



Prevalence of Anemia in Patients with Chronic Obstructive Pulmonary Disease in a Tertiary Care Centre

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Abstract

Background: *Chronic Obstructive Pulmonary Disease (COPD) is defined as a common, preventable and treatable disease. COPD is known to be associated with secondary polycythemia but anemia is also common and less studied in these patients. So we conducted a study to see the prevalence anemia in COPD patients.*

Methods: *A Cross sectional observational study performed in the Department of Pulmonary Medicine, Department of Biochemistry, Nizam's Institute Of Medical Sciences (NIMS), Hyderabad, Telangana. The study group consisted of 120 patients who presented to the outpatient department of NIMS hospital during study period. Hemogram, Renal function test, Liver function test, BMI calculation, Dyspnea scoring according to modified Medical Research Council (mMRC), 6minute walk test were done in confirmed cases of COPD.*

Results: *Total 120 patients included in the study. Mean age of the study group was 60.13 ± 7.9 , with age ranging from 43 - 80 years. Of the total population, anemia was present in 24 (20%) patients and polycythemia was present in 8 (6.67%) patients. Mean haemoglobin values for anemic, Polycythemia and normal patients were 13.48 ± 2.47 gm/dl, 18.13 ± 0.64 gm /dl and 14.16 ± 0.93 gm/dl respectively. In anemic patients, most of them, i.e. 22 (91.67%) had normocytic normochromic (NCNC) anemia and 2 (8.33%) patients had microcytic hypochromic (MCHY) anemia.*

Conclusion: *Anemia occurs more frequently than polycythemia in patients with COPD. The most common type of anemia associated with COPD is normocytic normochromic anemia. Most of the anemic patients were in GOLD Grade III severity. Anemic COPD patients have a significantly lower BMI, FEV1 % predicted values, dyspnea by mMRC dyspnea scale and exercise capacity by 6MWD, compared to nonanemic COPD patients.*

Keywords: Anemia, COPD.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of disability and death all over the world. It is responsible for a huge social and economic burden for the health care infrastructure. COPD is the fourth leading cause of death in the world⁽¹⁾.

According to the Global Obstructive Lung Disease (GOLD) guidelines Chronic Obstructive Pulmonary Disease (COPD) is defined as a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. (GOLD guidelines 2017, www.goldcopd.org) As per the report of Global Burden of Disease Study (GBDS), It is expected to become the 3rd most leading cause of death and the 5th leading cause of loss of 'Disability Adjusted Life Years' (DALYs) by 2020⁽²⁾.

The exact burden of COPD was unknown but data from various countries between the years 1998 and 2004 was shown that the prevalence of 7.6% of which chronic bronchitis accounted for 6.8% and emphysema accounted for 1.8%⁽³⁾. The prevalence of COPD is increasing in countries at all over the world⁽⁴⁾. It is the result of cumulative exposures to risk factors over decades. Often, the prevalence has directly been related to the prevalence of tobacco smoking and outdoor, occupational and indoor air pollution – resulting from the chulas, burning of wood and other biomass fuels. COPD is prevalent among non-smokers, especially women in rural areas of the world where indoor air pollution is generated by burning biomass for heating and cooking⁽⁵⁾.

The economic burden of the disease is quite high. According to GOLD the cost incurred on respiratory diseases was 6% in the US and COPD accounted for 56% of the total costs. In figures direct costs incurred were estimated to be 29.4 billion dollars and indirectly 20.5 billion dollars respectively. In India the burden was estimated at

169 billion in 2001 and the number would expect to be increase at least by 50% by 2016⁽⁶⁾.

Systemic effects and/or comorbidities contribute to the overall increase in the morbidity, economic burden, and mortality of COPD^(7,8). Systemic manifestations and comorbidities commonly reported in COPD include cardiovascular disease, diabetes, and hypertension, anemia, reduction in skeletal muscle strength, cachexia, gastro oesophageal reflux, depression, impaired cognition and anxiety⁽⁹⁾.

COPD is traditionally known to be associated with polycythemia, which occurs less frequently nowadays, because of the more rigorous correction of hypoxemia⁽⁹⁾. Recent studies have described that anemia is frequent than expected and associated with increased mortality^(10,11). Anemia has been extensively studied in patients with chronic renal failure, malignancy and chronic heart failure, but little attention has been given to it in COPD.

There is a paucity of information in the current literature describing the prevalence of anemia and its impact on the COPD population. The purpose of the present study is to determine the prevalence of anemia in patients with COPD.

Materials & Methods

This Cross sectional Observational study performed in the Department of Pulmonary Medicine, Department of Biochemistry, Nizam's Institute Of Medical Sciences (NIMS), Hyderabad, Telangana.

Inclusion Criteria

- Age 40 years or more with history suggestive of COPD (cough with sputum production in chronic bronchitis and breathlessness in emphysema), physical findings suggestive of airway obstruction (rhonchi, decreased intensity of breath sounds and prolonged expiration).
- Spirometry confirmed diagnosis of COPD as per Global Initiative For Chronic Obstructive Lung Disease (GOLD)

- criteria, (post bronchodilator FEV₁/FVC ratio <0.7)
- Willingness of the patient to participate in this study.

Exclusion Criteria

- Current or past diagnosis of asthma (defined as an increase in FEV1 >12% and >200mL above the baseline value after administration of a bronchodilator).
- Patients with cancer, thyroid disease, severe liver disease, chronic kidney disease, chronic heart failure, rheumatoid arthritis, GI hemorrhage or blood loss of any other cause and patients with a known vitamin B12 or folic acid deficiency.
- Inability to complete the lung function test.
- All patients with insufficient mental capacity that preclude obtaining an informed consent from them.

The study group consists of 120 patients who presented to the outpatient department of NIMS hospital, who met our inclusion and exclusion criteria. Obtained a detailed history from all these patients about smoking including passive smoking, occupational history, Biomass fuel exposure and general history and clinical examination of all these patients was performed and recorded.

Patients of COPD whose diagnosis was confirmed by clinical history, radiology of chest, and pulmonary function test were enrolled into the study. Hemogram, Renal function test ,Liver function test, BMI calculation, Dyspnea scoring according to modified Medical Research Council (mMRC), 6minute walk test were done in confirmed cases of COPD. Additional investigations were done depending on the patients requirement.

Patients were categorized in to 3 groups based on the Haemoglobin values

1. Anemic, with Hb levels <13 g/dL for males and <12 g/dl for females (World Health Organization definition of anemia) ⁽¹²⁾.
2. Polycythemic with Hb levels >17 g/dL and >15 g/dL for males and females, respectively ⁽¹³⁾.
3. Normal.

Further patients were grouped in to anemic and nonanemic patients. Polycythemic patients were included in the group with normal Hemoglobin levels.

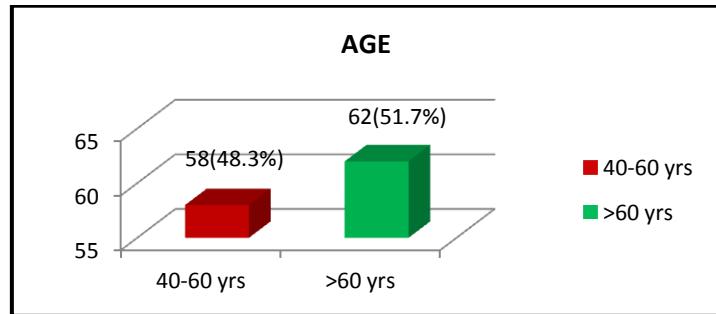
Statistical analysis

Results were given as mean ± SD for continuous data and as percentages for categorical data. The differences between-groups were calculated using a two-sided independent t-test or Chi-squared statistic where appropriate. Linear regression analyses controlling for age, FEV1, BMI were performed to identify the independent association of anemia with the MRC dyspnea scale and the 6MWD test. To analyze relationships between variables, Student t test and simple regression analyses were performed. A p-value <0.05 was considered statistically significant. SPSS statistics 20.0 version was used for data analysis.

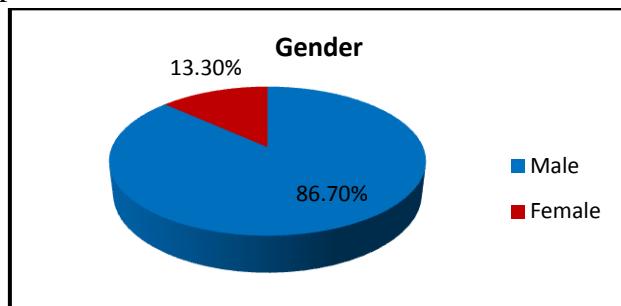
Results

This is an institution based study and was conducted in department of pulmonary Medicine, Nizam's Institute of Medical Sciences (NIMS), Hyderabad between January 2015 and December 2015.

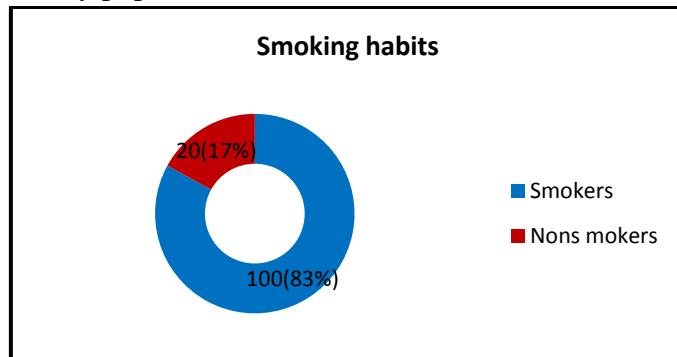
The total number of patients (n) included in the study was 120, diagnosed to have COPD constituting both males and females, including smokers as well as non-smokers visiting the outpatient department.

Figure 1: Age distribution of study population

Mean age of the study group was 60.13 ± 7.9 , with age ranging from 43 - 80 years.

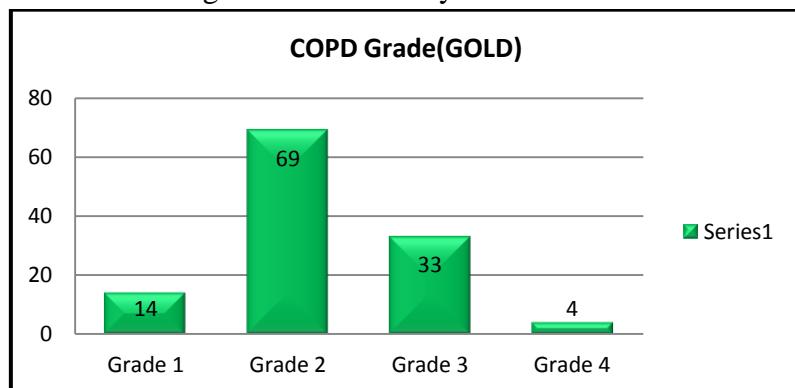
Figure 2: Gender of study population

Male and female constituted 86.70% (104) and 13.30% (16) respectively of the total patients (n=120).

Figure 3: Smoking habits of study population

The number of smokers in the selected population were 100 (83%) and all of them were males. 20 (17%) patients were non-smokers. Out of 100

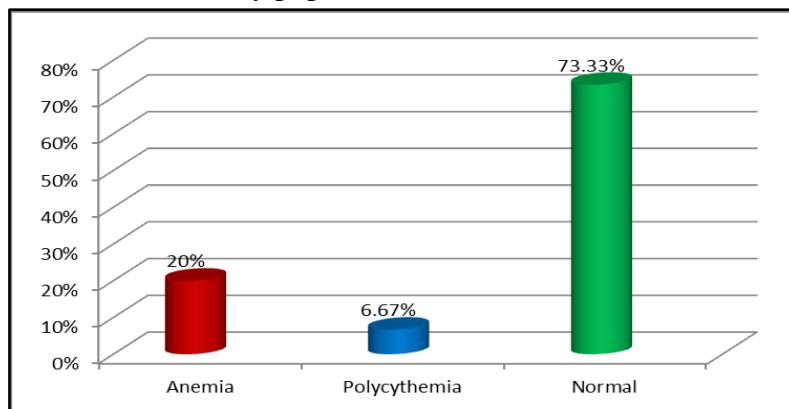
smokers in males 32 were ex-smokers and 68 were smoking actively. The time since giving up smoking varied from person to person.

Figure 4: Patient distribution according to COPD severity

Among this study group, the majority of patients were having Moderate COPD (Grade II) i.e. 57.5% (n=69), followed by Severe COPD (Grade III) in

27.5% (n=33), Mild COPD (Grade I) in 11.67% (n=14) and Very severe COPD (Grade IV) in 3.3% (n=4) patients.

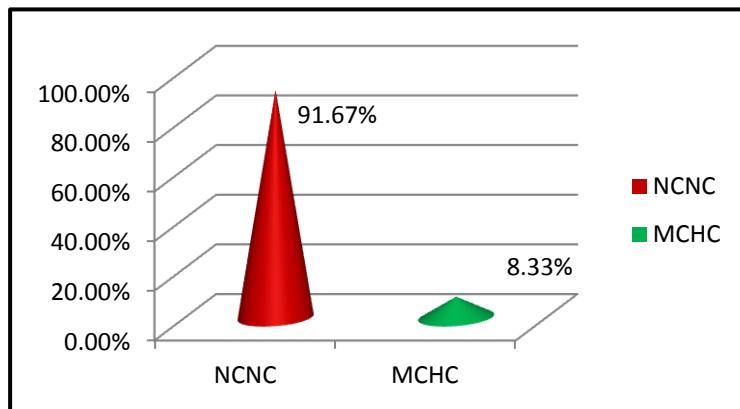
Figure 5: Hemoglobin distribution of study population



Of the total population, anemia was present in 24 (20%) patients and polycythemia was present in 8 (6.67%) patients. Mean haemoglobin values for

anemic, Polycythemia and normal patients were 13.48 ± 2.47 gm/dl, 18.13 ± 0.64 gm /dl and 14.16 ± 0.93 gm/dl respectively.

Figure 6: Type of anemia based on peripheral smear



In anemic patients, most of them, i.e. 22 (91.67%) patients had normocytic normochromic (NCNC)

anemia and 2 (8.33%) patients had microcytic hypochromic (MCHY) anemia.

Table 3: Characteristics of anemic and nonanemic patients

| Variable | Anemic | Nonanemic | P value |
|-----------------------------|------------------|--------------------|---------|
| Subjects (n) | 24 | 96 | |
| Age (years) | 65.63 ± 7.47 | 58.76 ± 7.39 | < 0.001 |
| Hb (gm/dl) | 9.46 ± 1.41 | 14.48 ± 1.44 | < 0.001 |
| PCV (vol%) | 30.63 ± 4.70 | 43.98 ± 4.91 | < 0.001 |
| RBC(mill/ mm ³) | 3.46 ± 0.50 | 4.69 ± 0.73 | < 0.001 |
| BMI (Kg/m ²) | 21.38 ± 1.95 | 22.72 ± 2.01 | 0.005 |
| FEV1 % predicted | 40 ± 8.54 | 64.72 ± 12.90 | 0.001 |
| mMRC | 3.13 ± 0.54 | 2.13 ± 0.51 | < 0.001 |
| 6MWD (m) | 219 ± 46.40 | 333.67 ± 56.83 | < 0.001 |

Discussion

In this study of 120 COPD patients, male and female constituted 86.70% (104) and 13.30% (16), respectively. Mean age of the study group was 60.13 ± 7.9 , with an age range of 43 - 80 years (Figure 1). Male and female constituted 86.70% (104) and 13.30% (16) respectively of the total patients (n=120) (Figure 2). The number of smokers in the selected population was 100 (83%) and all of them were males (Figure 3). Most of our patients 57.5% (n=69) were having Grade II COPD severity (Figure 4).

In this study, 20% (24/120) of the patients were having co-existing anemia. This was similar to the frequency of 17% reported by Cote et al, 18% by Parveen et al, 21% by Halpern et al and 23% by John et al. The mean \pm SD of Hb in the whole group was 13.48 ± 2.47 gm/dL. Mean Hb levels for anemic and nonanemic patients were 9.46 ± 1.41 gm/dL and 14.48 ± 1.44 gm/dL, respectively ($p < 0.0001$). These results are consistent with another study by John et al with mean Hb of 11.9 ± 0.4 g/dl and 14.7 ± 0.2 g/dl ($p < 0.0001$) in anemic and non-anemic patients respectively. In the study by Cote et al, the mean Hb level was 11.8 ± 1.0 g/dL and 15.0 ± 1.2 g/dL ($p < 0.0001$) in anemic and non-anemic patients respectively.

The most common type of anemia was found to be normocytic normochromic anemia (91.67%). Microcytic anemia was present in 8.33% of anemic patients (Figure 6). This was similar to the study done by Parveen et al (88.9% vs 11.1%). Packed cell volume (PCV) and Red cell counts

were significantly lower in anemic COPD patients (Table 3).

A significant proportion (87.5%) of anemic COPD patients was smokers. Among smokers (n=100) anemia was present in 21% of the patients and polycythemia was present in 7% of patients, on analysis, it was observed that smoking predisposing to anemia was statistically insignificant. Among non-smokers 15% (20) had anemia and 5% (1) had polycythemia and the results were statistically significant ($P = 0.049$) suggesting that smoking predisposes to polycythemia.

Anemic patients were significantly older (65.63 ± 7.47 versus 58.76 ± 7.39 ; $p < 0.001$) than nonanemic patients, which was comparable to the study done by Cote et al (72.8 ± 9.3 and 69.5 ± 8.8 ; $p=0.0003$). BMI was also significantly lower in anemic patients. The Most of the anemic patients were in GOLD Grade III severity. FEV1 % predicted was significantly lower (40 ± 8.54 versus 64.72 ± 12.90 ; $p < 0.001$) in anemic COPD patients. Dyspnea and exercise capacity by 6MWD differed significantly between anemic and nonanemic patients. Mean MRC values were significantly higher (3.13 ± 0.54 versus 2.13 ± 0.51 ; $p < 0.001$) and mean 6MWD was significantly shorter (219 ± 46.40 m versus 333.67 ± 56.83 m; $p < 0.001$) in anemic patients compared with nonanemic patients (Table 3).

Polycythemia was present in 6.67% of the patients (Figure 5) compared to 6% in a study by Cote et al.

Table 4: Comparative studies

| Author | Study population | Prevalence of anemia |
|--------------------------------------|------------------|------------------------------------|
| Marathias John et al ⁽¹⁴⁾ | 101 | 13% |
| Gokul Krishnan et al ⁽¹⁵⁾ | 495 | 7.47% |
| Chambellan et al ⁽¹⁶⁾ | 2524 | 13% males and 8% females |
| Halpern et al ⁽¹⁷⁾ | 132,424 | 21% |
| Shorr et al ⁽¹⁸⁾ | 2404 | 33% |
| C.Cote et al ⁽¹⁹⁾ | 667 | 17% (Polycythemia in 6%) |
| Attaran et al ⁽²⁰⁾ | 80 | 16% |
| Boutou et al ⁽²¹⁾ | 294 | 15.6% (polycythemia in 10.2%) |
| Silverberg et al ⁽²²⁾ | 107 | 43.9% |
| Parveen et al ⁽²³⁾ | 200 | 18% |
| Present study | 120 | 20% (Polycythemia in 6.67%) |

Conclusion

From our study, we arrived to a conclusion that Anemia occurs frequently in patients with COPD. The most common type of anemia associated with COPD is normocytic normochromic anemia. Most of the anemic patients were in GOLD Grade III severity. Significant proportions (87.5%) of anemic COPD patients were smokers. Anemic COPD patients have a significantly lower BMI, FEV1 % predicted values, dyspnea by mMRC dyspnea scale and exercise capacity by 6MWD, compared to nonanemic COPD patients.

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