European Journal of Clinical Pharmacy

Print ISSN: 2385-409X, **Online ISSN**: 3105-0409
Website: https://farmclin.com/

Prevalence, Risk Factors, and Clinical Outcomes of Secondary Polycythemia in COPD Patients in a Tertiary Care Setting

Article History:

Name of Author:
Dr. Sada Saeed[1],Dr. Bushra Arif[2], Dr.Hala Afandi[3],Dr.Sabeen Sajjad[4],Dr.Hamid Nisar Khan[5],Dr. Fazal Mustaan[6]

Affiliation: *[1]Specialty Registrar, Pulmonology Ayub Teaching Hospital, Abbottabad, Pakistan*
[2]Pulmonology Department Ayub Teaching Hospital, Abbottabad, Pakistan
[3]Senior Registrar, Pulmonology Department, Rawal Institute of Health Sciences Islamabad
[4]Department of Medicine Ayub Teaching Hospital, Abbottabad, Pakistan
[5]Consultant Pulmonologist Ayub Teaching Hospital, Abbottabad, Pakista
[6]Trainee Registrar, Pulmonology Ayub Teaching Hospital, Abbottabad, Pakistan.

Corresponding Author:
Dr. Bushra Arif,

Email: *bushytauian@yahoo.com*

Received*:* 06-11-2025
Revised*:* 11-12-2025
Accepted*:* 16-12-2025
Published*:* 27-12-2025

Abstract: ***Background:*** Chronic obstructive pulmonary disease is often complicated by a state of chronic hypoxemia, which may result in secondary polycythemia as a compensatory body reaction. However, little information is available about the prevalence and risk factors for this complication and its implications among local populations of Pakistan. ***Objective:*** To determine the prevalence, risk factors, and clinical outcomes of secondary polycythemia in patients with COPD at a tertiary care hospital .***Methods:*** The study is a cross-sectional analytical study, and it was conducted at the Medical Teaching Institution, Ayub Medical Complex Abbottabad, from January 1, 2022, to December 1, 2022. In this study, 220 patients were included after spirometric confirmation of COPD. Demographic characteristics, smoking habits, disease severity according to GOLD classification, oxygen saturation levels (SpO_2), hematologic parameters, and outcomes were documented. Secondary polycythemia was identified based on gender-specific hemoglobin and hematocrit levels. Statistical analysis was performed using SPSS software for descriptive statistics, chi-square test, independent t-test, and multivariate logistic regression analysis .***Results:*** The mean age of participants was 62.6 ± 9.8 years, with 70.0% males. Secondary polycythemia was observed in 11.8% of patients. It was significantly associated with hypoxemia ($p < 0.001$), advanced COPD ($p < 0.001$), and increased hospitalization rates ($p < 0.001$). Patients with polycythemia had lower SpO_2 and FEV1 levels ($p < 0.001$). On multivariate analysis, hypoxemia emerged as the only independent predictor (OR = 43.28, $p < 0.001$).***Conclusion:*** Secondary polycythemia is a clinically relevant complication in COPD and is strongly associated with hypoxemia and increased disease burden. Early identification and management of hypoxemia may help reduce the risk and improve clinical outcomes.

Keywords: COPD, secondary polycythemia, hypoxemia, prevalence, risk factors, outcomes.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a serious public health problem that continues to cause substantial morbidity and mortality and utilize extensive healthcare resources [1]. COPD is now being recognized as one of the most important causes of mortality, especially in low- and middle-income countries, where exposure to cigarette smoke, biomass fuels, and environmental toxins is common [2,3]. In South Asian countries, including Pakistan, COPD is further complicated by delayed diagnosis and treatment, and a high prevalence of risk factors [4,5]. It is in this context that the patients are seen in the late stages of the disease process with systemic manifestations involving different body systems, thereby necessitating the evaluation of the patient [6]. One of the important manifestations of the progression of COPD is the development of chronic hypoxemia, which is the result of the sustained decrease in airflow and the defective gas exchange process [7]. This sustained decrease in the level of oxygen in the blood eventually triggers the body's compensatory mechanisms to maintain the level of tissue oxygenation [8]. While the compensatory mechanisms are beneficial in the early stages of the disease process, the sustained effect of the disease process eventually manifests in the form of maladaptive changes [9].

The compensatory changes in the disease process are in the form of the development of secondary polycythemia, which is defined as the increase in the level of red blood cells in the blood in response to the sustained decrease in the level of oxygen in the blood [10,11]. This process is mediated through the sustained increase in the level of erythropoietin in the blood [12]. This increase in the level of hematocrit in the blood is a double-edged sword. While this sustained increase in the level of hematocrit in the blood is advantageous in the short term, it also has the adverse effect of causing disturbances in the blood circulation process. This is of immense clinical concern in the context of patients with COPD, as this factor has the direct potential of affecting the progression of the disease process [13].

The implications of the disease process are immense in the context of patients with COPD and the development of secondary polycythemia [14]. The sustained increase in the level of hematocrit in the blood has the adverse effect of leading to several complications, including the development of hyperviscosity syndrome, the development of thromboembolic phenomena, and the development of pulmonary hypertension [15].

All these may result in a deterioration in functional capacity, increased hospitalizations, and adverse outcomes. However, this is often not recognized in routine practice, especially in resource-constrained environments[16].

The prevalence and risk factors for secondary polycythemia in patients with COPD have been explored in the existing literature to some extent. However, the prevalence rates and risk factors have been inconsistent [17,18]. This inconsistency can be due to differences in the population studies and the diagnostic criteria. In addition, the availability of studies from developing countries like Pakistan is scarce. In addition to this, there is a lack of studies that have explored the relationship between the prevalence and risk factors for secondary polycythemia and clinical outcomes in one population of patients. In this regard, the current study aims to fill this knowledge gap by investigating the prevalence of secondary polycythemia and its associated risk factors and clinical outcomes in patients with chronic obstructive pulmonary disease in a tertiary care hospital in Abbottabad, Pakistan. Tertiary care hospitals are those that provide medical care to patients who have already been treated in a primary care hospital and require specialized care for their medical conditions. In this regard, patients attending a tertiary care hospital for chronic obstructive pulmonary disease will have more severe disease and a greater number of associated risk factors. This will provide a more accurate clinical scenario for patients with chronic obstructive pulmonary disease in general.

The current study aims to determine the prevalence of secondary polycythemia and its associated risk factors and clinical outcomes in patients with chronic obstructive pulmonary disease in a tertiary care hospital in Abbottabad, Pakistan.

MATERIALS AND METHODS

This was a cross-sectional analytical study that was conducted in the Medical Teaching Institution, Ayub Medical Complex Abbottabad, Pakistan. The period for which this study was conducted was from the 1st of January 2022 to the 1st of December 2022. This study was aimed at assessing the prevalence of secondary polycythemia and its associated risk factors and clinical outcomes in patients with chronic obstructive pulmonary disease. Ethical approval was obtained before the start of the study. Informed consent was obtained from the patients. Confidentiality of patient information was maintained throughout the study period.

The sample size was calculated using a formula for prevalence-based studies. It was estimated that the prevalence of secondary polycythemia was going to be 15%. The confidence level was set at 95%. The margin of error was set at 5%. The minimum sample size was estimated to be 196 patients. In this study, a total of 220 patients were included.

The study population consisted of patients aged 40 years and above, of either gender, with a confirmed diagnosis of COPD. The diagnosis was made on the basis of spirometric values, with the FEV1/FVC ratio being less than 0.70. The patients were recruited from outpatient clinics as well as inpatient departments. The inclusion criterion for the patients was the presence of documented evidence of the diagnosis of COPD, and the patient should either be stable or present with acute exacerbations. The exclusion criterion was the presence of any condition known to independently alter the hematological parameters, such as primary polycythemia, hematological malignancy, chronic renal disease, congenital heart disease, or history of recent transfusion of blood products within the preceding three months. The data was collected using a structured proforma, and the data collection was done on the basis of patient presentation. The data collected included demographic information such as age, gender, and residential area, along with the history of smoking quantified in terms of pack years and the duration of disease since the diagnosis. The clinical evaluation of the patient included the assessment of symptoms, peripheral oxygen saturation using pulse oximetry, and arterial blood gas analysis. The laboratory investigations included the determination of the level of hemoglobin and the hematocrit level. The severity of the disease was determined by spirometry, and the severity was graded based on the GOLD classification. The history of the frequency of acute exacerbations over the preceding year and the history of hospitalizations due to acute exacerbations were also documented.

The secondary polycythemia was operationally defined by elevated levels of hemoglobin and hematocrit. The criteria for secondary polycythemia were set as values greater than 16.5 g/dL for men and values greater than 16.0 g/dL for women for hemoglobin. For hematocrit values, the criteria for secondary polycythemia were set as values greater than 49% for men and values greater than 48% for women. The hypoxemia was defined by a peripheral saturation of oxygen (SpO2) of less than 90% breathing room air and/or a partial pressure of arterial oxygen (PaO2) of less than 60 mmHg. The severity of COPD was defined by GOLD staging based on FEV1 values after bronchodilator. Acute exacerbations of COPD were defined by episodes of increased symptoms of COPD that necessitated additional therapy. Hospitalization was defined by hospital admission for COPD-related complications.

The Statistical Package for the Social Sciences (SPSS), version 25.0, was used for entering and analyzing the data. Descriptive statistics were computed for the entire set of variables. The results for the continuous variables were expressed as mean values ± SD. The results for the categorical variables were expressed as frequency and percentages. Comparative studies between patients with and without secondary polycythemia were done using the t-test for continuous variables and the chi-square test for categorical variables. Multivariate logistic regression was used to determine the risk factors for secondary polycythemia while adjusting for confounders. The results were expressed as odds ratio with its 95% confidence interval. The results were considered significant if the p-value was ≤0.05.

RESULTS

A total of 220 patients with known chronic obstructive pulmonary disease (COPD) were included in the study. The mean age of the patients included in the study was 62.6 years ± 9.8 years. The majority of patients included in the study were males (70.0%), and the mean body mass index (BMI) was 24.7 kg/m² ± 3.9 kg/m². The majority of patients included in the study had moderate to severe disease. The percentage of patients included in the study was 40.0% for GOLD stage II and 35.0% for GOLD stage III. The percentage of patients included in the study with hypoxemia was 30.5%. The baseline characteristics of patients included in the study are mentioned in Table 1.

Table 1: Baseline Characteristics of the Study Population (n = 220)

Variable	Value
Age (years)	62.6 ± 9.8
BMI (kg/m²)	24.7 ± 3.9
FEV_1 (% predicted)	49.8 ± 18.6
SpO_2 (%)	91.2 ± 3.4
Hemoglobin (g/dL)	15.2 ± 1.6
Male gender	154 (70.0%)
Female gender	66 (30.0%)
Smoking status	
— Current smokers	102 (46.4%)
— Former smokers	63 (28.6%)
— Never smokers	55 (25.0%)

GOLD stage	
— Stage I	22 (10.0%)
— Stage II	88 (40.0%)
— Stage III	77 (35.0%)
— Stage IV	33 (15.0%)
Hypoxemia (SpO_2 <90%)	67 (30.5%)
Secondary polycythemia	26 (11.8%)

The secondary polycythemia was identified in 26 patients, giving a prevalence of 11.8%. Patients with polycythemia had lower oxygen saturation levels and more severe disease than those without polycythemia.

In the bivariate analysis, secondary polycythemia was associated with markers of disease severity and hypoxemia. The percentage of patients with secondary polycythemia who had hypoxemia was significantly higher than those without polycythemia (92.3% vs 22.2%, $p < 0.001$). Patients with secondary polycythemia had more advanced COPD (GOLD III-IV) than those without polycythemia (88.5% vs 45.8%, $p < 0.001$). Patients with secondary polycythemia had a higher percentage of hospitalizations than those without polycythemia (69.2% vs 28.9%, $p < 0.001$), as shown in Table 2.

Table 2: Association of Secondary Polycythemia with Clinical Variables

A. Categorical Variables

Variable	Polycythemia Yes (n=26)	Polycythemia No (n=194)	p-value
Hypoxemia (SpO_2 <90%)	24 (92.3%)	43 (22.2%)	<0.001
Normal SpO_2	2 (7.7%)	151 (77.8%)	
GOLD Stage III–IV	23 (88.5%)	89 (45.8%)	<0.001
GOLD Stage I–II	3 (11.5%)	105 (54.2%)	
Hospitalization	18 (69.2%)	56 (28.9%)	<0.001
No Hospitalization	8 (30.8%)	138 (71.1%)	

Continuous Variables

Variable	Polycythemia Yes (Mean ± SD)	Polycythemia No (Mean ± SD)	p-value
SpO_2 (%)	87.8 ± 2.5	91.8 ± 3.1	<0.001
FEV_1 (% predicted)	39.6 ± 8.2	55.1 ± 17.4	<0.001
Hemoglobin (g/dL)	17.3 ± 0.9	14.1 ± 1.2	<0.001
Age (years)	60.2 ± 8.7	62.9 ± 9.9	0.15
BMI (kg/m^2)	23.9 ± 3.6	24.4 ± 4.0	0.57

In terms of continuous variables, patients with polycythemia were found to have lower mean oxygen saturation (87.8% vs. 91.8%, $p < 0.001$) and lower FEV1 (% predicted) (39.6% vs. 55.1%, $p < 0.001$). Hemoglobin was found to be higher in the polycythemia patient group compared to the non-polycythemia patient group (17.3 vs. 14.1 g/dL, $p < 0.001$). There were no significant differences found for the continuous variables of age, BMI, smoking, ICU admission, or the presence of comorbidities ($p > 0.05$).

Multivariate logistic regression analysis was performed to identify the independent predictors of secondary polycythemia. After adjusting for all the possible confounding variables, the only independent predictor for secondary polycythemia was found to be hypoxemia. The patient group with hypoxemia was found to have very high odds for the development of secondary polycythemia ($p < 0.001$, OR = 43.28, 95% CI: 7.12-263.4). The results of the regression analysis are presented in Table 3.

Table 3: Multivariate Logistic Regression Analysis for Predictors of Secondary Polycythemia

Variable	Odds Ratio (OR)	95% Confidence Interval	p-value
Age (years)	0.98	0.92 – 1.02	0.36
BMI (kg/m^2)	0.93	0.81 – 1.07	0.34
Pack-years	1.01	0.98 – 1.03	0.49
Hypoxemia (SpO_2 <90%)	**43.28**	**7.12 – 263.4**	**<0.001**
GOLD Stage (III–IV)	1.08	0.20 – 5.61	0.92

Overall, the results suggest that secondary polycythemia in COPD is strongly related to chronic hypoxemia and is associated with disease severity and hospitalization rates.

DISCUSSION

The present study assessed the prevalence, risk factors, and outcomes of secondary polycythemia in patients suffering from COPD and identified various determinants and outcomes in a tertiary care setting. The results show that secondary polycythemia is a clinically important complication and is prevalent in 11.8% of patients suffering from COPD. More importantly, this study identified chronic hypoxemia as a key determinant for secondary polycythemia and emphasized its link to disease severity and poor outcomes.

The prevalence of secondary polycythemia in this study is similar to previous reports and ranges from 5-20%. The prevalence may be related to various factors, including disease characteristics and improved management strategies for COPD patients [17–19]. Compared to previous studies, this study may show a slightly lower prevalence due to improved management and monitoring of patients suffering from COPD. More importantly, this study identified that patients suffering from COPD and experiencing hypoxemia have a significantly greater risk for developing secondary polycythemia. Hypoxemia is identified as a key predictor for secondary polycythemia in this study. More specifically, patients experiencing less than 90% oxygen saturation levels have a greater probability for developing secondary polycythemia. Hypoxemia is identified as the only predictor for secondary polycythemia in this study.
The link between secondary polycythemia and hypoxemia is evident and is related to erythropoietin levels and compensatory mechanisms for low oxygen levels in patients suffering from COPD. The link is evident and is related to erythropoietin levels and compensatory mechanisms for low oxygen levels [15].

While there was a significant association between the severity of disease, as measured by the GOLD staging system, and polycythemia in the bivariate analysis, this was not sustained in the regression analysis. This suggests that the role of disease severity is mediated through hypoxemia and is not independent. This is an important distinction because polycythemia is not caused by the severity of airflow limitation but is caused by the degree of hypoxemia [20]. This is an important clinical distinction because one must focus on hypoxemia rather than airflow limitation in the assessment of polycythemia risk in patients with chronic obstructive pulmonary disease.

Another interesting observation from this study is that patients with secondary polycythemia have a significantly higher rate of hospitalization. This is an important observation because polycythemia is clearly having an important clinical role in patients with chronic obstructive pulmonary disease. Polycythemia is often considered to be one of the markers for chronic obstructive pulmonary disease because blood viscosity is known to be high in patients with polycythemia. This can lead to problems in patients with chronic obstructive pulmonary disease because blood is known to be thicker. While there was no significant association with ICU admission, this could be because of other factors [17].

Interestingly, age, BMI, and smoking exposure were not independently associated with secondary polycythemia in this study. Smoking, which is a well-known risk factor for COPD, indirectly contributes to secondary polycythemia by inducing hypoxemia, which is a major risk factor for the condition. Similarly, age, BMI, and other demographic and anthropometric factors, while possibly influencing the course of the disease, do not directly contribute to secondary polycythemia, especially after accounting for the effects of oxygenation[21,22].

The results of this study have a number of clinical implications for the management of patients with COPD. The results of the study highlight the importance of routine monitoring of oxygen saturation levels in patients with COPD, as the detection of hypoxemia as the major risk factor for secondary polycythemia can help in the timely management of the condition, thereby reducing the risks of secondary polycythemia and its associated complications. The results of the study also highlight the fact that patients with COPD should be monitored for secondary polycythemia, especially in the late stages of the disease, as timely management of the condition can help in improving patient outcome.

It should, however, be noted that this study has some limitations, which include the fact that the study was a single-center study, which might limit the generalization of the results to other populations. The fact that the study was a cross-sectional study might also limit the establishment of causality between the variables. Furthermore, the fact that some confounding variables might have affected the results, despite the efforts made to include all relevant variables, should also be noted.

The study has shown that secondary polycythemia is a relatively common condition among COPD patients, which is associated with hypoxemia, the severity of the disease, and increased hospitalization rates.

CONCLUSION

This research has proved that secondary polycythemia is an important complication in the clinical course of chronic obstructive pulmonary disease, with a prevalence of 11.8% in the tertiary hospital setting.

The research has also proved that chronic hypoxemia is the main and independent predictor of secondary polycythemia.

Patients with secondary polycythemia were found to have more severe disease and higher rates of hospitalization, thus confirming the association of secondary polycythemia with increased disease severity and poor clinical outcomes. The research has proved that secondary polycythemia may be an important clinical marker for the presence of hypoxemia in the clinical course of COPD.

It is very important to monitor the level of oxygen saturation in the management of patients with COPD, and the early detection of hypoxemia may help in the prevention of secondary polycythemia and its complications. Further research is recommended to evaluate the impact of secondary polycythemia on the mortality rate in the clinical course of COPD.

REFERENCES

1. Doke PP. Chronic respiratory diseases: a rapidly emerging public health menace. Indian J Public Health. 2023;67(2):192–6.
2. Mei F, Dalmartello M, Bonifazi M, Bertuccio P, Levi F, Boffetta P, et al. Chronic obstructive pulmonary disease (COPD) mortality trends worldwide: An update to 2019. Respirology. 2022;27(11):941–50.
3. Halpin DM. Mortality of patients with COPD. Expert Rev Respir Med. 2024;18(6):381–95.
4. Ghorpade D, Salvi S. Awareness of COPD in low-and middle-income countries and implications for treatment. Expert Rev Respir Med. 2024;18(9):721–33.
5. Khan KS, Jawaid S, Memon UA, Perera T, Khan U, Farwa UE, et al. Management of chronic obstructive pulmonary disease (COPD) exacerbations in hospitalized patients from admission to discharge: a comprehensive review of therapeutic interventions. Cureus. 2023;15(8).
6. Agusti A, Ambrosino N, Blackstock F, Bourbeau J, Casaburi R, Celli B, et al. COPD: providing the right treatment for the right patient at the right time. Respir Med. 2023;207:107041.
7. Rodríguez-Pérez J, Andreu-Martínez R, Daza R, Fernández-Arroyo L, Hernández-García A, Díaz-García E, et al. Oxidative stress and inflammation in hypoxemic respiratory diseases and their comorbidities: molecular insights and diagnostic advances in chronic obstructive pulmonary disease and sleep apnea. Antioxidants. 2025;14(7):839.
8. Domnik NJ, Phillips DB, James MD, Ayoo GA, Taylor SM, Scheeren RE, et al. Compensatory responses to increased mechanical abnormalities in COPD during sleep. Eur J Appl Physiol. 2022;122(3):663–76.
9. Lacasse Y, Joseph V, Casaburi R, Maltais F. Translating the mechanisms of hypoxia to long-term oxygen prescription in COPD: A proposal. Chest. 2025.
10. Tiller NB, Porszasz J, Casaburi R, Rossiter HB, Ferguson C. Critical power and respiratory compensation point are not equivalent in patients with COPD. Med Sci Sports Exerc. 2023;55(6):1097.
11. Nielsen BB, Springborg CJ, Jacobsen PA, Weinreich UM. Anemia and polycythemia in patients hospitalised with acute exacerbations of chronic obstructive pulmonary disease: prevalence, patient characteristics, and risk of readmission and mortality. Eur Clin Respir J. 2025;12(1):2546672.
12. Alsagheer BMB, Kanawati MMR, Ali DH, Al-Bardan H. Secondary polycythemia in patients with chronic obstructive pulmonary disease. 2023.
13. Thapa KB, Paudel A, Dhital S, Shrestha A, Ojha L, Shrestha A. Polycythemia among Patients with Chronic Obstructive Pulmonary Disease Admitted to the Department of Medicine in a Tertiary Care Center: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2023;61(260):343.
14. Nielsen BB, Springborg CJ, Jacobsen PA, Weinreich UM. Anemia and polycythemia in patients hospitalised with acute exacerbations of chronic obstructive pulmonary disease: prevalence, patient characteristics, and risk of readmission and mortality. Eur Clin Respir J. 2025;12(1):2546672.
15. Tariq S, Ismail D, Thapa M, Goriparthi L, Pradeep R, Khalid K, et al. Chronic Obstructive Pulmonary Disease and Its Effect on Red Blood Cell Indices. Cureus. 2023 Mar 13. doi:10.7759/cureus.36100
16. Wu S, Yi Q, Luo Y, Wei H, Ge H, Liu H, et al. Hemoglobin and clinical outcomes of in-hospital patients with severe acute exacerbation of chronic obstructive pulmonary disease: a multicenter cohort study. Front Med. 2025;12:1674268.
17. Li J, Xiong Y, Li S, Ye Q, Han Y, Zhang X, et al. Prevalence and risk factors of pulmonary embolism in COPD patients complicated with secondary polycythemia. Int J Chron Obstruct Pulmon Dis. 2024;2371–85.
18. Nielsen BB, Springborg CJ, Jacobsen PA, Weinreich UM. Anemia and polycythemia in patients hospitalised with acute exacerbations of chronic obstructive pulmonary disease: prevalence, patient characteristics, and risk of readmission and mortality. Eur Clin Respir J. 2025;12(1):2546672.
19. Krecak I, Lekovic D, Arsenovic I, Dabcevic N, Ivankovic I, Holik H, et al. Prevalence of Chronic

Obstructive Pulmonary Disease and Asthma in Polycythemia Vera and Essential Thrombocythemia and Its Prognostic Implications. J Clin Med. 2025;14(23):8416.
20. Thapa KB, Paudel A, Dhital S, Shrestha A, Ojha L, Shrestha A. Polycythemia among Patients with Chronic Obstructive Pulmonary Disease Admitted to the Department of Medicine in a Tertiary Care Center: A Descriptive Cross-sectional Study. JNMA J Nepal Med Assoc. 2023;61(260):343.
21. Ilkkilic K, Karadogan D, Telatar TG, Cure O, Klisic A. Effect of smoking and smoking cessation on hematological parameters in polycythemic patients. Open Med. 2025;20(1):20251181.
22. Panjwani A, Burle VS, Raj R, Thomas S, Gorantla V. Secondary polycythemia and venous thromboembolism: a systematic review. F1000Research. 2023;12:758.

