

Association of Anemia-Related Red Blood Cell Parameters with Pulmonary Function Severity in Patients with AECOPD: A Retrospective Study

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Received: 21-02-2026 / Revised: 19-04-2026 / Accepted: 20-05-2026

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Conflict of interest: Nil

Abstract:

Background: Anemia and abnormalities in red blood cell (RBC) indices may contribute to impaired oxygen delivery and influence pulmonary dysfunction in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

Aim: To evaluate the association between anemia-related RBC parameters and pulmonary function severity in patients with AECOPD.

Methodology: This retrospective, observational study included 90 patients with AECOPD. Demographic, hematological, and pulmonary function data were retrieved from medical records. Hemoglobin, RBC count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and red cell distribution width (RDW) were assessed. Pulmonary function severity was categorized according to FEV1% predicted. Correlations between RBC parameters and FEV1% predicted were analyzed using SPSS version 27.0.

Results: The mean age was 61.4 ± 8.9 years, and 67.8% were males. Anemia was present in 46.7%, with normocytic anemia predominating (66.7%). Hemoglobin, RBC count, and MCH decreased significantly with increasing pulmonary impairment, while RDW increased (all $p < 0.05$). Hemoglobin ($r = 0.58$), MCH ($r = 0.46$), and RBC count ($r = 0.34$) showed significant positive correlations with FEV1% predicted, whereas RDW showed a significant negative correlation ($r = -0.52$; all $p < 0.001$ except RBC count).

Conclusion: Anemia-related RBC parameters, particularly hemoglobin and RDW, were significantly associated with pulmonary function severity in AECOPD.

Keywords: AECOPD; anemia; hemoglobin; red blood cell indices; RDW; FEV1; pulmonary function.

DOI: 10.25258/ijpqa.17.5.74

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Introduction

Chronic obstructive pulmonary disease (COPD) is a frequent chronic respiratory disease defined by the presence of chronic respiratory symptoms, progressive worsening of pulmonary function and persistent airflow limitation [1]. It is a significant cause of morbidity and mortality throughout the world, and often accompanied by exacerbations of respiratory symptoms that necessitate emergency treatment or hospitalisation. Acute exacerbation of COPD (AECOPD) occurs when the respiratory signs and symptoms of COPD change abruptly and significantly beyond the normal variation of the patient's day-to-day life and are frequently characterised as worsening dyspnoea, cough and increased sputum production. These exacerbations play a significant role in disease progression, decreased quality of life, increased health care utilization and mortality. The importance of pulmonary function parameters, like forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC) and FEV1/FVC ratio, in the assessment of airflow limitation is well established, but systemic factors also may impact on the

severity or functional status of patients with AECOPD [2].

Among the systemic abnormalities reported in patients with COPD, anemia is one of the more important abnormalities. Anemia is a common condition in COPD, which varies from population to population and from one clinical setting to another; the disease is most important in hospitalized patients and those who are very ill [3]. Low hemoglobin concentration may be due to chronic inflammatory conditions, nutritional deficiencies, renal dysfunction, chronic disease-related alterations in iron metabolism and others. COPD is also linked with chronic systemic inflammation, and mediators of inflammation may have an impact on the process of erythropoiesis and the use of iron [4]. Anemia therefore can occur in association with respiratory dysfunction, and may also deplete the physiological reserve of those who are having an acute exacerbation.

The main protein which carries oxygen from the lungs to the peripheral tissues and carbon dioxide

from the tissues to the lungs is hemoglobin. So a decrease in hemoglobin level may reduce the ability of the blood to carry oxygen, even if the arterial oxygen saturation is relatively maintained [5]. A decrease in oxygen-carrying capacity may have other physiological effects in patients with COPD, who may have a reduced gas exchange and ventilation-perfusion abnormalities. Patients may be more hypoxic, have higher cardiac work, or be less able to exercise, and may develop dyspnea, which may lead to poorer clinical outcomes [6]. This interaction is especially critical during AECOPD when the demand for air is amplified and the capacity to ensure the delivery of adequate oxygen may be further reduced.

Routinely available red blood cell (RBC) indices include hemoglobin concentration and information about erythrocyte morphology and characteristics that may reflect underlying hematological abnormalities. The complete blood count includes commonly reported parameters such as mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and red cell distribution width (RDW) [7]. These parameters are investigated as markers of systemic inflammation, nutritional deficiency, oxidative stress and altered erythropoiesis, among which RDW is one that reflects the degree of variation in erythrocyte size, or anisocytosis. RDW has been linked to disease activity and poor prognosis of various chronic cardiopulmonary diseases, such as COPD.

It has been suggested that RBC parameters might have important clinical implications other than diagnosing and classifying anemia. In different COPD populations, increased RDW has been correlated with decreased exercise capacity, impaired pulmonary function, increased COPD exacerbation frequency, hospitalization, and mortality [8]. Likewise, decreased hemoglobin and changes in erythrocyte indices can affect oxygen transport and tissue oxygenation, which can have an impact on functional capacity. The association of specific RBC parameters with the degree of pulmonary dysfunction in an acute exacerbation of the disease, however, is not fully understood.

PFTs can be used to objectively measure the extent of airflow limitation in COPD [9]. FEV1 is a common measure of the severity of airflow obstruction, FVC and FEV1/FVC ratio are used to help characterise ventilatory impairment. In AECOPD patients, pulmonary function can be significantly reduced due to increased airway inflammation, bronchoconstriction, mucus hypersecretion and dynamic hyperinflation. In addition, the presence of anemia can have a further impact on the patient's physiologic response to respiratory insufficiency. However, severity of pulmonary function is not solely dependent on hemoglobin concentration, but other factors like age, smoking history, nutritional status,

comorbidities and systemic inflammation may affect both hematological and respiratory parameters.

Thus, the possible relationship between anemia-related parameters of RBC and severity of pulmonary function is clinically significant. If hematological parameters — also easily available laboratory tests — can be identified that correlate with more severe pulmonary disease, they could give further data from standard tests and may help to identify patients with increased risk for poor functional status [10]. Of particular interest may be RDW as this is cheap, readily available and can be a marker of several different biological processes related to chronic disease. However, the results of previous studies have not been uniform, perhaps because of variations in populations, disease severity, definitions of anemia and clinical settings.

The relationship between anemia-related RBC parameters and objective measures of pulmonary function, therefore, can be analysed in a retrospective evaluation of patients with AECOPD. The evaluation of hemoglobin, RBC count, MCV, MCH, MCHC and RDW in combination with pulmonary function parameters could be important to understand if certain haematological characteristics are related to increased respiratory impairment. This evaluation could also help to improve understanding of the systemic hematological abnormalities that interact with respiratory dysfunction in AECOPD. Based on this, the present study was conducted to assess the correlation of anemia-related RBC parameters with severity of pulmonary function in AECOPD patients, especially the correlation of hematological parameters, which are routinely measured, with objective assessment of pulmonary function.”

Methodology

Study Design: This study was conducted as a retrospective, observational, single-center cohort study to evaluate the association between anemia-related red blood cell (RBC) parameters and pulmonary function severity among patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Previously recorded clinical, hematological, and pulmonary function data were retrieved from hospital medical records. The study assessed the relationship between hemoglobin concentration, RBC count, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), red cell distribution width (RDW), and the severity of airflow limitation.

Study Area

1. The study was conducted in the Department of Physiology, Government medical college, Bettiah, west Champaran, Bihar, India

Study Duration: The study was conducted over a period of one year from January 2024 to December 2024

Study Participants: The study participants comprised patients with a documented diagnosis of AECOPD who fulfilled the predefined inclusion criteria and had complete records of hematological investigations and pulmonary function assessment.

Inclusion Criteria

- Patients aged ≥ 40 years with a documented diagnosis of COPD and acute exacerbation.
- Patients who fulfilled the clinical criteria for AECOPD, including worsening of dyspnea, cough, and/or sputum beyond usual day-to-day variation.
- Patients who had undergone pulmonary function testing after clinical stabilization.
- Patients with documented post-bronchodilator FEV1/FVC < 0.70 , confirming persistent air-flow limitation.
- Patients with a complete blood count performed during hospitalization, including hemoglobin and relevant RBC indices.
- Patients with sufficiently complete medical records for analysis.

Exclusion Criteria

- Patients with active or recent significant blood loss, including gastrointestinal or other major bleeding.
- Patients with known hematological malignancies, hemolytic anemia, myelodysplastic syndromes, or other established causes of severe anemia.
- Patients with severe renal dysfunction or severe liver disease likely to independently influence hemoglobin concentration.
- Patients who had received a blood transfusion within the preceding three months.
- Patients with other chronic respiratory diseases significantly affecting pulmonary function, such as bronchiectasis, pulmonary fibrosis, or extensive post-tubercular lung disease.
- Patients with incomplete or insufficient clinical, hematological, or pulmonary function records.

Sample Size: A total of 90 patients fulfilling the predefined eligibility criteria were included in the study. The participants were selected retrospectively from available hospital records after screening according to the inclusion and exclusion criteria.

Procedure: Relevant information was retrospectively extracted from the patients' medical records using a structured data collection format. Demographic characteristics, including age and sex, and

available clinical characteristics were recorded. Hematological parameters obtained from the complete blood count were reviewed, including hemoglobin (Hb), RBC count, MCV, MCH, and RDW. Patients were classified as anemic or non-anemic according to the recorded hemoglobin concentration, and the morphological pattern of anemia was assessed using MCV where applicable. Pulmonary function data obtained after clinical stabilization were reviewed, with particular emphasis on post-bronchodilator forced expiratory volume in one second (FEV1), FEV1% predicted, and FEV1/FVC ratio. Pulmonary function severity was categorized according to FEV1% predicted into mild ($\geq 80\%$), moderate (50–79%), severe (30–49%), and very severe ($< 30\%$) air-flow limitation. The relationship between individual RBC parameters and pulmonary function severity was subsequently evaluated. All collected information was anonymized before analysis to maintain patient confidentiality.

Statistical Analysis: Data were analyzed using IBM SPSS Statistics version 27.0. Continuous variables were assessed using the Shapiro–Wilk test and expressed as mean $\pm$ SD or median (IQR). Categorical variables were presented as frequencies and percentages. Group comparisons used t-test, Mann–Whitney U, chi-square, or Fisher's exact test. Pearson/Spearman correlation assessed relationships between RBC parameters and FEV1% predicted. Logistic regression identified independent associations with severe pulmonary impairment. A p-value < 0.05 was considered statistically significant."

Result

Table 1 presents the demographic and baseline characteristics of the 90 study participants. The mean age of the study population was 61.4 ± 8.9 years, indicating a predominantly older adult population. Males constituted the majority of participants, accounting for 61 (67.8%), while females represented 29 (32.2%). The mean BMI was 22.8 ± 3.4 kg/m². The mean hemoglobin concentration was 11.8 ± 1.7 g/dL, while the mean RBC count was $4.21 \pm 0.61 \times 10^6/\mu\text{L}$. Regarding red blood cell indices, the mean MCV was 87.6 ± 8.9 fL and the mean MCH was 28.1 ± 3.2 pg. The mean RDW was $15.1 \pm 2.4\%$, indicating variation in red blood cell size within the study population. The mean FEV1% predicted was $52.7 \pm 19.6\%$, reflecting reduced pulmonary function in the participants. Overall, the table demonstrates the demographic profile and baseline hematological and pulmonary characteristics of the study population.

Table 1: Demographic and baseline characteristics of study participants (N=90)

Variable	Value
Age (years), mean $\pm$ SD	61.4 $\pm$ 8.9
Male, n (%)	61 (67.8%)
Female, n (%)	29 (32.2%)
BMI (kg/m ²), mean $\pm$ SD	22.8 $\pm$ 3.4
Hemoglobin (g/dL), mean $\pm$ SD	11.8 $\pm$ 1.7
RBC count ($\times 10^6/\mu\text{L}$), mean $\pm$ SD	4.21 $\pm$ 0.61
MCV (fL), mean $\pm$ SD	87.6 $\pm$ 8.9
MCH (pg), mean $\pm$ SD	28.1 $\pm$ 3.2
RDW (%), mean $\pm$ SD	15.1 $\pm$ 2.4
FEV1% predicted, mean $\pm$ SD	52.7 $\pm$ 19.6

Table 2 presents the distribution of patients according to pulmonary function severity based on FEV1% predicted. Among the 90 study participants, the largest proportion had moderate pulmonary function impairment, with 34 (37.8%) patients having an FEV1% predicted of 50–79%. This was followed by severe impairment, observed in 27 (30.0%) patients with FEV1% predicted between 30–49%. Mild impairment, defined as FEV1% predicted $\geq 80\%$, was present in 18 (20.0%) patients, while 11 (12.2%) patients had very severe impairment with FEV1%

predicted $<30\%$. Thus, moderate and severe pulmonary impairment together accounted for 61 (67.8%) of the participants, indicating that the majority of the study population had clinically significant reduction in pulmonary function. Overall, the findings demonstrate a broad distribution of pulmonary function severity, with moderate impairment being the most frequently observed category and very severe impairment representing the smallest proportion of patients.

Table 2: Distribution of patients according to pulmonary function severity

Pulmonary function severity	FEV1% predicted	n	%
Mild	$\geq 80\%$	18	20
Moderate	50–79%	34	37.8
Severe	30–49%	27	30
Very severe	$<30\%$	11	12.2
Total	—	90	100

Table 3 compares anemia-related RBC parameters according to pulmonary function severity. Hemoglobin concentration showed a significant progressive decline with increasing pulmonary impairment, decreasing from 12.9 ± 1.3 g/dL in the mild group to 10.3 ± 1.4 g/dL in the very severe group ($p < 0.001$). Similarly, RBC count decreased significantly across severity categories, from $4.52 \pm 0.54 \times 10^6/\mu\text{L}$ in mild impairment to $3.81 \pm 0.58 \times 10^6/\mu\text{L}$ in very severe impairment ($p = 0.002$). MCH also demonstrated

a significant reduction, from 29.4 ± 2.8 pg in the mild group to 25.8 ± 3.3 pg in the very severe group ($p < 0.001$). In contrast, MCV showed a gradual decline from 89.4 ± 7.8 fL to 84.7 ± 10.1 fL, but the difference was not statistically significant ($p = 0.184$). Conversely, RDW increased progressively with worsening pulmonary function, from $13.8 \pm 1.7\%$ in the mild group to $17.2 \pm 2.6\%$ in the very severe group ($p < 0.001$)."

Table 3. Comparison of anemia-related RBC parameters according to pulmonary function severity

Parameter	Mild (n=18)	Moderate (n=34)	Severe (n=27)	Very severe (n=11)	p-value
Hemoglobin (g/dL)	12.9 $\pm$ 1.3	12.1 $\pm$ 1.5	11.2 $\pm$ 1.5	10.3 $\pm$ 1.4	<0.001
RBC count ($\times 10^6/\mu\text{L}$)	4.52 $\pm$ 0.54	4.31 $\pm$ 0.56	4.02 $\pm$ 0.61	3.81 $\pm$ 0.58	0.002
MCV (fL)	89.4 $\pm$ 7.8	88.1 $\pm$ 8.3	86.4 $\pm$ 9.6	84.7 $\pm$ 10.1	0.184
MCH (pg)	29.4 $\pm$ 2.8	28.7 $\pm$ 2.9	27.1 $\pm$ 3.1	25.8 $\pm$ 3.3	<0.001
RDW (%)	13.8 $\pm$ 1.7	14.6 $\pm$ 1.9	16.0 $\pm$ 2.4	17.2 $\pm$ 2.6	<0.001

"Table 4 presents the prevalence and morphological pattern of anemia among the 90 study participants. Anemia was present in 42 (46.7%) patients, while 48 (53.3%) patients had no anemia. Among the 42 anemic patients, normocytic anemia was the predominant morphological pattern, observed in 28 (66.7%)

patients. Microcytic anemia was identified in 9 (21.4%) patients, whereas macrocytic anemia was present in 5 (11.9%) patients. Thus, approximately two-thirds of the anemic participants demonstrated a normocytic pattern, while microcytic and macrocytic patterns accounted for smaller proportions.

Overall, the findings indicate that nearly half of the study population had anemia, with normocytic

anemia being the most frequently observed morphological type.

Table 4: Prevalence and morphological pattern of anemia

Anemia status / type	n	%
Anemia present	42	46.7
No anemia	48	53.3
Total	90	100
Among anemic patients (n=42):		
Microcytic anemia	9	21.4
Normocytic anemia	28	66.7
Macrocytic anemia	5	11.9
Total anemic patients	42	100

Table 5 presents the correlation of anemia-related RBC parameters with FEV1% predicted. Hemoglobin showed a moderate positive correlation with FEV1% predicted ($r=0.58$), which was statistically significant ($p<0.001$), indicating that higher hemoglobin levels were associated with higher FEV1% predicted values. RBC count also demonstrated a significant positive correlation with FEV1% predicted ($r=0.34$, $p=0.001$), although the strength of association was weaker. MCH showed a moderate positive correlation ($r=0.46$, $p<0.001$), indicating a

significant relationship with pulmonary function. In contrast, MCV demonstrated a weak positive correlation ($r=0.15$), which was not statistically significant ($p=0.158$). RDW showed a moderate negative correlation with FEV1% predicted ($r=-0.52$, $p<0.001$), suggesting that higher RDW values were associated with lower FEV1% predicted values. Overall, hemoglobin, RBC count, MCH, and RDW showed statistically significant correlations with pulmonary function, whereas MCV did not.

Table 5: Correlation of RBC parameters with FEV1% predicted

RBC parameter	Correlation coefficient (r)	p-value
Hemoglobin	0.58	<0.001
RBC count	0.34	0.001
MCV	0.15	0.158
MCH	0.46	<0.001
RDW	-0.52	<0.001

Discussion

In the present retrospective study, we found that the clinically relevant association between anemia-related red blood cell (RBC) parameters and pulmonary function severity was found in patients who suffered from an acute exacerbation of chronic obstructive pulmonary disease (AECOPD). The mean age of the study population was 61.4 ± 8.9 years, and the majority were male (67.8%). The mean hemoglobin concentration was 11.8 ± 1.7 g/dL and mean FEV1% predicted was $52.7 \pm 19.6\%$. Substantial respiratory dysfunction was seen in the study population with moderate to severe pulmonary impairment present in 67.8% of participants. Anemia has also been identified as an important systemic comorbidity by previous studies in COPD. A sub-analysis of 683 COPD patients by Cote et al. 2007 [11] revealed that 17% were anemic, and that anemic COPD patients had lower functional capacity compared to normoanemic patients, with a 6-minute walk distance of 265m in the anemic group compared to 325m in the normoanemic group."

"One of the most significant discoveries was that the amount of hemoglobin decreased as the lungs were

worse. There was a moderate positive correlation between hemoglobin and FEV1% predicted in mild ($r=0.58$, $p<0.001$) and very severe ($r=0.58$, $p<0.001$) impairment groups, but the mean hemoglobin level in the latter group was significantly lower at 10.3 ± 1.4 g/dL than in the moderate group at 12.9 ± 1.3 g/dL ($p<0.001$). This is a similar finding to Hoepers AT. The association between anemia and inflammation and lowered physiological status in COPD was shown by (2015) [12]. Guo et al., 2015 [13] also found decreased lung function and exercise capacity in severe COPD patients with anemia. The higher correlation found in the present study might be due to the fact that acute exacerbation patients were included, and the systemic inflammation and physiological stress might increase the hematological abnormalities. However, the study design is retrospective, which does not prove a causal link between decreased hemoglobin and the deterioration of the lung.

Anemia was more prevalent in participants (46.7%) than in some previous COPD studies. The prevalence of anemia has been reported in 6.2% of patients with stable COPD by Boutou AK et al. (2015) [14] and 31.6% of the COPD population in the North

of India by Bhatta et al. (2018). This increased prevalence in the present study could be linked to the fact that AECOPD patients had been recruited and the moderate-to-severe percentage of pulmonary impairment. The same has been reported by Shorr et al. (2008) [15] who also highlighted the importance of anemia as a comorbidity in COPD and its contribution to the disease burden. Variations in prevalence of anemia from one study to another may be due to differences in severity of disease, population characteristics, nutritional status, and/or clinical setting.

RBC count also decreased significantly from $4.52 \pm 0.54 \times 10^6/\mu\text{L}$ in mild impairment to $3.81 \pm 0.58 \times 10^6/\mu\text{L}$ in very severe impairment ($p=0.002$). It was positively correlated with FEV1% predicted ($r=0.34$, $p=0.001$), suggesting that the lower the number of red blood cells, the lower the pulmonary function. The decrease in RBC mass can lead to a decrease in oxygen-carrying capacity and further reduce tissue oxygen delivery in patients with compromised respiratory gas exchange. RBC count also may be influenced by other factors, including smoking, nutritional status, inflammation, hydration, and comorbid conditions, however, which were not fully controlled in the present study.

MCH significantly decreased from mild impairment (29.4 ± 2.8 pg) to very severe impairment (25.8 ± 3.3 pg) ($p<0.001$) and was correlated with FEV1% predicted ($r=0.46$, $p<0.001$). This indicates that decreased hemoglobin of the RBC was correlated with declined pulmonary function. John et al. (2005) reported on abnormalities of the erythropoietic status of COPD patients and Guo et al. (2015) showed the functional consequences of anaemia in severe COPD. The current results also suggest that some of the individual RBC indices, like MCH, might be useful in obtaining further information about the pulmonary damage beyond the total hemoglobin concentration.

However, in contrast to this, there was no significant association between pulmonary function and MCV. MCV was lower in very severe impairment, 84.7 ± 10.1 fL, compared to mild, 89.4 ± 7.8 fL, but this was not significant ($p=0.184$), and had a poor correlation with FEV1% predicted ($r=0.15$, $p=0.158$). This may be partially explained by the predominance of normocytic anemia (66.7% of anemic participants), microcytic (21.4%) and macrocytic (11.9%) anemia. Therefore, RBC size measured as mean may not be sufficiently indicative of hematological abnormalities related to pulmonary dysfunction.

RDW was the opposite with rising from $13.8 \pm 1.7\%$ in mild impairment to $17.2 \pm 2.6\%$ in very severe impairment ($p<0.001$). The other variables showing a significant negative correlation with RDW were FEV1% predicted ($r=-0.52$, $p<0.001$). This result was similar to previous studies that identified that

higher RDW is correlated with clinically relevant abnormalities in COPD. In AECOPD patients, Hu et al. (2019) [16] found that $\text{RDW} \geq 13.75\%$ was related to an increased in-hospital mortality hazard with a risk ratio of about 4.30. Also, Epstein et al. 2018 [17] discovered that elevated RDW was associated with adverse results in AECOPD hospitalizations. While these studies concentrated primarily on prognosis and not lung function, they do corroborate the present result that may suggest that RDW is a marker of systemic disease burden.

The elevated RDW may be due to a heterogeneous process of erythropoiesis associated with inflammation, nutritional deficiencies, altered iron availability, and/or increased RBC turnover. In the present study however, iron status, vitamin B12, folate, and other complete inflammatory markers were not evaluated; therefore, the exact mechanism cannot be determined. Overall, hemoglobin had the highest positive correlation with FEV1% predicted ($r=0.58$), followed by MCH ($r=0.46$), and RBC count ($r=0.34$), and RDW had a significant inverse correlation ($r=-0.52$). No significant relationship between pulmonary function was observed with MCV. The results indicate that the abnormalities observed in anemia parameters, such as hemoglobin, MCH, RBC count and RDW may be helpful as complementary data to the pulmonary function severity in AECOPD. The retrospective design and relatively small sample size, however, restricts the ability to make causal interpretations, and larger prospective studies including nutritional, inflammatory, iron-status and comorbidity related variables are warranted."

Conclusion

The present study demonstrated a significant association between anemia-related red blood cell parameters and pulmonary function severity in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD). Nearly half of the participants (46.7%) had anemia, with normocytic anemia being the predominant pattern. Hemoglobin, RBC count, and MCH progressively decreased with increasing pulmonary impairment, while RDW increased significantly. Hemoglobin showed the strongest positive correlation with FEV1% predicted ($r=0.58$, $p<0.001$), whereas RDW demonstrated a significant negative correlation ($r=-0.52$, $p<0.001$). MCV was not significantly associated with pulmonary function. These findings suggest that routinely available hematological parameters, particularly hemoglobin, MCH, RBC count, and RDW, may provide useful complementary information regarding pulmonary function severity in AECOPD. Further prospective studies with larger populations are warranted.

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