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Red Cell Distribution Width as a Prognostic Marker in ICU-Admitted Chronic Obstructive Pulmonary Disease Patients: Correlation with Inflammatory Profile and Clinical Outcomes

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ABSTRACT

Background: Red cell distribution width (RDW), a measure of the variability in erythrocyte size, has emerged as a potential biomarker of systemic inflammation and adverse outcomes in various critical illnesses. However, its prognostic significance in critically ill patients with chronic obstructive pulmonary disease (COPD) remains underexplored.

Objective: To find out the association of RDW with clinical severity, inflammatory markers, and outcomes in critically ill COPD patients admitted to the intensive care unit (ICU).

Methodology: A prospective observational cohort study was conducted on 240 COPD patients admitted to the ICU. Patients were stratified into two groups based on RDW values at admission: normal RDW (n=98) and elevated RDW (n=142). Demographic data, clinical characteristics, laboratory parameters, severity scores (APACHE II, SOFA), interventions, and outcomes were analyzed. Correlations between RDW and key clinical variables were assessed.

Results: Results showed that patients with elevated RDW were significantly older (70.1 ± 9.6 vs. 64.2 ± 8.5 years) and had lower Body Mass Index and haemoglobin levels. Elevated RDW was associated with higher inflammatory markers (CRP: 56.8 ± 29.1 mg/L vs. 43.6 ± 25.3 mg/L, $p=0.002$), lower serum albumin (2.9 ± 0.6 g/dL vs. 3.4 ± 0.4 g/dL, $p<0.001$), and increased white blood cell counts. Severity scores were significantly higher in the elevated RDW group ($p<0.001$).

Conclusion: Elevated RDW is strongly associated with increased inflammation, disease severity, and worse outcomes in severe COPD cases. RDW may serve as a simple, cost-effective prognostic marker to aid early risk stratification and guide clinical management in this high-risk population.

Keywords: RDW; COPD; Prognostic Marker; Correlation; ICU

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is characterized by persistent respiratory issues and airflow limitation stemming from airway abnormalities or alveolar damage worldwide.¹ According to the Global Initiative for Chronic Obstructive Lung Disease (GOLD), annually about 300 million individuals suffer from this respiratory condition, resulting in nearly 3.2 million fatalities annually around the world. Critically ill patients suffer greatly from COPD with exacerbations and systemic problems, often landing them in intensive care unit beds. Understanding biomarkers that forecast disease severity, nasty complications, and outcomes is crucial for improving clinical management in this population.²

One new biomarker is Red Cell Distribution Width (RDW), which measures circulating erythrocytes' size variability (anisocytosis). RDW has long been utilized in the differential diagnosis of anaemia and is a typical part of a complete blood count (CBC). Recent research, however, has shown that increased RDW is a prognostic sign for a variety of systemic diseases, such as sepsis, acute respiratory distress syndrome (ARDS), cardiovascular disorders, and chronic inflammatory syndromes, in addition to being a marker of hematologic malfunction. Although the pathophysiological rationale for this connection is still being studied, it is thought to be related to bone marrow malfunction, oxidative stress, systemic inflammation, and nutritional deficiencies, all of which are common in critically sick patients.³

Patients with COPD are more likely to have these issues, especially at the time when they are having acute exacerbations or need urgent care. Nowadays, it is generally accepted that COPD is a systemic illness, with comorbidities, like hypoxemia and chronic inflammation, which are key factors in its development and consequences. These comorbidities may directly or indirectly impact red blood cell shape and erythropoiesis, which could change RDW. Furthermore, infections, cardiovascular illness, malnourishment, and renal dysfunction are common coexisting disorders in critically sick COPD patients, and these conditions can all raise RDW values. Studying RDW in this population may help to know the severity of the illness and the level of inflammation, and even forecast clinical outcomes like the length of time spent in the intensive care unit, the necessity for mechanical ventilation, or death.⁴

Despite the importance of RDW as a therapeutic agent, very little is known about RDW's function in critically ill COPD patients. RDW is mostly studied in general ICU cohorts or connected with pneumonia and sepsis. Few studies have been conducted to know the importance of RDW in patients with stable COPD or during acute flare-ups, and even fewer have looked at its significance in patients in critical care. RDW is a straightforward,

affordable, and frequently accessible metric that can potentially be a useful assistant in the risk assessment and treatment of patients with COPD in critical care environments. Therefore, this study aimed to bridge this knowledge gap by assessing the red cell distribution width in critically sick COPD patients and investigating its relationship to clinical parameters, comorbidities, and outcomes.

Objective

To find the association of RDW with clinical severity, inflammatory markers, and outcomes in severe COPD cases admitted to the ICU.

Methodology

A prospective observational cohort study was conducted in the Combined Military Hospital (CMH), Malir Cantt from January 2022 to August 2023. A total of 240 adult patients with an age of more than 39 years who had been admitted to the ICU because of an acute exacerbation or respiratory failure and had a confirmed diagnosis of COPD were enrolled in this study. Clinical history, symptoms, and spirometric evidence (post-bronchodilator FEV₁/FVC ratio <0.70) were used to diagnose and categorize COPD by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) specifications.

Strong inclusion and exclusion criteria were followed during this study. All confirmed COPD patients of age 40 years or above admitted to the ICU due to acute exacerbation of COPD, respiratory failure, or corresponding critical illness were eligible for this study. In contrast, exclusion criteria were established as patients with haematological diseases (e.g., thalassemia, sickle cell anaemia), who had received a recent blood transfusion within 4 weeks before ICU admission or who had active malignancy, chemotherapy and chronic liver disease or end-stage renal disease with the necessity for dialysis were excluded from this study.

For data purposes, a specialized proforma was created. Data like patients' demographic information, such as age, sex, smoking history, BMI and clinical information, like duration of COPD, exacerbation frequency, and comorbidities (e.g., diabetes, hypertension, coronary artery disease) were recorded. Different laboratory investigations like Complete Blood Count (CBC) with RDW (expressed as RDW-CV and RDW-SD), serum electrolytes, and inflammatory markers were also recorded.

First data was entered in a specially designed Microsoft Excel sheet and transported to SPSS version 25 for analysis. Mean $\pm$ standard deviation (SD) or median (interquartile range) were used for continuous variables, whereas categorical variables were presented as frequencies and percentages. Significant association was declared positive at a p-value of <0.05.

An ethical certificate (IRB No. 0201, 2022) was obtained from the Research Department, Karachi Institute of Medical Sciences for study purposes.

Results

A total of 240 critically ill COPD patients were included in this study. Patients were stratified into two groups based on Red Cell Distribution Width (RDW). One group

consisted of 98 patients with normal RDW (<14.5%) (NRDW), and the other group included 142 patients with Elevated RDW (≥14.5%) (ERDW). The mean age of the participants was 67.5 ± 9.8 years. Patients in the ERDW group were significantly older (70.1 ± 9.6 years) compared to those in the NRDW group (64.2 ± 8.5 years), with a p-value <0.001, indicating a strong statistical difference. Males were more numerous (175 (72.9%)) than females (Figure 1).

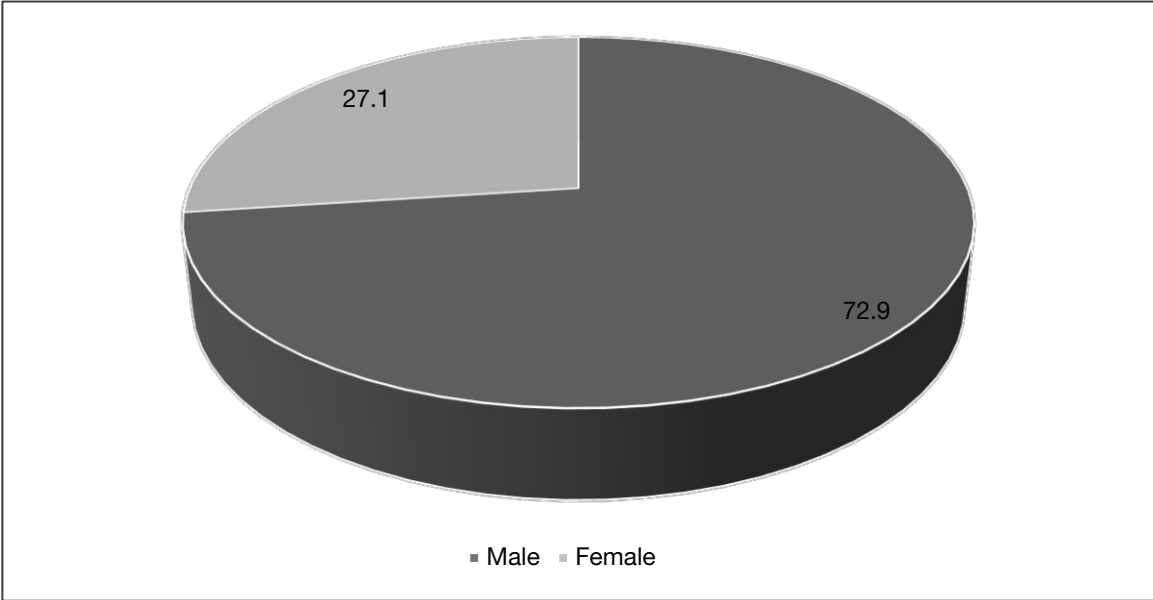


Figure 1. Gender base distribution of study cases

Based on gender, there was no statistically significant difference between the NRDW group (73.5%) and the ERDW group (72.5%, p-value = 0.87). A large proportion of the population had a history of smoking (75.8%). Smoking rates were comparable between the two groups—77.5% in the normal RDW group and 74.6% in the elevated RDW group (p-value = 0.61). This non-significant difference implies that smoking history was not

a differentiating factor for RDW levels among critically ill COPD patients in this cohort (Figure 2). The mean BMI of the participants was 21.4 ± 3.9 kg/m², reflecting a generally low-to-normal body weight status. Patients with elevated RDW had a significantly lower BMI (20.7 ± 4.1 kg/m²) than those with normal RDW (22.3 ± 3.5 kg/m², p = 0.003). This indicates that malnutrition or low nutritional reserve may be associated with elevated RDW,

Table 1. Baseline demographic and clinical characteristics of study cases

Variable	Total (n=240)	Normal RDW (n=98)	Elevated RDW (n=142)	p-value
Age (years)	67.5 ± 9.8	64.2 ± 8.5	70.1 ± 9.6	<0.001
Male gender (%)	72.9%	73.5%	72.5%	0.87
Smoking history (%)	75.8%	77.5%	74.6%	0.61
BMI (kg/m²)	21.4 ± 3.9	22.3 ± 3.5	20.7 ± 4.1	0.003
Duration of COPD (years)	7.2 ± 4.3	6.7 ± 4.1	7.6 ± 4.5	0.07

possibly reflecting chronic inflammation or cachexia seen in advanced levels of COPD. The average duration of COPD was 7.2 ± 4.3 years across the entire group. Patients in the ERDW group had slightly longer disease duration (7.6 ± 4.5 years) than those in the NRDW group (6.7 ± 4.1 years), although this difference did not reach statistical significance ($p = 0.07$) (Table 1).

Results showed that the mean hemoglobin level across all patients was 12.1 ± 1.9 g/dL. Patients with elevated RDW had significantly lower hemoglobin levels (11.5 ± 2.1 g/dL) compared to those with normal RDW (12.8 ± 1.6 g/dL, $p < 0.001$). As expected, the RDW was significantly higher in the ERDW group ($16.7 \pm 1.5\%$) compared to the NRDW group ($13.4 \pm 0.7\%$, $p < 0.001$). The average RDW in the

Table 2. Hematological and Biochemical Parameters of the study participants

Parameter	Total	Normal RDW	Elevated RDW	p-value
Hemoglobin (g/dL)	12.1 ± 1.9	12.8 ± 1.6	11.5 ± 2.1	<0.001
RDW (%)	15.3 ± 2.1	13.4 ± 0.7	16.7 ± 1.5	<0.001
WBC count ($\times 10^9/L$)	11.8 ± 4.6	10.9 ± 4.2	12.4 ± 4.7	0.01
CRP (mg/L)	51.2 ± 28.5	43.6 ± 25.3	56.8 ± 29.1	0.002
Serum Albumin (g/dL)	3.1 ± 0.5	3.4 ± 0.4	2.9 ± 0.6	<0.001

study population was $15.3 \pm 2.1\%$, reinforcing that anisocytosis (variation in red blood cell size) is common in this cohort, particularly in sicker patients. The overall WBC count was $11.8 \pm 4.6 \times 10^9/L$, indicating elevated levels consistent with systemic inflammation or infection. WBC counts were significantly higher in the elevated RDW group ($12.4 \pm 4.7 \times 10^9/L$) compared to the NRDW group ($10.9 \pm 4.2 \times 10^9/L$, p -value = 0.01). The mean CRP level was 51.2 ± 28.5 mg/L in the total cohort, with significantly higher values in the elevated RDW group (56.8 ± 29.1 mg/L) compared to the NRDW group (43.6 ± 25.3 mg/L, p -value = 0.002). CRP is a sensitive marker of systemic inflammation, and its association with RDW suggests that RDW elevation may reflect an underlying inflammatory burden, common in acute exacerbations of COPD and critical illness. Serum albumin, a marker of nutritional status and systemic inflammation, was significantly lower in the elevated RDW group (2.9 ± 0.6 g/dL) compared to the normal RDW group (3.4 ± 0.4 g/dL,

$p < 0.001$). The mean level across all patients was 3.1 ± 0.5 g/dL. Hypoalbuminemia is a known predictor of poor outcomes in ICU patients and is closely linked to malnutrition, inflammation, and disease severity, all of which may contribute to RDW elevation (Table 2).

The mean Acute Physiology and Chronic Health Evaluation II (APACHE II) score was 19.3 ± 5.2 across the cohort. Patients with elevated RDW had significantly higher scores (20.5 ± 5.3) compared to those with normal RDW (17.6 ± 4.8 , $p < 0.001$). The Sequential Organ Failure Assessment (SOFA) score, which quantifies the extent of organ dysfunction, was significantly higher in the elevated RDW group (8.3 ± 3.0) than in the normal RDW group (6.2 ± 2.5 , $p < 0.001$), with a total mean of 7.4 ± 2.9 . The overall proportion of patients requiring mechanical ventilation was 76.7%. A substantially higher proportion of patients in the elevated RDW group (85.2%) required mechanical ventilation compared to the normal RDW group (64.3%, $p < 0.001$). Vasopressors were needed in 45.4% of the total

Table 3. Comparison of Intensive Care Unit Severity Scores and Supportive Management Measures

Variable	Total	Normal RDW	Elevated RDW	p-value
APACHE II Score	19.3 ± 5.2	17.6 ± 4.8	20.5 ± 5.3	<0.001
SOFA Score	7.4 ± 2.9	6.2 ± 2.5	8.3 ± 3.0	<0.001
Mechanical Ventilation (%)	76.7%	64.3%	85.2%	<0.001
Vasopressor Use (%)	45.4%	31.6%	54.2%	<0.001
Corticosteroid Therapy (%)	83.3%	80.6%	85.2%	0.38

cohort, with significantly more usage in the elevated RDW group (54.2%) versus the normal RDW group (31.6%, $p < 0.001$). The use of corticosteroids was common across both groups, with an overall prevalence of 83.3%, slightly higher in the elevated RDW group (85.2%) than the normal RDW group (80.6%). Still, this difference was insignificant ($p = 0.38$) (Table 3). The average ICU stay for all patients was 9.6 ± 4.1 days. Patients with elevated RDW stayed significantly longer (10.8 ± 4.3 days) than those with normal RDW (7.8 ± 3.6 days) (Table 4). Outcomes and Prognosis of study cases

Outcome Measure	Total	Normal RDW	Elevated RDW	p-value
ICU Length of Stay (days)	9.6 ± 4.1	7.8 ± 3.6	10.8 ± 4.3	<0.001
Duration of Ventilation	6.4 ± 2.9	5.3 ± 2.4	7.2 ± 3.1	<0.001
ICU Mortality (%)	28.3%	14.3%	38.0%	<0.001
30-Day Mortality (%)	33.8%	19.4%	43.0%	<0.001
Readmission within 30 days (%)	11.2%	6.1%	14.8%	0.04

readmission rate was 11.2% overall, significantly higher in the elevated RDW group (14.8%) than in the normal RDW group (6.1%, $p = 0.04$) (Table 4). Table 5 presents the Pearson correlation coefficients (r) between Red Cell Distribution Width (RDW) and a range of clinical, laboratory, and outcome variables. All correlations reported are statistically significant ($p < 0.001$), underscoring the robust associations between RDW and disease severity, inflammation, and patient prognosis indicators. Positive Correlations ($r > 0$) of RDW were found with age ($r = +0.31$), indicating that older patients tended to have higher RDW levels. Similarly, a moderate positive correlation was observed between RDW and C-reactive Protein (CRP) ($r = +0.36$), a key inflammatory biomarker. RDW showed a strong positive correlation with the Sequential Organ Failure Assessment (SOFA) score ($r = +0.41$), suggesting that higher RDW levels are associated with more severe multi-organ dysfunction. This reinforces RDW as a marker of physiological deterioration. The positive correlation between RDW and APACHE II ($r = +0.38$) score further supports RDW's role as an indicator of overall disease severity and ICU burden. Higher RDW values correspond with acute physiological derangement, chronic health impairment, and ICU. A moderate correlation with ICU length of stay ($r = +0.34$) indicates that patients with elevated RDW are more likely to have prolonged ICU admissions. Negative Correlations ($r < 0$) of RDW were found between RDW and that of Serum Albumin ($r = -0.42$). This is a strong inverse correlation. Since albumin is a marker of

days, $p < 0.001$). The mean duration of ventilation in the total cohort was 6.4 ± 2.9 days, with the elevated RDW group requiring significantly longer ventilation (7.2 ± 3.1 days) compared to the normal RDW group (5.3 ± 2.4 days, $p < 0.001$). Overall ICU mortality was 28.3%, but was significantly higher in the elevated RDW group (38.0%) versus the normal RDW group (14.3%, $p < 0.001$). Mortality at 30 days was 33.8% overall, with a striking increase in the elevated RDW group (43.0%) compared to the normal RDW group (19.4%, $p < 0.001$). The 30-day

nutritional status and inflammation, this finding suggests that hypoalbuminemia is common in patients with elevated RDW, linking RDW with malnutrition and systemic illness and Hemoglobin ($r = -0.37$) which was also inversely correlated with RDW, confirming that higher RDW is associated with anemia, particularly anemia of chronic disease or mixed anemia patterns often found in critically ill patients (Table 5).

Discussion

Chronic obstructive pulmonary disease (COPD) is a progressive illness that frequently results in acute exacerbations that require critical care. It is characterized by chronic inflammation, airflow limitation, and systemic symptoms. For early identification of risks and better therapeutic care, it is essential to find accurate and conveniently accessible prognostic indicators in critically sick COPD patients.5 The frequently reported Red Cell Distribution Width (RDW) component of complete blood count has become a promising biomarker for assessing inflammation, malnutrition, and the overall disease burden. When we looked at the clinical relevance of RDW in critically seriously ill individuals with COPD, we discovered that higher RDW was substantially linked to worse clinical outcomes, systemic inflammation, and increased disease severity. Our cohort of 240 critically sick COPD patients' baseline characteristics shows significant clinical and demographic distinctions between individuals with higher RDW and those with normal RDW. It is remarkable that while

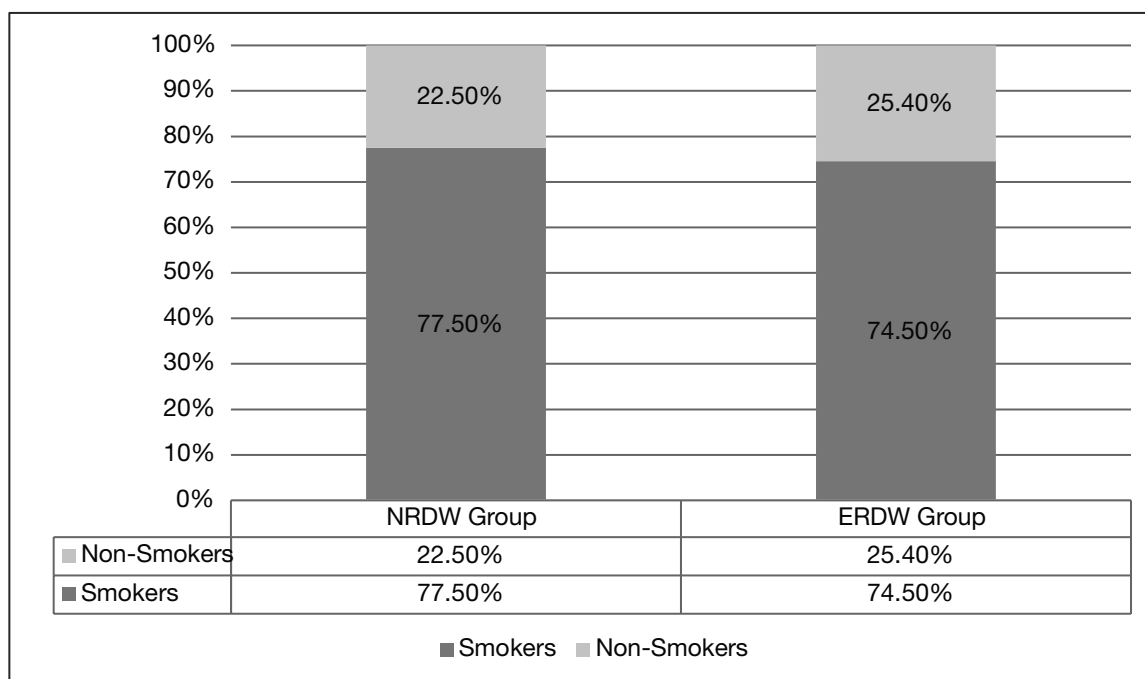


Figure 2. Smoking history of study cases

other factors, including gender distribution, smoking history, and length of COPD, did not statistically differ across the groups, greater RDW was significantly linked to older age and lower body mass index (BMI). Patients with normal RDW (64.2 ± 8.5 years, $p < 0.001$) were substantially younger than those with increased RDW (70.1 ± 9.6 years). This is consistent with earlier research by Persson et al (2020)6 and Hunziker et al. (2012)7, which found that age was a significant determinant of RDW. RDW readings in older individuals are probably raised due to chronic inflammation, age-related alterations in erythropoiesis, and increasing comorbidities. Increased oxidative stress and bone marrow inefficiency are also linked to ageing, which could help to explain the correlation.

The percentage of males was approximately the same in both RDW groups (73.5% in normal RDW and 72.5% in elevated RDW, $p = 0.87$), and there was no significant difference in smoking history (77.5% compared to 74.6%, $p = 0.61$). These results conform to studies conducted by Seyhan et al. (2013)8 and Kurt et al. (2015)9, which found no significant correlation between the level of RDW and the gender or smoking history of the COPD patient. Smoking is a well-recognized risk for developing COPD. Still, the relationship of tobacco on RDW seems to be indirect, possibly mediated by inflammation or hypoxia as opposed to direct cellular effects. There was one statistically significant difference in BMI, where it was noted that patients in the elevated RDW group had a lower average BMI (20.7 ± 4.1 kg/m²) than those with normal

RDW (22.3 ± 3.5 kg/m², $p = 0.003$). Low BMI can indicate frailty, malnutrition, systemic inflammation, and depletion, all of which can influence erythropoiesis and red blood cell size variability. This association is corroborated by findings from Ho et al. (2016)10, who reported that COPD patients with lower BMI tend to have higher RDW values and worse clinical outcomes. Furthermore, in advanced stages of COPD, malnutrition and cachexia are known to hinder erythropoiesis, resulting in anisocytosis. However, patients with elevated RDW did have a slightly longer average duration of COPD (7.6 ± 4.5 years) than those with normal RDW (6.7 ± 4.1 years). Although the difference was not statistically significant ($p = 0.07$), those with higher RDW did have a longer average duration. This tendency indicates that the progression of chronic disease might stratify or unmask some underlying systemic inflammation leading to increased RDW. These are the same tendencies observed in Huang et al. (2021)11, where a longer disease course was tied to increased RDW, but often depended on sample size and study design for statistical significance.

The elevation in the RDW group was significantly lower than the normal RDW group (11.5 ± 2.1 g/dL versus 12.8 ± 1.6 g/dL, $p < 0.001$). This increase aligns with the existing correlation between anisocytosis and anaemia. Anaemia in COPD is multifactorial, usually because of chronic inflammation, disorders of iron metabolism, and nutritional deficiency. This corroborates the results of Persson et al. (2020)6 and Seyhan et al. (2013)8, who noted that RDW tends to increase with the level of

anaemia in both stable and exacerbated forms of COPD. Additionally, another study indicated that increased RDW is not limited to iron-deficiency anaemia but is found in chronic disease anaemia, which is common in advanced COPD.¹²

As predicted, RDW levels were notably greater in the high RDW group ($16.7 \pm 1.5\%$) than in the normal group ($13.4 \pm 0.7\%$, $p < 0.001$). This validation of group classification and attestation to RDW as a valid marker of variation in erythrocyte size would be expected, given the characteristics of severe COPD and critical illness, which include impaired erythropoiesis from inflammation, oxidative stress, and nutritional deficiencies. Prior research, such as Hunziker et al. (2012)⁷ and Zurauskaite et al. (2018)¹³, found raised RDW as an independent predictor of mortality in the ICU for a broad spectrum of diagnoses, its prognostic significance in critically ill patients being underlined. WBC count was remarkably elevated in patients with increased RDW ($12.4 \pm 4.7 \times 10^9 /L$) than patients with normal RDW ($10.9 \pm 4.2 \times 10^9 /L$, $p = 0.01$), indicating a higher inflammatory or infective process in these patients. Increased WBC counts tend to accompany acute COPD exacerbation and systemic infection. The same tendencies were noticed by Seyhan et al. (2013)⁸, who revealed that WBC count correlated moderately with RDW in exacerbation of COPD. This confirms the hypothesis that RDW could be a part of a more general systemic inflammatory response. As a robust inflammatory biomarker, CRP was raised significantly in the high-RDW group (56.8 ± 29.1 mg/L) versus the normal RDW group (43.6 ± 25.3 mg/L, $p = 0.002$). This again supports the link between RDW and inflammation. Kurt et al. (2015)⁹ identified that RDW correlated with CRP in patients with acute COPD exacerbation. Likewise, Huang et al. (2021)¹¹ identified that RDW and CRP elevated together predicted poorer

clinical outcomes in ICU patients. These results indicate that RDW may be used as a surrogate marker for systemic inflammation, particularly in resource-poor environments where CRP determination may not be easily accessible.

Serum albumin concentrations were profoundly lower in the high RDW group (2.9 ± 0.6 g/dL) than in the normal RDW group (3.4 ± 0.4 g/dL, $p < 0.001$). Hypoalbuminemia indicates malnutrition, catabolism, and systemic inflammation, all of which are highly linked with unfavorable outcomes for critical illness. Our results corroborate those of research in 2018, which added that hypoalbuminemia with increased RDW indicated poorer survival in septic and respiratory failure patients. Our correlation analysis also validated this negative correlation between RDW and albumin ($r = -0.42$, $p < 0.001$), emphasizing RDW's association with nutritional and inflammatory state.¹⁴

Our results clearly show a correlation between increased red cell distribution width (RDW), increased ICU severity scores, and increased demand for supportive interventions in critically ill COPD patients. These findings further implicate that RDW is not just a hematologic variability marker but also correlates with clinical severity and resource use in intensive care units. The APACHE II (Acute Physiology and Chronic Health Evaluation II) score, which is one of the most utilized severity-of-illness indexes, was substantially greater in the group with elevated RDW (20.5 ± 5.3) than in the group with normal RDW (17.6 ± 4.8 ; $p < 0.001$). This suggests that patients with elevated RDW were more seriously ill when they were admitted to the ICU in general. This correlation aligns with findings by Hunziker et al. (2012),⁷ and Deniz et al. (2022),¹⁵ which revealed that raised RDW values correlate strongly with increased APACHE II score and risk of mortality in ICU patients. The increase in RDW can be seen as the cumulative effect of systemic stress,

Table 5. Statistical Correlation between RDW and Key Clinical Variables

Variable	Correlation Coefficient ®	p-value
Age	+0.31	<0.001
CRP	+0.36	<0.001
SOFA Score	+0.41	<0.001
APACHE II Score	+0.38	<0.001
ICU Length of Stay	+0.34	<0.001
Serum Albumin	-0.42	<0.001
Hemoglobin	-0.37	<0.001

hypoxia, and inflammation, which also affect APACHE II scoring parameters.

In the same way, SOFA score was much lower in high-RDW patients (8.3 ± 3.0) than in normal-RDW patients (6.2 ± 2.5 ; $p < 0.001$). The SOFA score measures the level of organ dysfunction in six organ systems, and its increase in the high-RDW group suggests a higher level of multi-organ impairment. This result is consistent with Zurauskaite et al.'s (2018)¹³ research, which found a positive correlation between RDW and SOFA score, particularly among septic and respiratory failure patients. The correlation could be attributed to RDW's sensitivity to tissue hypoxia, systemic inflammation, and renal or hepatic impairment, influencing SOFA scoring. The percentage of patients that needed mechanical ventilation was much greater in the increased RDW group (85.2%) compared to the normal RDW group (64.3%; $p < 0.001$). This indicates that greater RDW is correlated with more profound respiratory compromise necessitating ventilatory support. Past research, such as that conducted by Kurt et al. (2015),⁹ and another study in 2021¹⁶, also noted that COPD patients with high RDW at exacerbation or during ICU admission had increased intubation or non-invasive ventilation requirements. The mechanisms underlying these might include hypoxia-induced disturbances of red cell production and augmented respiratory muscle fatigue.

More of the high RDW patients needed vasopressor therapy (54.2%) than in the normal RDW group (31.6%; $p < 0.001$), indicating more hemodynamic instability. RDW is associated with hypotension and inadequate perfusion in critically ill patients previously, and it is likely related to the same systemic inflammatory condition and microcirculatory disturbance that produce both increased RDW and the requirement for vasopressors. This is consistent with evidence in 2022¹⁷ research, which indicated elevated RDW values among septic shock patients who needed vasopressors, highlighting its use as a predictor of circulatory failure. Although considerable for both groups, Corticosteroid use was not significantly different between high and normal RDW patients (85.2% vs. 80.6%; $p = 0.38$). This is consistent with typical management in COPD exacerbations and severe illness in which corticosteroids are routinely given irrespective of RDW status. Other research (e.g., Seyhan et al., 2013)⁸ has not identified an association between RDW and corticosteroids.

Our research shows that increased red cell distribution width (RDW) is independently related to increased morbidity in critically ill patients with COPD. The patients with increased RDW had a markedly increased ICU length of stay (LOS) in comparison to the patients with normal RDW (10.8 ± 4.3 vs. 7.8 ± 3.6 days; $p < 0.001$). Extended ICU stay is usually a surrogate indicator of more severe disease, complications, and slower recovery. Hunziker et al. (2012),⁷ and Deniz et al (2022),¹⁵ who identified RDW

independently predicted extended ICU and hospital LOS in septic and critically ill groups, this correlation has been equally noted. RDW can only be supposed to indicate a chronic inflammatory condition and physiological derangement causing delayed recovery. The length of mechanical ventilation was also markedly longer in the high RDW group (7.2 ± 3.1 days) than in the normal RDW group (5.3 ± 2.4 days; $p < 0.001$). This result implies that severe or long-standing respiratory failure is more frequent in patients with elevated RDW. These findings are consistent with those of Kurt et al. (2015)⁹, who demonstrated that high RDW was a predictor of longer ventilation duration among COPD patients admitted for acute exacerbations. RDW could indicate associated factors like hypoxemia, systemic inflammation, and poor respiratory muscle strength, which are weaning-limiting factors.

ICU mortality was much greater among patients in the high RDW group (38.0%) than in the normal RDW group (14.3%; $p < 0.001$). This reaffirms RDW's prognostic strength and is our analysis's most clinically useful result. Many studies within various ICU patient populations have supported this correlation. Zurauskaite et al. (2018)¹³ confirmed RDW was an independent predictor of ICU mortality even after controlling for APACHE II and SOFA scores. Kim et al. (2015)¹⁸ also observed that elevated RDW was associated with higher short-term mortality in critically ill COPD patients. These observations indicate that RDW can be used as an indicator of total physiological reserve and burden of illness. The 30-day mortality was also significantly higher among the high-ranking RDW group (43.0%) compared to the normal RDW group (19.4%; $p < 0.001$). This suggests that RDW possesses predictive value extending beyond the ICU admission and beyond, and may be used as a marker of prognosis post-discharge. Elevated RDW was also found in a study conducted in 2021,¹⁶ to have an association with increased 30-day mortality among patients presenting with acute exacerbation of COPD. Mechanisms can include chronic inflammation, nutritional deficiencies, and comorbidities that extend beyond the acute phase. Patients with increased RDW had a statistically significantly higher readmission rate within 30 days (14.8%) than those with normal RDW (6.1%; $p = 0.04$). Readmission is frequently related to incomplete recovery, poor follow-up, or ongoing functional impairment. In one such study by Yao et al. (2022)¹⁹, elevated RDW was a predictor of readmission in patients with heart failure and COPD, possibly an indicator of the weight of chronic systemic inflammation and frailty.

Our study emphasizes the association analysis between red cell distribution width (RDW) and different clinical and biochemical markers of severity and prognosis in critically ill patients with chronic obstructive pulmonary disease (COPD). Such findings accentuate the prospective utility of RDW as an integrative biomarker for underlying

inflammation, nutritional indicators, and systemic derangement. RDW was positively correlated moderately with age ($r = +0.31$, $p < 0.001$), indicating that elderly patients have higher RDW values. This is consistent with earlier research by Salvagno et al. (2015)²⁰ and Persson et al (2020)⁶, which proved that RDW rises with age, possibly because of age-related inflammation, comorbidities, or decreased erythropoiesis. In COPD, ageing could enhance RDW increases because of cumulative oxidative stress and chronic systemic inflammation. The positive correlation between RDW and CRP ($r = +0.36$, $p < 0.001$) underscores the direct association between systemic inflammation and anisocytosis. Such observations have been noted in various studies, such as Zhou et al. (2014),²¹ and another in 2021,²² where RDW was reported to be higher with increased CRP levels among patients with COPD and sepsis. Inflammatory cytokines such as IL-6 could interfere with erythropoiesis and cause elevation of RDW, which lends credence to the view that RDW is an inflammatory-sensitive marker.

RDW was positively correlated with both SOFA ($r = +0.41$, $p < 0.001$) and APACHE II ($r = +0.38$, $p < 0.001$) scores, which are established severity indices in critical care. This reinforces findings from studies in 2022¹⁷ and another study by Kim et al. (2015),¹⁸ which demonstrated that higher RDW levels are associated with increased organ dysfunction and severity of illness in ICU populations. These associations justify the application of RDW as a surrogate disease severity marker and may also contribute to risk stratification. A moderate correlation between ICU length of stay and RDW ($r = +0.34$, $p < 0.001$) suggests that patients with elevated RDW will need longer intensive care. This result aligns with research like Hunziker et al. (2012),⁷ which described hospital stay prolongation in patients with increased RDW, especially in sepsis and critical illness. Increased RDW could represent a pattern of delayed recovery, ongoing inflammation, and metabolic stress contributing to hospital prolongation.

There was a strong inverse correlation between RDW and serum albumin ($r = -0.42$, $p < 0.001$). Low serum albumin indicates suboptimal nutritional status and chronic inflammation, negatively impacting erythrocyte morphology and survival. Tonelli et al. (2019)²³ and Gómez-Rosero et al. (2021)²⁴ have documented this in their studies. These results underscore the multifactorial origin of increased RDW, which encompasses nutritional deficiencies and systemic inflammation. RDW was also negatively correlated with haemoglobin ($r = -0.37$, $p < 0.001$), demonstrating that anisocytosis is often coupled with anaemia. This connection is well-documented in the literature. Research by Rhodes et al. (2011),²⁵ and Yao et al. (2022),¹⁹ found that patients who were anaemic, particularly those with chronic disease or inflammation, tend to have elevated RDW values. Mechanistically, this could be due to ineffective erythropoiesis or bone marrow stress.

Conclusion

In conclusion, the present study highlights that elevated Red Cell Distribution Width in critically ill COPD patients serves as more than just an indicator of anemia. It reflects a complex interplay of systemic inflammation, physiological stress, aging, and nutritional deficiencies. The strong associations observed between RDW and established clinical severity scores and inflammatory biomarkers underscore its potential role as a simple, cost-effective prognostic marker. Incorporating RDW into routine assessment may enhance risk stratification and guide timely clinical interventions in the management of critically ill COPD patients.

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