Hematological and clinical profiling of chronic obstructive pulmonary disease: a comprehensive study

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Abstract

Chronic obstructive pulmonary disease (COPD) presents as a multifaceted clinical landscape with various hematological manifestations. Among these, polycythemia and anemia pose distinct challenges. While the prevalence of polycythemia has decreased in recent years, anemia remains a prevalent concern, impacting patient outcomes. This study investigated the incidence and clinical characteristics of polycythemia in COPD patients, focusing on a diverse cohort in India. Methodological approaches included comprehensive evaluations of clinical parameters, pulmonary function, and hematological profiles. Results revealed significant variations in COPD severity, pulmonary function, and respiratory symptoms among patients with different hemoglobin levels. The findings shed light on the complex interplay between hematological variations and clinical manifestations in COPD, providing valuable insights for disease management strategies.

Introduction

Chronic obstructive pulmonary disease (COPD), a significant global health concern, is often accompanied by a range of comorbidities, including cardiovascular diseases, anemia, and polycythemia [1]. While historically prevalent, the occurrence of polycythemia in COPD has decreased due to improved healthcare and hypoxemia correction. Anemia now emerges as a common issue, associated with higher mortality rates [2]. It has been well-established that advanced cases of COPD lead to secondary polycythemia due to erythrocytosis induced by hypoxia [3]. Polycythemia is linked to complications such as pulmonary hypertension and endothelial dysfunction [4]. A negative association is found in these patients with high hematocrit and age, forced expiratory volume in the first second (FEV1) predicted, and FEV1/forced vital capacity (FVC) ratio, while positive correlations were observed with male gender, current smoking status, partial pressure of carbon dioxide (pCO_2), and body mass index (BMI) in COPD patients [5]. Despite its impact, a thorough analysis of polycythemia incidence and characteristics, and COPD severity, particularly in high-COPD-burden countries like India, is lacking. Factors contributing to polycythemia include smoking and chronic hypoxemia [6,7], although underlying mechanisms remain unclear. The study seeks to address this gap by investigating the occurrence and clinical features of polycythemia in COPD patients in India.

Materials and Methods

This observational, cross-sectional study enrolled 367 COPD patients after institutional ethical approval. Patients, aged over 40

years, demonstrating polycythemia, clinical stability, and obstructive airway diseases (OAD), were recruited from a tertiary care hospital, New Delhi, India, over 1 year. Informed consent was obtained from all patients. Exclusion criteria encompassed individuals with alternative obstructive respiratory diseases, such as bronchial asthma, as well as those with cardiac or renal conditions, active pulmonary tuberculosis, post-tubercular OAD, and individuals on long-term oxygen therapy (LTOT). Baseline investigations included complete blood count, serum electrolytes, liver and renal function tests, fasting blood sugar, sputum for acid-fast bacilli, and chest X-ray (PA view). According to the World Health Organization guidelines (2016), polycythemia was defined as hemoglobin levels exceeding 16.5 gm/dL in males and 16 gm/dL in females, with hematocrit levels surpassing 52% in males and 48% in females. Normochromic hemoglobin levels were within the range of 12-16 gm/dL for females and 13-16.5 gm/dL for males. Anemia was diagnosed with hemoglobin levels below 12 gm/dL for females and below 13 gm/dL for males. Specialized examinations focused on various parameters, including demographics, smoking history, COPD duration, peripheral oxygen saturation (SpO_2), respiratory and pulse rates, BMI, arterial blood gas analysis, spirometry, modified Medical Research Council (MMRC) dyspnea scale, and electrocardiogram (ECG). These parameters provided a comprehensive understanding of the study cohort, aiding in the analysis of potential associations and patterns.

Results

Study population overview

The study involved 367 participants, reflecting a diverse age distribution with a mean age of 58±8.5 years. Participants were categorized into distinct age groups, with the highest percentage (31.1%) falling in the 61-65-year range and the lowest (7.4%) in the 40-45-year range. Gender distribution showed 77.4% male and 22.6% female participants. Participants were categorized into three hemoglobin groups: normochromic (73.6%), anemic (17.4%), and polycythemia (9%). Detailed demographic details are provided in Table 1.

Analysis of clinical symptoms

Examining respiratory symptoms, we found variability across the cohorts. Cough was reported most frequently by anemic patients, followed by those in the polycythemia and normochromic groups. Shortness of breath was also prevalent among all groups, with anemic patients reporting the highest incidence. Wheezing and chest pain showed varying prevalence among the groups, suggesting potential cardiovascular implications. ECG abnormalities were noted in both the anemic and normochromic groups, whereas fewer cases were observed in the polycythemia group. These abnormalities primarily included pulmonale and right ventricular hypertrophy. Additionally, some cases in all groups showed ST elevation and prolonged PR intervals. Hypoxemia was most prevalent in the normochromic group, while smoking history distribution differed among the groups. The detailed findings of these characteristics have been summarised in Table 1.

Clinical characteristics

Significant variations were observed in BMI among the three groups. Polycythemia patients exhibited the highest BMI compared to normochromic and anemic patients. Additionally, differences in the grading of COPD and MMRC grading were noted among the groups. Among anemic patients, the majority of patients (62.5%) exhibited severe COPD, followed by 25% with

Table 1. Demographic and clinical characteristics of COPD patients by hemoglobin levels.

Total patients (n=367)				
Male	284 (77.4%)			
Female	83 (22.6%)			
Parameter	**Normochromic**	**Anemic**	**Polycythemia**	**p**
Body mass index				
Mean BMI (kg/m^2)	23.40	19.88	26.23	
Grading of COPD, n (%)				
Mild	3 (1.1)	0	1 (3.1)	0.005
Moderate	43 (15.9)	8 (12.5)	10 (30.3)	
Severe	183 (67.8)	40 (62.5)	11 (33.3)	
Very severe	41 (15.2)	16 (25)	11 (33.3)	
MMRC grading, n (%)				
Grade 1	0	0	1 (3)	<0.001
Grade 2	176 (65.2)	7 (10.9)	25 (75.8)	
Grade 3	83 (30.7)	47 (73.4)	6 (18.2)	
Grade 4	11 (4.1)	10 (15.6)	1 (3)	
Respiratory symptoms, n (%)				
Cough	195 (72.25)	64 (100)	28 (84)	<0.001
Shortness of breath	196 (72.2)	64 (100)	31 (93.9)	<0.001
Wheezing	133 (49.2)	41 (64)	13 (39)	0.039
Chest pain	77 (28)	22 (34)	4 (12)	0.06
ECG abnormalities	46 (17)	10 (5.7)	3 (9)	0.494
Hypoxemia	240 (88.8)	49 (76.5)	26 (78)	0.019
Smoking history	240 (83.7)	64 (100)	29 (87.8)	0.002

BMI, body mass index; COPD, chronic obstructive pulmonary disease; MMRC, modified medical research council; p-value of less than 0.05 was considered statistically significant.

very severe COPD and 12.5% with moderate severity. In the normochromic group, 67.8% patients had severe COPD, among these, 15.2% patients were classified as very severe. In the polycythemia group, 33.3% patients had severe COPD, with an equal number of patients categorized as very severe. Patients with normal hemoglobin levels had a higher incidence of severe COPD compared to the polycythemia group, with a significantly lower incidence of very severe COPD (p=0.005). The MMRC grading distribution across the three hemoglobin groups revealed varied severity levels: the normochromic group had predominantly moderate to severe COPD, while the anemic and polycythemia groups showed diverse distributions across mild to very severe categories. Specifically, anemic patients experienced severe symptoms more frequently. While patients having polycythemia had moderate symptoms followed by severe and very severe symptoms (Table 1). These findings highlight the distribution of COPD severity across hematological groups, underscoring the interplay between pulmonary function and hematological profiles in this diverse patient cohort.

Hematological analysis

A comparative analysis between patients having polycythemia and anemia revealed distinct patterns across various health parameters. Patients in the polycythemia group (mean age: 56.39±7.5 years) were slightly younger than those in the anemic group (mean age: 57.75±7.8 years). Polycythemia patients exhibited better pulmonary function compared to anemic patients. Arterial blood gas analyses showed significant differences in pH, pCO_2, partial pressure of oxygen (pO_2), HCO_3, and the base excess levels between the two groups. Patients with polycythemia had lower pO_2 but higher pCO_2 compared to anemic patients. Additionally, patients with polycythemia had higher base excess values and bicarbonate levels, indicating differences in acid-base balance. Such patients also exhibited higher SpO_2 compared to anemic patients.

Patients with polycythemia were in the younger age group and had better lung function (FEV1%) when compared to the normochromic group. Interestingly, blood gas analysis of polycythemia individuals showed higher levels of CO_2, bicarbonate, and base excess, but lower oxygen levels. Furthermore, polycythemia individuals experienced higher SpO_2 compared to the normochromic group. These findings suggest distinct health profiles associated with different blood cell characteristics, highlighting the need for further exploration of these relationships. The details of these findings have been tabulated in Table 2.

Discussion

COPD remains a significant public health concern, motivating our investigation into the association between hematological profiles and COPD severity. This study represents the first comprehensive analysis of hemoglobin levels in 367 COPD patients in India, revealing concurrent patterns of both anemia and polycythemia. In our COPD population, 9% of patients had polycythemia, while 17% displayed anemia, which is almost double. These results are consistent with existing research, demonstrating a 23.5% prevalence of anemia [8], and are in concordance with a separate study reporting a 14% prevalence of anemia and 5% prevalence of polycythemia in individuals with COPD [9]. This trend may reflect advancements in COPD management, including the widespread use of LTOT, which has been associated with improved oxygenation and a potential reduction in the stimulus for excessive red blood cell production [10,11]. Malnutrition is common in COPD patients and contributes to lower hemoglobin levels and the development of anemia, reflecting the systemic inflammatory nature of COPD. Anemia is associated with lower mean BMI, which is consistent with existing literature highlighting the link between anemia and malnutrition. Conversely, the polycythemia group exhibited a higher mean BMI, which correlates with studies suggesting a positive correlation between BMI and hematocrit [12]. The higher BMI in polycythemia patients aligns with decreased ventilatory drive, contributing to elevated hypoxemia and hypercapnia levels [13]. Additionally, anemic individuals in our study showed a correlation with COPD severi-

Table 2. Comparative clinical profiles among three hematological groups.

Variable	Polycythemia	Anemia	Normochromic	P	
N	33 (27M/6F)	64 (45M/19F)	270 (212M/58F)	P *vs.* A	P *vs.* N
Age	56.39±7.545	57.75±7.8	58.36±8.874	0.414	0.22
Hemoglobin	17.521±1.3467	11.278±0.899	13.793±0.653	<0.00001	<0.00001
BMI	26.233±1.582	19.88±1.481	23.40±1.411	<0.00001	<0.00001
FEV_1%	39.27±16.436	32.92±9.33	36.50±10.954	0.01698	0.198
FVC	2.27±0.677	2.04±0.441	2.292±0.531	0.0434	0.855
FEV_1/FVC	54.06±11.570	50.38±88.635	50.333±9.387	0.080	0.0369
pH	7.373±0.029	7.398±0.055	7.383±0.458	0.0144	0.192
pCO_2	53.30±4.38	44.64±14.89	47.818±13.075	0.00153	0.0173
pO_2	63.93±6.89	72.61±16.27	67.931±17.83	0.0043	0.2
HCO_3	29.885±1.68	26.364±5.632	27.161±4.741	0.0007	0.00198
Base excess	4.379±2.340	1.945±4.93	2.111±4.117	0.0087	0.002126
Duration of COPD	5.64±4.053	5.009±4.852	6.38±4.473	0.526	0.366
Smoking index	390.5±400	605.61±454.87	450±384.05	0.02	0.213
O_2 saturation	89.61±3.807	82.94±8.463	85.47±6.486	0.000041	0.000391

M, male; F, female; P, polycythemia; A, anemia; N, normochromic; BMI, body mass index; FEV_1, forced expiratory volume in the first second; FVC, forced vital capacity; COPD, chronic obstructive pulmonary disease; pCO_2, partial pressure of carbon dioxide; pO_2, partial pressure of oxygen; data is presented as mean ± standard deviation; p-value of less than 0.05 was considered statistically significant.

ty, leading to increased hospital admissions and subjective dyspnea. Patients with polycythemia exhibited less pronounced COPD severity and primarily manifested moderate dyspnea. This observation aligns with reports suggesting that polycythemia in COPD patients may be a compensatory response to chronic hypoxia, which is aimed at enhancing oxygen-carrying capacity and tissue oxygenation [3].

Individuals with polycythemia exhibited lower pO_2 levels, indicating heightened susceptibility to hypoxia, which potentially contributes to erythrocytosis. Our study supports a previous report where hypoxemia triggers HIF-1 (hypoxia-inducible factor-1, transcription factor) in COPD, leading to polycythemia by upregulating erythropoietin [14]. Higher pCO_2 levels in COPD patients with polycythemia may result from compensatory responses to chronic hypoxia, leading to respiratory acidosis. Elevated base excess and HCO_3 levels suggest metabolic compensation for chronic respiratory acidosis. Despite lower pO_2 levels, polycythemia patients showed higher SpO_2 levels due to increased oxygen-carrying capacity of elevated red blood cell count [15]. Polycythemia is associated with better pulmonary function parameters, possibly due to enhanced tissue oxygenation. Anemic individuals exhibited a higher prevalence of respiratory symptoms, potentially due to reduced oxygen-carrying capacity and smoking history [16]. Conversely, individuals with polycythemia had a higher occurrence of ECG abnormalities, likely linked to increased red blood cell mass and associated cardiovascular effects [17].

The present study's strengths include its diverse COPD patient cohort, comprehensive analysis of clinical parameters, and robust statistical comparisons between various hemoglobin levels. While the present study's single-center design and homogeneous ethnic population may limit generalizability, we tried to ensure internal validity and minimize biases. Future multi-center studies with diverse ethnic cohorts will be crucial for validating and extending our findings to broader populations.

Conclusions

Our Indian study challenges previous observations by revealing a lower prevalence of polycythemia compared to anemia in COPD patients. This shift underscores the importance of considering hematological profiles in COPD management, particularly in the Indian population. Additionally, our findings indicate differences in the distribution of COPD severity between anemia and polycythemia, with anemia predominantly associated with severe cases. Interestingly, polycythemia shows a balanced distribution between severe and very severe COPD. Moreover, polycythemia is associated with better pulmonary function parameters, suggesting potential adaptive advantages in managing hypoxic conditions. The lower prevalence of respiratory symptoms in polycythemia compared to anemia underscores the complex interplay between hematological variations and clinical manifestations in COPD. This comprehensive analysis provides valuable insights into the diverse patterns of hematological alterations and their implications for COPD management in the Indian context.

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