of chronic disease we used various other parameters like as Table(3).^[11]

Statistical analysis : Data were analyzed using IBM SPSS Statistics Version 19 for Windows . A value of $p < 0.05$ was considered statistically significant .The results were presented as mean \pm standard deviation (SD) for all variables that were normally distributed and as median with data range when not normally distributed. Differences

between groups were analysed using the independent samples t test, and between. Correlations between parameters were calculated with Spearman's correlation test.

RESULTS:

Among 107 COPD patients there was 21 anemic patients(19.62%) . The distribution of anemia in males and females was 57% and 43% respectively. Male/Female ratio was 1.3/1 in anemic patients while was 2/1 in non-anemic ones . That was statistically not significant($p=0.3$). Median age was 62 in anemic patients ,and 60 in non-anemic ones. That is statistically not significant, too.($p =0.2$) Table(1)

Mean hemoglobin was(10.86 \pm 0.98) in anemic patients while was (14.11 \pm 1.2) in non anemic ones. That was statistically significant with 'p' value of(0.0001) . Table(2)

Inflammatory anemia was the most common type of anemia in COPD patients 60% Table(4).

Correlation was found with the following :number of acute exacerbations in the past year (P value =0.0001)($r = - 0.5$), British medical Research Council dyspnea scale (P value=0.002) ($r = - 0.4$), severity of anemia with severity of dyspnea ($p=0.03$)while there was no correlation with forced expiratory volume in one second % predicted (FEV1%; ($p=0.6$)Table(5)

DISCUSSION:

The prevalence of anemia identified in our study (19.62%), That is higher than the 12.3% prevalence observed among COPD patients in Marcello Ferrari study^[14] and the 6.2% prevalence in Lorena Comeche Casanova study^[15]while is nearby to that reported in .K.Potillo and Shaheena Parveen studies of COPD patients.^[12-13]

Most COPD patients have anemia mild in grade (hemoglobin more than 10 mg/dl). Like.^[12-13-14-15]

Most common type seen is anemia of chronic disease (ACD) or inflammation That,s like.^[12-13-14-15]

The mechanism of anemia development in COPD might be similar to that in other chronic diseases. It has been shown that mediators of the immune and inflammatory response, such as tumor necrosis factor, IL-6, and interferon were potentially involved in the development of anemia in chronic illness.^[13]

The effects of anemia in COPD: The relationship between anemia and adverse clinical outcomes is wide recognized in other chronic disease states. The hemoglobin is the principal oxygen transport molecule. Any decrease in hemoglobin levels results in a corresponding reduction in the oxygen-carrying capacity of the blood which cause dyspnea and that it contributes to functional limitation in the anemic individual.

There is a comparison study done by C.Cote, M.D Zilberberg and S. H. Mody;^[16] they showed Dyspnea and functional status differed significantly between anemic and non-anemic patients. Mean MRC values were significantly higher (2.8 ± 0.9 versus 2.6 ± 0.8 ; $p=0.04$) in anemic compared with non-anemic patients.

Anemia in our study has significant correlation with number of exacerbation. Similar results have been in studies conducted by Shaheena Parveen.^[13]

CONCLUSION:

Prevalence of anemia among COPD patients is significantly higher and associated with poor clinical and functional status. Thus ,treatment of anemia may improve quality of life in these patients .Further studies are needed for determination of exact prevalence of anemia and its physiologic effects in COPD.

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TABLES:**Table (1): Comparison between Anemic and non-Anemic patients Features**

	Anemic	Non-anemic	Pvalue
N	21	86	0.002
Gender(M\F)	12/9	58/28	0.3
Age(median)	62	60	0.2

Table(2): Hematological Findings in Patients with COPD:

	Anemic	Non anemic	Pvalue
Hb	10.86±0.98	14.11±1.2	0.0001

Table (3):Differentiation between inflammatory and iron deficiency Anemia:

	Iron Deficiency	Inflammation
Serum Ferritin (mcg/l)	<15	30-200
Total Iron Binding Capacity	>360	<300

Table(4):Types of Anemia in COPD Patients

Type of Anemia	number of patients	Percentile Values
Inflammatory	13	61.90%
Iron deficiency	9	28.57%
Mixed	2	9.52%

Table(5): Comparison of spiromrtry , mMRC and exacerbations in Anemic and Non-anemic Patients:

	Anemic	Non-Anemic	P value	r
FEV1% [Range20-82]	61	55	0.2	-0.1
Exacerbations\y [1-10]	4	1	0.0001	-0.5
mMRC[Range1-5]	4	3	0.002	-0.4

COPD: chronic obstructive pulmonary disease.

FEV1% : forced expiratory volume in one second% predicted

mMRC: modified British Medical Research Council dyspnea scale.

Hb :Hemoglobin