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INCIDENCE OF POLYCYTHEMIA AMONG PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE ADMITTED TO THE DEPARTMENT OF MEDICINE IN TERTIARY CARE HOSPITAL

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Abstract

Background: *Secondary polycythemia is a recognized hematological complication of chronic hypoxic lung disease, particularly chronic obstructive pulmonary disease (COPD). Elevated hematocrit increases whole blood viscosity and predisposes patients to thromboembolic and cardiovascular complications. Local data on the prevalence of this complication among hospitalized patients in Pakistan remain scarce. This study was conducted to determine the prevalence of polycythemia among patients with COPD and to evaluate its association with demographic and clinical characteristics.*

Materials and Methods: *This prospective observational study was conducted in the Department of Medicine, Federal Government Polyclinic Hospital, Islamabad, over four months. A total of 200 consecutive adult patients (aged ≥40 years) admitted with a diagnosis of COPD, defined according to GOLD spirometric criteria, were enrolled using non-probability consecutive sampling. Demographic data, smoking status, biomass fuel exposure, resting oxygen saturation, and GOLD stage were recorded. Polycythemia was defined using 2016 WHO diagnostic thresholds. Comparisons between patients with and without polycythemia were performed using the independent-samples t-test, chi-square test, or Fisher's exact test. A p-value <0.05 was considered statistically significant.*

Results: *Among 200 patients with COPD, the mean age was 64.8 ± 8.7 years, with a male predominance (67.0%). Polycythemia was present in 16 patients (8.0%). Polycythemia was significantly more common among males than females (93.8% vs. 64.7%; p = 0.018) and among current smokers than others (87.5% vs. 56.5%; p = 0.015). Patients with polycythemia had significantly lower resting oxygen saturation than those without (84.7 ± 2.8% vs. 89.8 ± 3.9%; p < 0.001). No significant difference was observed for age or body mass index.*

Conclusion: *Secondary polycythemia remains a clinically relevant complication among hospitalized patients with COPD, occurring in 8.0% of this cohort. Male sex, current smoking, and severe resting hypoxemia were the principal factors*

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associated with its occurrence. Routine assessment of hemoglobin, hematocrit, and oxygen saturation may facilitate early identification of at-risk patients and guide timely optimization of long-term oxygen therapy and smoking cessation.

INTRODUCTION:

Chronic obstructive pulmonary disease (COPD) is a common, preventable, and treatable respiratory disorder characterized by persistent airflow limitation resulting from chronic airway inflammation and progressive destruction of the lung parenchyma.[1] It represents a major global public health challenge, affecting several hundred million individuals worldwide and ranking among the leading causes of morbidity, mortality, and healthcare utilization.[2] The burden of COPD continues to rise with population ageing, persistent tobacco smoking, occupational exposures, and biomass fuel combustion, and is disproportionately borne by low- and middle-income countries.[3]

The pathological hallmark of COPD is chronic airway inflammation accompanied by emphysematous destruction of alveolar architecture, mucus hypersecretion, and progressive impairment of gas exchange.[4] As airflow obstruction advances, ventilation-perfusion mismatch and chronic hypoxemia become increasingly prominent, particularly in patients with severe disease. Sustained tissue hypoxia stimulates renal erythropoietin secretion and compensatory bone marrow erythropoiesis, a physiological adaptation intended to preserve tissue oxygen delivery.[5] When this compensatory response becomes excessive, it may culminate in secondary polycythemia, an increase in hemoglobin concentration and hematocrit driven by chronic hypoxic stimulation rather than an intrinsic myeloproliferative disorder.

Although secondary polycythemia may transiently improve oxygen-carrying capacity, the accompanying rise in whole blood viscosity impairs microvascular perfusion and predisposes patients to thromboembolic events, pulmonary hypertension, and cardiovascular complications.[6] In a large COPDGene cohort of patients with moderate-to-severe COPD, secondary polycythemia was found in 9.2% of men and 3.5% of women, and was independently associated with male sex, current smoking, impaired diffusing capacity, and severe resting hypoxemia, while continuous and nocturnal long-term oxygen therapy (LTOT) were associated with a reduced risk.[7]

Long-term oxygen therapy, established by two landmark trials as the only intervention proven to improve survival in hypoxemic COPD, has substantially reduced the prevalence of secondary polycythemia in high-income settings.[8,9] However, in resource-limited countries such as Pakistan, where COPD is frequently diagnosed at an advanced stage and access to spirometry, pulmonary rehabilitation, and LTOT remains limited, chronic hypoxemia and its hematological consequences may persist more frequently than reported in high-income populations. Reported prevalence of polycythemia among patients with COPD varies considerably, from approximately 4% to 10%, depending on disease severity, smoking status, oxygen therapy use, and diagnostic criteria.[7] Evidence describing this complication among hospitalized patients in Pakistan remains scarce.

Hemoglobin and hematocrit estimation are inexpensive, readily available investigations that can be performed in virtually all healthcare settings, including resource-constrained hospitals, and their routine assessment may facilitate early identification of patients who warrant further evaluation for chronic hypoxemia, optimization of long-term oxygen therapy, and reinforcement of smoking cessation. Given the substantial burden of COPD in Pakistan and the paucity of local data on this complication, the present study was conducted to determine the prevalence of secondary polycythemia among patients with COPD admitted to the Department of Medicine of a tertiary care hospital and to evaluate its association with demographic characteristics, smoking status, disease severity, and resting oxygen saturation.

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MATERIALS AND METHODS:

This prospective observational study was conducted in the Department of Medicine, Federal Government Polyclinic Hospital (FGPH), Islamabad, from February 2025 to May 2025. The study was carried out following approval from the institutional ethics committee, and informed consent was obtained from all participants or their legal representatives prior to enrollment. Patient data were anonymized to maintain confidentiality.

A total of 200 consecutive patients were enrolled using a non-probability consecutive sampling technique. Adult patients aged ≥40 years admitted with a diagnosis of COPD during the study period were eligible for inclusion. COPD was diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, based on documented post-bronchodilator spirometry demonstrating a forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) ratio of <0.70, or a previously established diagnosis supported by spirometric records and ongoing COPD-specific treatment.[1] Patients with primary polycythemia (polycythemia vera), congenital cyanotic heart disease, chronic kidney disease receiving erythropoietin therapy, known obstructive sleep apnea, active pulmonary tuberculosis, interstitial lung disease, hematological malignancies, recent blood transfusion within the preceding three months, pregnancy, or severe dehydration were excluded.

Demographic and clinical data; age, sex, body mass index (BMI), smoking status, cumulative smoking exposure (pack-years), biomass fuel exposure, and duration of COPD, were recorded using a structured proforma. Resting peripheral oxygen saturation (SpO_2) was measured using a calibrated pulse oximeter after the patient had remained at rest for at least five minutes while breathing room air, whenever clinically feasible. Disease severity was classified according to the GOLD staging system using the most recent spirometric assessment available in the patient's medical record.

Venous blood samples were collected under aseptic conditions and analyzed in the hospital laboratory using an automated hematology analyzer to determine hemoglobin concentration, hematocrit, red blood cell count, white blood cell count, and platelet count. Polycythemia was defined according to the 2016 World Health Organization diagnostic thresholds as a hemoglobin concentration >16.5 g/dL or hematocrit >49% in men, and a hemoglobin concentration >16.0 g/dL or hematocrit >48% in women.[10]

Data were entered into and analyzed using Statistical Package for the Social Sciences (SPSS) version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables were assessed for normality and are presented as mean ± standard deviation (SD), whereas categorical variables are expressed as frequencies and percentages. Comparisons between patients with and without polycythemia were performed using the independent-samples t-test for normally distributed continuous variables, and the chi-square test or Fisher's exact test for categorical variables, as appropriate. A p-value <0.05 was considered statistically significant.

RESULTS:

A total of 200 patients with chronic obstructive pulmonary disease (COPD) admitted to the Department of Medicine during the study period were included in the final analysis. The mean age of the study population was 64.8 ± 8.7 years, with a predominance of males (67.0%). The mean body mass index (BMI) was 22.3 ± 4.1 kg/m^2. Current smokers constituted 59.0% of the cohort, while 29.0% had a history of biomass fuel exposure. The mean duration of COPD was 8.3 ± 4.9 years, and the mean resting peripheral oxygen saturation (SpO_2) was 89.4 ± 4.2%, as shown in Table 1.

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Table 1. Baseline Demographic and Clinical Characteristics of the Study Population (n=200)

Variable	Value
Age (years), Mean ± SD	64.8 ± 8.7
Male, n (%)	134 (67.0)
Female, n (%)	66 (33.0)
BMI (kg/m²), Mean ± SD	22.3 ± 4.1
Current smokers, n (%)	118 (59.0)
Former smokers, n (%)	46 (23.0)
Never smokers, n (%)	36 (18.0)
Smoking exposure (pack-years), Median (IQR)	32 (24–45)
Biomass fuel exposure, n (%)	58 (29.0)
Mean resting SpO_2 (%)	89.4 ± 4.2
Duration of COPD (years), Mean ± SD	8.3 ± 4.9

Regarding disease severity, 9.0% of patients were classified as GOLD stage I, 37.0% as GOLD stage II, 35.5% as GOLD stage III, and 18.5% as GOLD stage IV. Overall, 16 patients (8.0%) fulfilled the predefined diagnostic criteria for polycythemia, as shown in Table 2 and Figure 1.

Table 2. Distribution of GOLD Severity Stage and Presence of Polycythemia

Variable	n (%)
GOLD I	18 (9.0)
GOLD II	74 (37.0)
GOLD III	71 (35.5)
GOLD IV	37 (18.5)
Polycythemia present	16 (8.0)
Polycythemia absent	184 (92.0)

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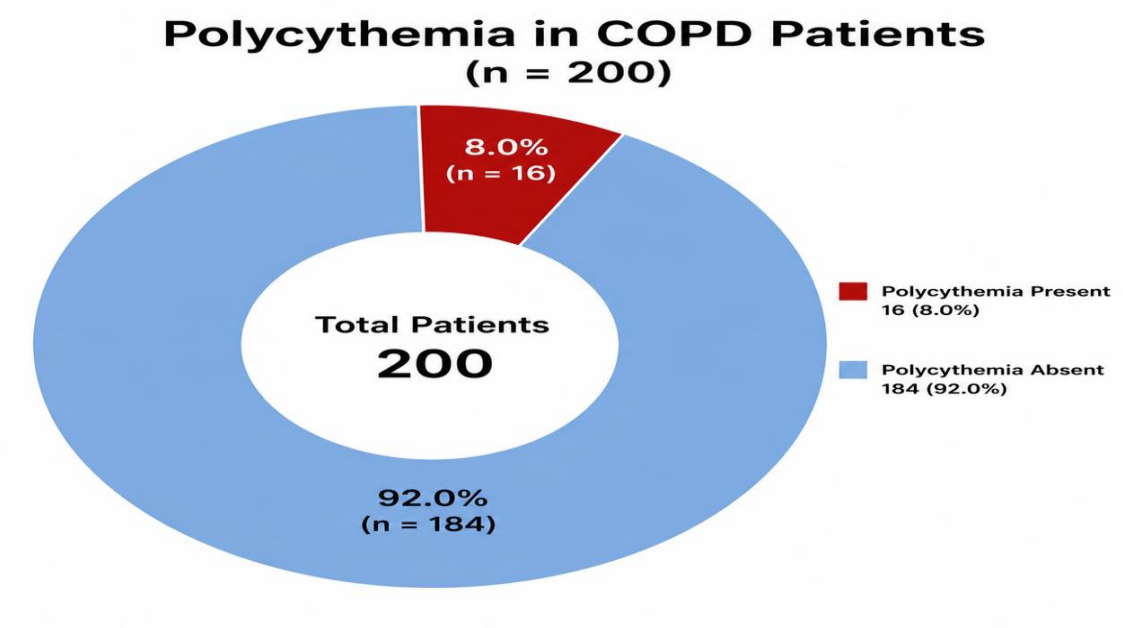

Figure 1. Polycythemia among patients with chronic obstructive pulmonary disease (COPD).

The mean hemoglobin concentration of the overall cohort was 14.8 ± 1.9 g/dL, with a mean hematocrit of 44.3 ± 5.3% and a mean red blood cell count of 5.01 ± 0.61 × 10^6/µL. The mean white blood cell count and platelet count were 10.4 ± 3.2 × 10^3/µL and 254 ± 68 × 10^3/µL, respectively, as shown in Table 3.

Table 3. Hematological Parameters of the Study Population

Variable	Mean ± SD
Hemoglobin (g/dL)	14.8 ± 1.9
Hematocrit (%)	44.3 ± 5.3
RBC count (×10^6/µL)	5.01 ± 0.61
WBC count (×10^3/µL)	10.4 ± 3.2
Platelets (×10^3/µL)	254 ± 68

Comparison of demographic characteristics between patients with and without polycythemia demonstrated no significant difference in mean age (65.7 ± 7.6 vs. 64.7 ± 8.8 years; p = 0.68) or BMI (21.8 ± 3.6 vs. 22.4 ± 4.2 kg/m^2; p = 0.59). However, polycythemia occurred significantly more frequently among males than females (93.8% vs. 64.7%; p = 0.018). Smoking status showed a significant association with the occurrence of polycythemia: among patients with polycythemia, 87.5% were current smokers compared with 56.5% in the non-polycythemia group (p = 0.015), and no patient with polycythemia was a never-smoker. Patients with polycythemia had significantly lower resting oxygen saturation compared with those without (84.7 ± 2.8% vs. 89.8 ± 3.9%; p < 0.001). These comparisons are summarized in Table 4.

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Table 4. Comparison of Demographic and Clinical Characteristics Between Patients with and Without Polycythemia

Variable	Polycythemia Present (n=16)	Polycythemia Absent (n=184)	p-value*
Age (years)	65.7 ± 7.6	64.7 ± 8.8	0.68
Male, n (%)	15 (93.8)	119 (64.7)	0.018
Female, n (%)	1 (6.2)	65 (35.3)	
BMI (kg/m²)	21.8 ± 3.6	22.4 ± 4.2	0.59
Current smoker, n (%)	14 (87.5)	104 (56.5)	0.015
Former smoker, n (%)	2 (12.5)	44 (23.9)	
Never smoker, n (%)	0 (0.0)	36 (19.6)	
Resting SpO_2 (%)	84.7 ± 2.8	89.8 ± 3.9	<0.001

* $p \leq 0.05$ was considered statistically significant.

DISCUSSION:

In this hospital-based study, the prevalence of secondary polycythemia among patients admitted with chronic obstructive pulmonary disease (COPD) was 8.0%, indicating that this complication remains clinically relevant despite advances in COPD management. Chronic hypoxemia resulting from progressive airflow limitation stimulates renal erythropoietin production, leading to increased erythrocyte mass as a compensatory mechanism to improve oxygen transport. Although this physiological adaptation may enhance oxygen-carrying capacity, excessive erythrocytosis increases blood viscosity and predisposes patients to thromboembolic events, pulmonary hypertension, and cardiovascular complications, particularly in resource-limited healthcare settings where access to specialized investigations may be restricted.

The prevalence observed in the present study lies within the wide range reported in the literature, although considerable variation exists across populations and clinical settings. Zhang et al., in the large COPDGene cohort of 1,928 predominantly outpatients with moderate-to-severe COPD, reported an overall prevalence of secondary polycythemia of 6.6% (9.2% among men and 3.5% among women).[7] A hospital-based study conducted in Nepal by Thapa et al., using an identical WHO-based definition of polycythemia among patients with COPD admitted to the department of medicine of a tertiary care hospital, reported a considerably higher prevalence of 23.8%.[12] Similarly, Abdelfattah et al., in a cohort of hospitalized patients with COPD in Egypt, reported polycythemia in 14% of patients.[13] Within Pakistan, Ullah et al. reported a prevalence of 10.8% among patients with COPD, which is closer to the prevalence observed in our cohort.[14] The prevalence found in the present study is thus intermediate between the outpatient COPDGene cohort and the hospital-based South Asian and Egyptian studies, which is consistent with the observation that inpatient cohorts, comprising patients with more advanced disease and longer-standing hypoxemia, tend to report a higher prevalence of polycythemia than outpatient populations. Differences in sample size, altitude, disease severity distribution, and duration of COPD across these studies may further account for the variation observed.

Male sex was significantly associated with polycythemia in the present study (93.8% vs. 64.7% among those without polycythemia; p = 0.018), consistent with the male predominance widely reported in the literature. Zhang et al.

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similarly demonstrated a strong association between male sex and secondary polycythemia (adjusted OR 3.60, 95% CI 2.20–5.90) in the COPDGene cohort.[7] Interestingly, Ullah et al. observed a comparatively less pronounced sex disparity in their Pakistani cohort.[14] This regional variation suggests that, alongside male-predominant risk factors such as cigarette smoking, indoor air pollution and biomass fuel exposure may be an important additional contributor to hypoxemia-driven erythrocytosis among women in South Asian settings. In contrast, neither age nor body mass index demonstrated a significant association with polycythemia in our cohort, in keeping with previous reports suggesting that these demographic variables contribute less to erythrocytosis than the severity of chronic hypoxemia itself.

Current smoking showed a significant association with polycythemia in our cohort, with nearly nine out of every ten patients with polycythemia being active smokers. This finding is consistent with the COPDGene study, in which current smoking was identified as a significant correlate of polycythemia.[7] Cigarette smoking increases carboxyhemoglobin levels, thereby reducing effective oxygen delivery and stimulating erythropoietin-mediated erythropoiesis; continued smoking also accelerates disease progression and worsens gas-exchange abnormalities, further increasing the risk of secondary erythrocytosis. These findings, echoed across the COPDGene, Nepalese, and Egyptian cohorts described above, underscore the importance of comprehensive smoking cessation programs as an integral component of COPD management across diverse healthcare settings.[7,12,13]

Disease severity was another important correlate of polycythemia in our study, with GOLD stage III and IV disease accounting for the majority of cases, reflecting the progressive deterioration in pulmonary function and increasing severity of chronic hypoxemia with advancing COPD. Patients with polycythemia also had significantly lower resting oxygen saturation than those without (84.7 ± 2.8% vs. 89.8 ± 3.9%; $p < 0.001$). These observations are biologically plausible and are supported by Zhang et al., who found that severe resting hypoxemia was strongly associated with an increased risk of secondary polycythemia (adjusted OR 3.50, 95% CI 1.41–8.66).[7] Chronic tissue hypoxia remains the principal stimulus for erythropoietin secretion and compensatory erythrocyte production in COPD, and the accompanying rise in whole blood viscosity is the key mechanism linking polycythemia to microvascular and thromboembolic complications.[6]

Long-term oxygen therapy remains the only intervention shown to improve survival in COPD patients with severe resting hypoxemia.[8,9] In the COPDGene cohort, continuous and nocturnal supplemental oxygen use were associated with a substantially reduced risk of polycythemia, reinforcing current guideline recommendations regarding timely identification and treatment of chronic hypoxemia in patients with advanced disease.[7] Interestingly, secondary polycythemia does not appear to uniformly predict worse clinical outcomes: in the SPIROMICS cohort, Fawzy et al. reported that polycythemic patients experienced fewer severe exacerbations requiring hospitalization than their normocythemic counterparts, despite having more advanced physiological impairment.[11] Taken together with the higher prevalence rates reported in hospital-based South Asian and Egyptian cohorts,[12,13,14] these findings suggest that the clinical significance of elevated hematocrit in COPD is context-dependent, and that its principal value may lie in flagging patients with unrecognized severe hypoxemia who warrant closer evaluation, rather than serving as a uniform marker of prognosis across all settings.

The present study has several clinical implications. Complete blood count and pulse oximetry are inexpensive and universally available investigations that can facilitate early recognition of secondary polycythemia, even in resource-constrained hospitals. Routine assessment of hemoglobin, hematocrit, smoking status, and resting oxygen saturation among hospitalized patients with COPD may help identify individuals at increased risk who could benefit from further

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evaluation for chronic hypoxemia, optimization of long-term oxygen therapy, and intensified smoking cessation interventions.

This study has certain limitations. It was conducted at a single tertiary care center using a non-probability consecutive sampling technique, which may limit the generalizability of the findings to other populations. The cross-sectional design precludes assessment of causality or of longitudinal changes in hematological parameters with disease progression or treatment. Arterial blood gas analysis and pulmonary hemodynamic assessment were not routinely performed. Larger, prospective, multicenter studies employing multivariable analysis are warranted to validate these findings and to determine whether early detection and management of secondary polycythemia translate into improved long-term clinical outcomes.

CONCLUSION:

Secondary polycythemia was present in 8.0% of patients hospitalized with COPD in this cohort, and was significantly associated with male sex, current smoking, and severe resting hypoxemia. These findings support the incorporation of routine hemoglobin, hematocrit, and pulse oximetry assessment into the evaluation of hospitalized COPD patients, enabling early identification of individuals who may benefit from optimization of long-term oxygen therapy and smoking cessation. Larger, prospective, multicenter studies employing multivariable analysis are needed to confirm these associations and to clarify the prognostic significance of secondary polycythemia in COPD.

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