Association between anemia and COPD in Iranian population

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Abstract

Background and Aim: Chronic obstructive pulmonary disease (COPD) is one of the major causes of morbidity and mortality in adults. Anemia is known as comorbidity in many chronic diseases that can increase morbidity and mortality of COPD. Recent studies have shown that anemia may be more prevalent than expected in COPD patients and can increase disabilities of COPD. In this study we have evaluated the correlation between anemia and the severity of COPD in patients referred to teaching hospitals of the Tehran University of Medical Sciences (TUMS), Tehran, Iran.

Material and Method: In this cross-sectional study the severity of COPD in 760 patients with dyspnea who referred to teaching hospitals of Tehran University of Medical Sciences and 96 stable COPD patients were categorize using a GOLD criteria from mild to moderate, severe and very severe. Anemia was determined as hemoglobin <13 g/dL in men and <12 g/dL in women, respectively. Demographic characteristics, spirometry parameters and laboratory findings were compared between anemic and non-anemic groups using Student *t*-test and regression tests (SPSS v.18 software).

Results: The Mean age of patients was 65 ± 13.07 years (59.4% male). Overall prevalence of anemia was 27% and there was no correlation between severity of COPD and anemia. Anemic patients were significantly older than non-anemic patients (71.1 ± 8.5 years vs. 65.4 ± 12.8 years; p=0.030). RBC count of anemic patients were significantly lower than non-anemic group (4.3 ± 0.5 vs. $5.02 \pm 0.8 \times 10^6/\mu L$; p<0.001). Erythropoietin levels in anemic group was significantly higher than non-anemic group (16.33 ± 2.43 vs. 10.22 ± 2.67 mu/ml; p<0.001) and there was a significant inverse correlation of hemoglobin vs erythropoietin (r= -0.8).

Conclusion: there was a high prevalence of anemia in COPD patients. Anemia can increase disabilities of COPD. Thus, treatment of anemia may improve quality of life in these patients. Further comprehensive studies are needed for determination of exact prevalence of anemia and its physiologic effects in COPD.

Keywords: COPD, Anemia.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is one of the major causes of morbidity and mortality in adults. As a result of oxygen deficiency, polycythemia is common in patients with COPD, but prevalence rate of anemia in COPD patients is reported about 13-33 %.[1-4] COPD can affect main extrapulmonary organs, including heart, brain, and musculoskeletal system. It has been shown that there is an increase in level of proinflammatory cytokines, including interleukin-1 (IL-1), interleukin- 6 (IL-6) and tumor necrosis factor-a (TNF-a). [5-6] Anemia is a known comorbidity in some disorders, including chronic renal failure, congestive heart failure, infections and cancer, and increases morbidity and mortality and impacts the quality of life. [7-11] Anemia can be a poor prognostic factor in COPD patients. [14] Recently, some studies have been shown that anemia may be more prevalent than previous estimations in COPD patients. It has been

shown that 10-15 percent of patients with severe forms of COPD concurrently suffer anemia. [12] In another cohort study, a direct association between hemoglobin levels and mortality of COPD patients was shown. [13] It has also showed that anemia can be associated with limitation in physical activity and worsen dyspnea in chronic disorders. [15] There are limited and controversial information about the relationship between the anemia and COPD, thus in the current study we tried to investigate the relation between anemia and severity of COPD.

Methods & Materials

In this study, 760 COPD patients who were referred to pulmonary clinic of teaching hospitals of Tehran University of Medical Sciences, including 96 stable COPD were investigated during 2010 to 2012. Spirometry was used to confirm the COPD in the patients. All COPD patients were clinically stable and under therapy. 74 patients with mean age of 65±13.07 (23 to 87 years old) entered the study. Patients who had no history of infection or had not been admitted during past 3 months, had no phlebotomy history during last year, had no coexisting diseases, including cancer, thyroid disease, liver or kidney disease and sever heart diseases, and had no history of active bleeding or other hemorrhages and folic acid or vitamin B12 deficiency were included in this study. Demographic characteristics (age, gender and smoking status), laboratory variables (complete blood count and differential), plasma ferritin level, reticulocyte index, plasma TSH level, blood urea nitrogen and plasma creatinine level, aspartate transaminase (AST) and alanine transaminase (ALT) levels, plasma erythropoietin (Epo), total iron binding capacity (TIBC), Serum iron, erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) were measured. Lung function tests were done. Cigarette smoking was measured as pack-years. By using Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria to determine, the severity of COPD, patients were classified into 4 groups (mild, moderate, severe, and very severe). Anemia was confirmed by hemoglobin <13 g/dL in men and < 12 g/dL in women, respectively, as explained previously. [14-17] This study was approved by institutional review board in Tehran University of Medical Sciences, Tehran, Iran.

Data Analysis

All statistical analysis, including prevalence rate, mean and standard deviation, were performed using SPSS version 18.0. Chi-square, T-test, regression, and correlation were used to determine the association between different variants.

Results

From 760 patients with dyspnea, 96 patients had an stable COPD, of those 74 patient had no other diseases. Forty-five patients were men (61%) and 29 were women (39%). Forty-three patients (58%) had a positive history of smoking and 31 patients had a history of inhalation of indoor air pollution, including cooking stoves or exposure to passive cigarette smoke. The mean cigarette consumption in smokers (with age of 20-65 years) was 36.6 ± 13.2 pack/year. Demographic characters of patients are shown in table 1.

Table1. Comparison between anemic and non-anemic patients' features

		Anemic group	Non-anemic group	P value
Mean age		71.1 ± 8.5	65.4 ±12.8	**0.03**
COPD Severity	Mild	0 (0.0%)	3 (4.1%)	> 0.05
	Moderate	9 (45%)	21 (40.5%)	
	Severe	7 (35%)	18 (33.8%)	
	Very severe	4 (20%)	12 (21.6%)	
Gender	Male	14 (70%)	31(57.4%)	> 0.05
	Female	6 (30%)	23 (42.6%)	
Smoking	Smoker	13 (65%)	30 (55.6%)	> 0.05
	Nonsmoker	7 (35%)	24 (44.4%)	

Based on the severity of COPD, patients were classified into 4 groups including: mild (4.1%), moderate (40.5%), severe (33.8%), and very severe (21.6%). Overall, 20 patients (27%) were identified to suffer concurrent anemia. The mean age of COPD patients with and

without anemia were 71.1 ± 8.5 vs. 65.4 ± 12.8 years (p=0.03), respectively. RBC count in anemic patients with COPD was significantly lower than non-anemic patients (4.3 ± 0.5 vs. 5.02 ± 0.8 million per micro-liter; p<0.001). ESR rate in anemic patients with COPD was significantly higher than non-anemic patients (29.15 ± 29.36 mm/hr vs. 17.42 ± 13.7 mm/hr; p=0.02). The erythropoietin level in anemic patients with COPD was significantly higher than non-anemic patients (16.33 ± 2.43 mu/ml vs. 10.22 ± 2.67; p<0.001) (Table 2).

Table2. Hematological findings in patients with COPD

Variable	Range	SD± Mean
Hb(g/dl)	9.2-19	1.8 ± 13.65
FEV1%	17.9-90	17 ±48.2
FEV1/FVC %	27.9-90	13.09 ± 56.4
WBC ($10^3/\mu L$)	3.4-21	3.5 ± 8.6
RBC ($10^6/\mu L$)	3.2-7.6	0.8 ± 4.8
Hct (%)	30.4-58	5.5 ± 43.4
Plt ($10^3/\mu L$)	105-394	16.9 ± 63.06
ESR (mm/hr)	1-25	9.5 ±20.65
BUN (mg/dl)	9-28	8.97 ± 19.2
Cr(mg/dl)	.6-1.6	0.6 ± 1.09
SGOT (IU/L)	10-42	8.3 ±33.7
SGPT(IU/L)	7-38	5.2 ± 28.8
EPO (mu/ml)	3-21	3.7 ± 11.75
Ferritine (ng/dl)	77-285	8.6 ± 90.5
BMI	15.57-43.96	6.9 ± 26.07

There was a reverse association between hemoglobin and erythropoietin levels. (r= -0.8) (Figure1)

Fig1. Relation between hemoglobin and erythropoietin levels in anemic and non-anemic
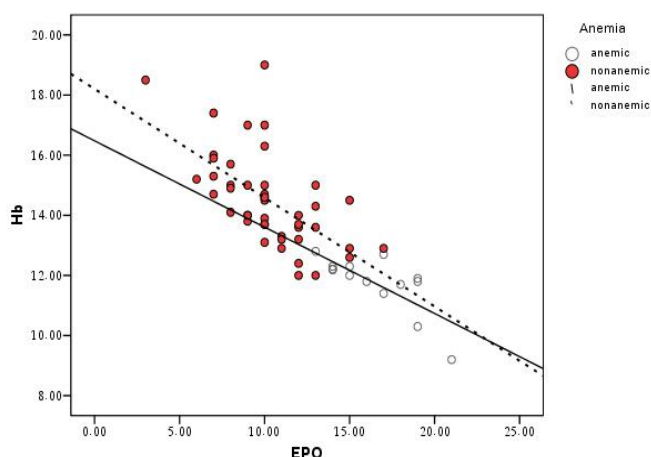
The severity of the COPD determined by spirometry was not significantly different between anemic and non-anemic groups (p>0.05) (Table 3).

Table3. Comparison of spirometric and laboratory results in anemic and non-anemic patients with COPD

	Anemic group	Non anemic group	P value
Age	8.5 ± 71.1	12.8 ±65.4	**0.03**
FEV1%	17.46 ± 49.37	17.37 ± 46.33	>0.05
FEV1/FVC %	13.92 ± 56.43	13.11 ± 56.09	>0.05
WBC ($10^3/\mu L$)	5.33 ± 9.87	2.67 ± 8.22	>0.05
RBC($10^6/\mu L$)	0.52 ± 4.22	0.72 ± 5.02	**<0.001**
Hct (%)	0.9 ±2.45	1.1 ± 2.1	>0.05
Plt ($10^3/ \mu L$)	66.51 ± 243.62	65.6 ± 237.4	>0.05
ESR (mm/hr)	29.36 ± 29.15	13.17 ± 17.42	**0.02**
BUN (mg/dl)	13.7 ± 2.94	6.53 ± 18.59	>0.05
Cr (mg/dl)	0.25 ± 1.02	0.24 ± 1.04	>0.05
SGOT (IU/L)	15.69 ± 26.3	43.9 ± 36.6	>0.05
SGPT(IU/L)	25.17 ± 24.1	38.64 ± 30.68	>0.05
EPO (mu/ml)	2.46 ± 16.33	2.67 ± 10.22	**<0.001**
Ferritin (ng/dl)	68.07 ± 80.56	53.23 ± 127.53	>0.05
BMI	6.1 ± 23.83	6.2 ± 25.58	>0.05

Discussion

The current study showed that the prevalence of anemia in COPD patients according to the WHO criteria was 27% .Previous studies have shown that prevalence of anemia in COPD patients can vary 10-15 %. In our study the prevalence of anemia was 27%, which is higher than the findings from previous studies [12, 19-21] that they mostly investigate greater sample size. However, most of those studies had been retrospective and were performed in several hospitals or different laboratories that failed to use the same clinical or laboratory methods to confirm the disease. In the current study, we examined all patients using a standard criteria for diagnosis of COPD and all laboratory procedures were performed at the same center by using the same diagnostic materials. Recently it has been shown that the high levels of erythropoietin in COPD patients indicates an erythropoietin resistance. [18] In that study, a reverse relationship was found between hemoglobin and erythropoietin level that attributed to a strong stimulating effect of sever hypoxia at higher stages of disease on erythropoietin production.[14] Several studies have been shown that regulation of blood

oxygen level and EPO production is a complicated process during which, different factors such as cytokines [22] or therapeutic agents, including the inhibitors of angiotensin converting enzyme or angiotensin receptor blockers [25, 26], can play an important role in inhibition of body responses to oxygen level changes. Chronic COPD has a greater role in initiation of anemia than a severe COPD. However, several studies stated that anemia can be induced by extensive inflammation following COPD or failure in response towards the erythropoietin.[6,16,17,21,22], but this hypothesis needs to be backed by more evidences. Dysfunction in transportation of the Iron reticuloendothelial resources can cause anemia in COPD patients. [23, 24]

Ageing has been also believed to be responsible for greater prevalence of anemia in COPD patients. [22,10,15,18] Annual costs for health services in anemic COPD patients are as twice more that non-anemic patients. [18] It has also been shown that anemic COPD patients had more comorbidities and mortalities. [10]. In addition to anemia, other health issues, including neurologic, respiratory and musculoskeletal disorders are more common in COPD patients. [10]

Conclusion

Our study showed that the prevalence of anemia in COPD patients is higher than that was previously stated by other studies (27%) and there was no significant relation between anemia and the severity of COPD. further investigation are required to better understand the association between the COPD and anemia and to gain a broader insights towards the impacts of these diseases in Iranian population.

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