**Original Article**

# Frequency of Anaemia in Chronic Obstructive Pulmonary Disease

**Muhammad Khalid Ch.,**[1] **Muhammad Younus,**[2] **Javeria Aijaz,**[3] **Ashfaq-ur-Rehman,**[4] **Sohail Anwar,**[5] **Sajjad Hassan,**[6] **Kashif Siddique,**[7] **M. Saqib Saeed**[8]

## Abstract

**Background:** Chronic obstructive pulmonary disease is a chronic inflammatory multisystem disease expected to cause anaemia. Anaemia of chronic disease is relatively common in COPD patients but is an under estimated issue.

**Study Objective:** To determine the frequency of anaemia in COPD patients.

**Study Setting:** Institute of Chest Medicine, Mayo Hospital, Lahore – a tertiary care university hospital affiliated with King Edward Medical University, Lahore.

**Study Design:** Cross sectional study.

**Sample Size:** One Hundred and two Patients of COPD diagnosed on standard Spirometric postbronchodilator FEV1/FVC % < 0.70.

**Sample Technique:** Purposive.

**Inclusion Criteria:** Clinically stable patients of all categories of COPD were included.

**Exclusion Criteria:** Patients of malignancy, chronic liver disease, chronic heart failure, G.I. hemorrhage, known vitamin $B_{12}$ or folic acid deficiency, myocardial infarction in last one month, unstable angina, unable to perform pulmonary function test and asthmatic patients were excluded.

**Results:** Out of 102 COPD patients anaemia was detected in 21 (20.58%), (Male 20, Female 1) cases.

Khalid M.C.[1]
Associate Professor, TB, Chest and Pulmonology
Institute of Chest Medicine, King Edward Medical
University / Mayo Hospital, Lahore

Younus M.[2]
Institute of Chest Medicine
King Edward Medical University, Lahore

Aijaz J.[3]
Department of Hematology
King Edward Medical University, Lahore

Rehman A.U.[4]
Institute of Chest Medicine
King Edward Medical University, Lahore

Anwar S.[5]
Institute of Chest Medicine
King Edward Medical University, Lahore

Hassan S.[6]
Institute of Chest Medicine
King Edward Medical University, Lahore

Siddique K.[7]
Institute of Chest Medicine
King Edward Medical University, Lahore

Saeed M.S.[8]
Institute of Chest Medicine
King Edward Medical University, Lahore

The criteria for anaemia diagnosis was Hb < 13 gm/dl in males and Hb < 12 gm/dl in females. Sixty seven (65.68%) were normal and 14 (13.72%) were policythemic (M – 13 and F: 1). Mean haemoglobin in anaemic patents was 10.14 ± 1.06 gm/dl with P. value of 0.00 which is highly significant. Amongst 21 anaemic patients, 15 patients were normocytic normochromic and 06 were microcytic hypochromic.

**Conclusion:** Anaemia is a relatively common finding in COPD patients.

**Key Words:** COPD (Chronic Obstructive Pulmonary Disease). Anaemia, Normocytic normochromic, Microcytic hyprochromic, Chronic disease.

## Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of chronic morbidity and mortality throughout the world. COPD is the fourth leading cause of death in the world. Its prevalence and mortality are increasing.[1] COPD is a preventable and treatable disease with some significant extra-pulmonary effects which may contribute to its severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and associated with abnormal inflammatory response of the lungs to noxious particles or gases.[2] Worldwide, cigarette smoking is the most important risk factor for COPD. Although in many countries air pollution resulting from wood burning and use of other biomass are also important risk factors. Inhaled smoke and other noxious particles cause lungs inflammation.[3] COPD is associated with significant extra-pulmonary systemic effects because of the release of pro-inflammatory cytokines like interleukin -1 (IL – 1), IL – 6, and tumor necrosis factor α (TNF – α).[4]

Anaemia is the deficiency in either red cell quantity or hemoglobin concentration in circulating blood, with the effect of reducing the oxygen-carrying capability of the blood. World Health Organization (WHO) has defined anaemia as a haematocrit of less than 39% in men and less than 36% in women.[5]

After iron deficiency, chronic inflammatory diseases are the most common conditions producing anaemia. Anaemia of chronic disease, also called anaemia of inflammation, has been associated primarily with infections, cancers, autoimmune conditions such as rheumatoid arthritis, inflammatory bowel disease and kidney diseases.[6] Anaemia of chronic disease is relatively common in COPD. Anaemia is such a common and simple clinical finding that we may underestimate its physiological relevance in COPD. There is emerging data suggesting that anaemia may be associated with increased disease severity, and perhaps mortality, in COPD.[7]

In chronic inflammatory disease states, anaemia results from several factors, including shortened RBC's survival, reduced iron utilization and an impaired bone marrow erythropoietic response.[8] There is good evidence that anaemia of chronic disease occurs in COPD. Patients with COPD have increased peripheral blood CRP, fibrinogen, TNF-α, IL-1β and IL-6, IL-8, MCP-α (monocyte chemotactic protein-α).[9]

COPD related inflammation can also impair the erythropoiesis. In COPD patients erthropoiesis is stimulated by hypoxia and depressed by the inflammatory markers, so it is the balance between the two that determines the hemoglobin level of the patients. Erythropoietin is the primary stimulating hormone for erthropoiesis. Recently it is observed that in anaemic COPD patients, levels of erythropoietin hormone are increased as compared to non-anaemic COPD patients which suggests the presence of resistance to the erythropoietin hormone function.[10]

Inadequate haemoglobin in patients of COPD can aggravate tissue hypoxia, increases the dyspnea, limits the exercise tolerance and all these carry negative prognosis.[11,12]

## Study Objective

The objective of the study was to determine the frequency of anaemia in COPD patients.

## Materials and Methods

### Study Setting

Institute of Chest Medicine, Mayo Hospital, Lahore – a tertiary care university hospital affiliated with King Edward Medical University, Lahore.

### Study Design

Cross Sectional Study.

### Sample Size

102 Patients of COPD diagnosed on standard Spirometric postbronchodilator $FEV_1 / FVC \% < 0.70$.

## Sample Technique

Purposive.

## Inclusion Criteria

Clinically stable patients of all categories of COPD were included.

## Exclusion Criteria

1. Cancer patients.
2. Chronic liver disease.
3. Chronic heart failure.
4. G.I. hemorrhage.
5. Known vitamin $B_{12}$ or folic acid deficiency.
6. Myocardial infarction in last one month.
7. Unstable angina.
8. Unable to perform pulmonary function testing.
9. Asthmatic patients.

## Anaemia was defined as:

Hb < 13 g/dl in males and Hb < 12 g/dl in females.

## Polycytemia was defined as:

Hb > 17g/dl in both males and females.

## Blood Sampling

Peripheral venous blood samples were collected between 09.00 am and 10.00 am. The samples were sent immediately for analysis to haematology laboratory, KEMU, Lahore.
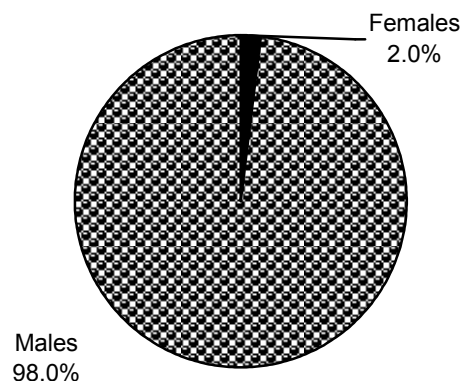
## Statistical Analysis

SPSS 15.0 was used for data analysis. Chi-squares test was used to see the relationship of qualitative variables with respect to hemoglobin status. ANOVA was used to see the mean difference of qualitative variables with respect to hemoglobin status.
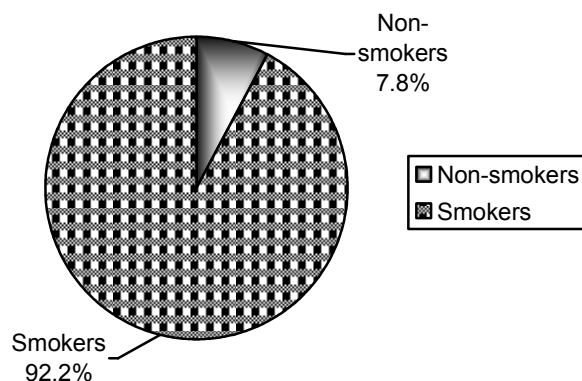P Value < 0.05 was taken as significant.

## Results

A total of 102 patients were included in the study. One hundred were males and 02 were females (Graph 1). Mean age for males was $57.36 \pm 8.81$ years and for females $40.50 \pm 6.36$ years. Out of 102 patients, 94 were smokers and 08 were non-smokers (Graph 2).

Amongst 102 patients, 21 (20.58 %) were anaemic (20 males, 01 female), 67 (65.68%) were normal (all males), 14 (13.72%) were Polycythemic (13 males and 01 – female).



**Graph 1:** Gender Distribution.



**Graph 2:** Smoking Status.

Mean haemoglobin in anaemic patients was $10.14 + 1.06$ gm/dl, in normal patients $14.13 \pm 0.81$ gm/dl, in polycytehmic $18.61 \pm 0.87$gm/dl with 'P' value of 0.00 which is highly significant. Mean haematocrit was $41.77 \pm 6.41$ and in 21 anaemic patients mean haematocrit was $34.67 \pm 5.67$, in patients with normal hemoglobin mean haematocrit was $43.42 \pm 4.58$ and in polycythemic patients mean hematocrit was $44.57 \pm 5.61$. Mean $FEV_1$ in anaemic patients was $1.13 \pm 0.36$ L, in normal patients $1.12 \pm 0.51$ and in polycythemic $0.95 \pm 0.35$ L with 'P' value 0.44 which is not significant statistically. Mean FVC in anaemic group $1.92 \pm 0.51$ L in normal patients $2.06 \pm 0.77$ L and in policythemic $2.22 \pm 0.57$ L with P value of 0.476 which is not significant (Table 1).

**Table 1:**

| | | Anaemia (n = 21) | Normal (n = 67) | Polycythemia (n = 14) | p-value |
|---|---|---|---|---|---|
| Age | | 56.38 ± 9.29 | 57.23 ± 8.77 | 57.00 ± 10.69 | 0.932 |
| Hb | | 10.14 ± 1.06 | 14.13 ± 0.81 | 18.61 ± 0.87 | 0.000* |
| FVC | | 1.92 ± 0.51 | 2.06 ± 0.77 | 2.22 ± 0.57 | 0.476 |
| FEV$_1$ | | 1.13 ± 0.36 | 1.12 ± 0.51 | 0.95 ± 0.35 | 0.444 |
| Gender | Male | 20 | 67 | 13 | 0.125 |
| | Female | 1 | 0 | 1 | |
| Mean Corpuscular Hemoglobin | Hypochromic | 6 | 34 | 7 | 0.232 |
| | Normochromic | 15 | 33 | 7 | |
| Mean Corpuscular Volume | Microcytic | 5 | 23 | 6 | 0.320 |
| | Normocytic | 16 | 44 | 8 | |

Amongst anaemic group, 15 patients were normocytic normochromic and 06 were microcytic hypochromic.

## Discussion

Anaemia of chronic disease is relatively common in COPD patients but is an underestimated issue. COPD is a chronic inflammatory multisystem disease leading to the expectation of anaemia. After iron deficiency, chronic inflammatory diseases are the most common conditions producing anaemia. Anaemia of chronic disease is typically of normocytic normochromic type.

In the present study, anaemia was present in 20.58% of COPD patients which is comparable with the study by Halprern TM et al[13] which showed the prevalence of anaemia of 21 % and with the study of Attaran D et all[14] from Iran which showed that 16 % of COPD patients are anaemic. A 2005 retrospective observational study of 2,524 severe COPD patients found that 12.6% of men and 8.2% of women were anaemic (haematocrit < 39% in men and < 36% in women), compared to 8.9% of men and 5.9% of women who were polycythemic (Hgb ≥ 55%).[10] In a 2007 retrospective analysis of 677 patients with COPD, anaemia was present in 17.1% of patients, and polycythemia was present in 5.9% of patients[12] which are comparable to our results. In our study 15(71.42%) patients have normocytic normochromic type of anaemia and 06 (28.57%) patients having microcytic hypo-

chromic anaemia which are comparable with the study by Pancirov D et al[15] which showed 83.40% patients had normocytic normochromic type of anaemia and 16.6% had microcytic hypochromic type of anaemia.

Anaemia of chronic disease is immune driven and mainly it is because of chronic systemic inflammatory response. The mechanism of anaemia development in COPD patients is similar to the other chronic diseases. It has been shown that immune and inflammatory markers like tumor necrosis factor α, IL – 6 and interferon gamma are potentially involved in the development of anaemia of chronic disease. The increased level of these inflammatory cytokines and C reactive proteins (CRP) lead to shortening of the erythrocyte life span, disturbed utilization of iron from reticuloendothelial stores and to the impairment of the compensational activity of bone marrow. Hence, bone marrow does not respond to enhanced erythropoietin formation. Resistance to erythropoietin emerges, leading to anaemia which is most commonly normocytic normochromic but seldom microcytic and hypochromic anaemia.[16] It is assumed that anaemia could be a significant prognostic factor in COPD patients, because decreased haemoglobin and haematocrit concentrations in these patients are associated with frequent and long-term hospitalization and increased mortality.[17]

In the recent years polycythemia is less commonly seen in COPD patients which may be because of better care and more use of long term oxygen therapy. In our study 14 (13.52%) patients had polycythemia which

are comparable with the studies of Shor AF et al, Cote C et al which showed the prevalence of polycythemia of 8% and 9% respectively.[18,19]

We suggest further lager studies to see the clinical impact of anaemia on COPD patients, its mechanism of development and impact of correction of anaemia on the COPD patients.

## Conclusion

Anaemia of chronic disease is a relatively common finding in COPD patients.

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