

Prevalence of anemia in patients with chronic obstructive pulmonary disease

Marzieh Nojomi¹, Arash Ehteshami Afshar², Mohsen Saberi³

ABSTRACT

Objective: Chronic obstructive pulmonary disease (COPD) is associated with significant morbidity and mortality worldwide. This disease affects the lungs and organs outside the lungs. The aim of this study was to determine the prevalence of anemia in patients who were referred to teaching hospitals of Tehran University of Medical Sciences, Tehran, Iran.

Methodology: Three hundred ninety two patients with COPD who attended to the teaching hospitals of Tehran University of Medical Sciences, from March to June 2009 were assessed. Laboratory and clinical data of patients was gathered from their medical records. We used global initiative for chronic obstructive lung disease criteria in order to categorize severity of disease in patients.

Results: The mean age of patients was 66.5 ± 12.3 years and 289 (73.7%) subjects were men. The overall prevalence of anemia was 36.7% (95% CI: 31%-41%). Twenty two females (21.4%) and 110 males (38.1%) were anemic. There was a positive correlation between age and hemoglobin level. In group two (COPD stages I to II), there was 43.5% prevalence of anemia versus 34.1% in group three (COPD stages III to IV).

Conclusion: There was a high prevalence of anemia in patients with COPD. Anemia can limit the physical activity of these patients and worsen dyspnea. Therefore, more attention needs to be given to anemia while managing these patients in clinics.

KEY WORDS: Anemia, Chronic obstructive pulmonary disease, Comorbidity, Prevalence.

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INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the major causes of substantial morbidity and mortality in older adult. COPD is characterized by progressive airflow limitation that is not completely reversible.¹ It is shown that patients with COPD were more likely to be old, heavy smokers and belong to lower social class.² The prevalence rate of chronic bronchitis is 20% and 18.5% among men and women who smoked 20 or more cigarette per day respectively.³

COPD affects many organs outside the lungs such as heart, brain, and musculoskeletal as a "systemic effect of COPD".⁴ It is shown that these systemic effects are because of increased level of pro-inflammatory cytokines such as interleukin 1 (IL-1), IL-6 and tumor necrosis factor Alpha (TNF- α).^{5,6} Important prognostic factors in COPD included:

1. Marzieh Nojomi, MD, MPH.
Professor of Community Medicine,
Fellow, Clinical Epidemiology,
Department of Community Medicine,
School of Medicine,
 2. Arash Ehteshami Afshar, MD,
 3. Amin Ehteshami Afshar, MD.
Professor of Internal Medicine,
Sub-specialist in Lung Disorders,
Rasoule Akram Hospital,
 - 1-3: Tehran University of Medical Sciences,
Tehran, Iran.
- Correspondence:
Dr. Marzieh Nojomi,
Department of Community Medicine, School of Medicine,
Tehran University of Medical Sciences,
Crossroads of Hemmat and Chamran Expressways: 15875-6171,
Tehran, Iran.
E-mail: mnojomi@tums.ac.ir
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severity of airflow obstruction, hypoxemia, hypercapnia and dyspnea, and some comorbidities such as congestive heart failure.⁷

Anemia as a known comorbidity in many chronic diseases can increase morbidity and mortality in cancer, congestive heart failure, chronic renal failure and hepatitis-C virus infection.⁸⁻¹¹ Recently, some studies showed that anemia may be more prevalent than expected in COPD patients. It is found that 10% to 15% of patients with severe forms of disease have anemia.¹² Also, a cohort study revealed a linear association between hemoglobin levels and mortality of COPD patients.¹³ Anemia can be as a poor prognostic factor in COPD patients.¹⁴

Often, the symptoms of anemia are not apparent in COPD patients. Another study showed that anemia can be associated with limitation in physical activity and worsen dyspnea in chronic disorders.¹⁵ In our setting, little is found about the prevalence of anemia in COPD patients. The aim of present study was to assess the prevalence of anemia and its association with some clinical symptoms and outcomes in a sample of patients with COPD in a hospital-clinic based study.

METHODOLOGY

This study was carried out on three hundred and ninety two patients with COPD admitted to teaching hospitals of Tehran University of Medical Sciences between 2002 to 2009. The study was conducted between March to June 2009. Outpatients with COPD were included. The ratio of inpatients to outpatients was one to eight. We used the medical records of patients to collect clinical and laboratory data. Patients informed consent was taken to participate in the study. The diagnosis of COPD was made based on ICD/9 coding. The COPD diagnosis was either established during the hospital admission or during referral to outpatient clinics. All patients with COPD were clinically stable and under therapy.

Spirometric classification of COPD severity based on GOLD criteria, 2008

Stage I: Mild	FEV1/FVC < 0.70 FEV1 ≥ 80% predicted
Stage II: Moderate	FEV1/FVC < 0.70 50% ≤ FEV1 < 80% predicted
Stage III: Severe	FEV1/FVC < 0.70 30% ≤ FEV1 < 50% predicted
Stage IV: Very severe	FEV1/FVC < 0.70 FEV1 < 30% predicted or FEV1 < 50% predicted plus chronic respiratory failure

Exclusion criteria were: Patients with other chronic diseases; cancer, severe renal or hepatic failure, heart failure, acute blood loss, history of folic acid or vitamin B12 deficiency, and having received blood products during previous three last months. We measured demographic characteristics (age, gender, smoking status) as well as clinical (severity and duration of disease) and laboratory variables (hemoglobin, mean corpuscular volume (MCV), and forced expiratory volume in one second (FEV₁). Anemia was defined as hemoglobin levels less than 13 g/dl and 12 g/dl in males and females respectively.¹⁶

Polycythemia was considered as hemoglobin levels more than 15 g/dl and 17 g/dl in females and males respectively. We used the complete blood count of patient had measured ± 4 weeks of measuring lung function tests. Cigarettes smoking was measured as pack year. By using Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, the patients with COPD were divided into four groups.¹⁷

The study approved by Institutional Review Board of Medical School of Tehran University of Medical Sciences, Tehran.

All statistical analysis was done using the 14.0 version of SPSS for windows (SPSS Inc., Chicago, IL). Tables of frequency distribution were used to present qualitative variables. Numeric variables were shown as mean ± standard deviation. The prevalence of anemia is presented with 95% confidence interval. The chi-square test was used to study relationship between nominal data. The independent sample t-test was used for comparing means of quantitative variables across two groups. One way analysis of variance (ANOVA) was used to perform between and within comparison of quantitative data across more than two groups. Significant level was considered at 0.05.

RESULTS

There were 392 patients (44 outpatients and 348 inpatients) with COPD in this cross-sectional study. The mean age of patients was 66.5±12.3 years and 289 (73.7%) subjects were men. Three hundred and sixty six (93.4%) patients had history of smoking with a mean pack year of 27.4±13.4. Table-I demonstrates the laboratory findings and lung function testing of patients with COPD.

Approximately 36.7% (95% CI: 31%-41%) (n=140) were identified as having anemia. Twenty two females (21.4%) and 110 males (38.1%) were anemic according to our definition with statistical

significant difference ($P=0.002$). About twenty six percent ($n=27$) of women and 20.8% ($n=60$) of men had polycythemia. The mean age of patients with COPD with and without anemia were 69.0 years (± 11.4) and 65.0 years (± 12.6) respectively. This difference was significant ($P=0.002$). Fig.1 shows the correlation between age and hemoglobin level ($r=0.28$, $P<0.01$).

According to GOLD ranking, COPD patients in this study were categorized as stages II and III. In stage II, prevalence of anemia was 43.5% versus 34.1% in stage III. This difference was not statistically significant. Fig.2 demonstrates the distribution of hemoglobin levels by severity of disease in patients with COPD. The difference between two means was not significant. The mean of MCV was 79.3 (± 8.3) in patients without anemia versus 80.6 (± 10.3) in anemic patients without any significant difference. Fifty five percent of patients had MCV less than 80. The anemia was not associated with smoking status and type of admission (inpatient versus outpatient).

DISCUSSION

This study showed that prevalence of anemia in patients with COPD was 36.7%. In our study, anemia as (defined according to the World Health Organization (WHO) criteria).¹⁶ was present in 21.4% and 38.1% of women and men respectively. Anemia in patients with COPD is reported in recent studies. The estimation of anemia in patients with COPD is between 10 to 15%.¹² It is shown that there is a linear correlation between hemoglobin level and mortality in patients with COPD.¹³ Recent studies showed that high levels of erythropoietin in patients with COPD indicating the presence of erythropoietin resistance.¹⁸

The prevalence of anemia in our study was more than the other studies.^{12,19-21} One possible explanation for this finding could be the stages of patients with COPD in this study. In the current study based on GOLD criteria, all patients were in stages of

moderate and severe, although, in one study the severe patients showed higher hemoglobin level than milder patients.¹⁹ The authors explained this finding as an effect of more severe hypoxia in higher stages of disease that is a strong stimulator for erythropoietin production and erythropoiesis. On the other hand, hemoglobin level in COPD reflect the balance between the stimulation of erythropoiesis by hypoxia and its depression by inflammation.¹⁴ The latter predicts higher prevalence of anemia in more severe patients due to extensive systemic inflammation. However, it is a hypothesis that need more studies to clarify. The other possible explanation for higher prevalence of anemia could be the higher proportion of inpatients and older subjects in the current study. The high prevalence of anemia in hospitalized patients was reported¹⁹, and the prevalence of anemia is known to increase with increasing age.²²

In the current study, we could not find any significant difference between stages of GOLD in patients. However, patients with COPD in this study categorized as stages two and three, due to not having any patients in stage one. John et al. showed that patients with COPD in the advanced stages had higher hemoglobin values than patients in lower stages with a significant difference.¹⁹ They showed this difference between group two and three too. However, in our study the prevalence of anemia was more in stage two than three, but the difference was not significant. We also found higher hemoglobin levels in stage three versus two. The possible explanation could be were the same as mentioned before; the more severe hypoxia in higher stages.

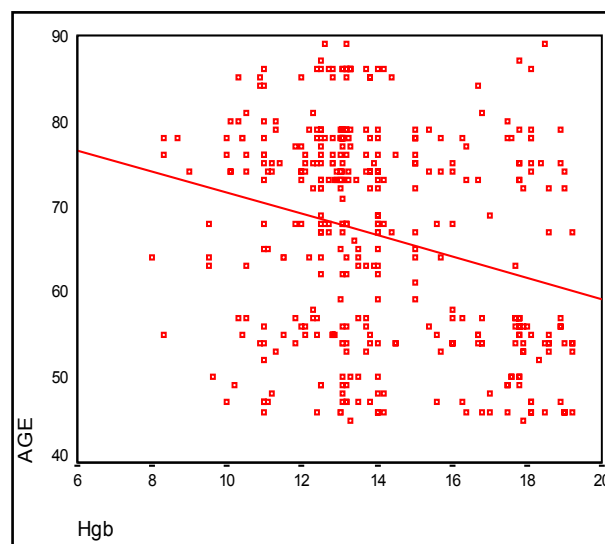


Fig.1: Correlation between age and hemoglobin level.

Table-I: Laboratory findings and lung function tests of COPD patients.

Variable	Mean	Standard deviation
Haemoglobin	14.0 gm/dl	2.5
MCV	79.8	9.1
Hct	40.2	9.4
MCH	28.4	3.3
FEV1(percent predicted)	54.9	8.7
FEV1/FVC (absolute)	66.3	15.0

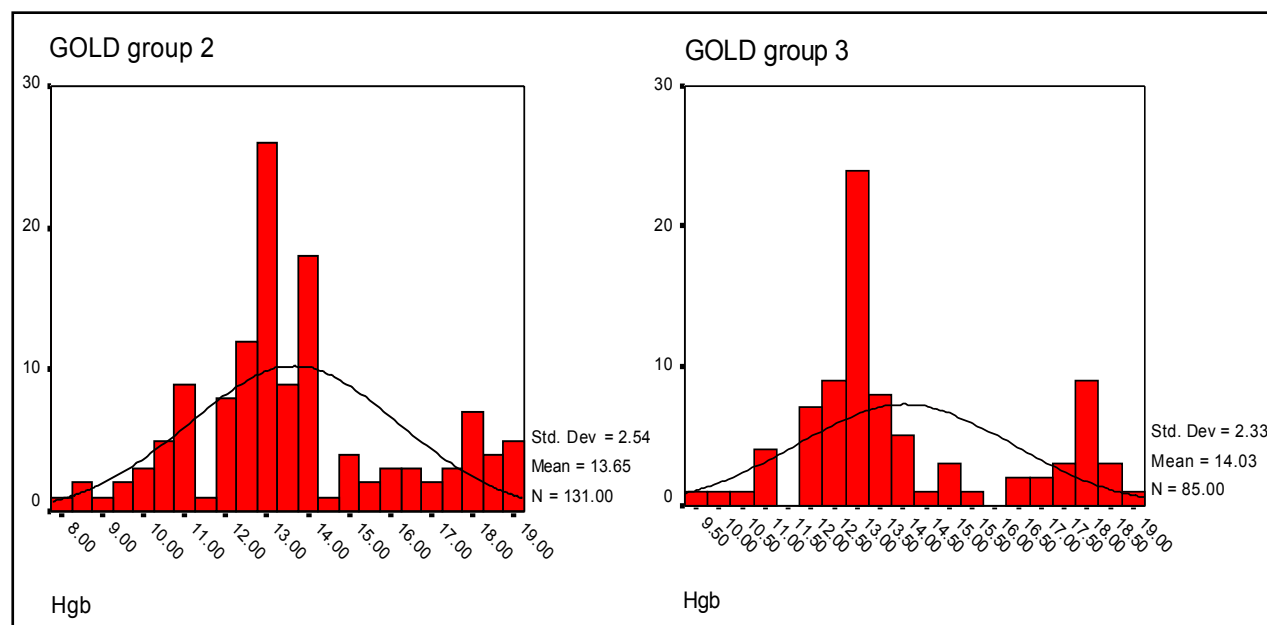


Fig.2: Distribution of hemoglobin levels in COPD patients according to GOLD ranking.
A: Group 2 (COPD stages I and II). B: Group 3 (COPD patients stages III and IV)

Fifty five percent of anemia in patients with COPD were microcytic in current study. Therefore, this type of anemia should be considered as an anemia of chronic disease. In our study older patients was more anemic than younger and there was a linear correlation between anemia and age. This finding is supported by another study too.²²

We could not find any association between anemia with smoking status and type of admission of patients. However, the proportion of outpatients was low versus inpatients and could be because of small power of detection of difference. The absence of correlation between smoking status and anemia was found in the study of John et al.¹⁹

The current study has two limitations related to the estimation of anemia prevalence in patients with COPD in a hospital-based survey. The first one is about method by which patients were selected. All patients with COPD were selected from teaching hospitals (outpatients and inpatients), therefore it was not a good distribution of entire spectrum of patients with COPD. As we saw, all patients were categorized as two or three stages of GOLD.

The second limitation was about the method of collecting data in which we used the records of patients. All laboratory and clinical variables gathered from medical records of patients and some important variables (such as type of drug therapies, nutrition status,..) did not measure. These limitation must be considered in future studies. On the other hand, the current study provides a proper

estimation of anemia prevalence in hospitalized patients with COPD that little is found about it in Tehran, Iran.

CONCLUSION

Our findings showed that the prevalence of anemia in patients with COPD are higher than other studies and need more consideration in management of these patients. Anemic patients tend to be older and were more likely to be male. The anemia was not associated with severity of disease, smoking status, and type of admission of the patients.

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