Section: General Medicine

Original Research Article

INFLAMMATION AND HYPOXIA AS PREDICTORS OF IN HOSPITAL MORTALITY IN ACUTE EXACERBATIONS OF COPD: A COMBINED BIOMARKER APPROACH

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ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide. Early identification of patients at high risk of adverse outcomes during acute exacerbations remains a clinical challenge. Systemic inflammation and hypoxia play key roles in disease progression and prognosis. **Materials and Methods:** We conducted a hospital-based observational study at Basaveshwara Medical College and Hospital from April 2024 through September 2025. A total of 60 consecutive adult patients admitted with acute exacerbation of COPD were included. Total leukocyte count (TLC), erythrocyte sedimentation rate (ESR), and oxygen saturation were recorded at admission. Hypoxia was defined as SpO_2 <90%. The primary outcome was in-hospital mortality. Predictive performance was evaluated using receiver operating characteristic (ROC) analysis and multivariable logistic regression. **Results:** The mean age of patients was 64.3±9.8 years, and 70% were male. Hypoxia was present in 46.7% of patients. In-hospital mortality occurred in 20%. Non-survivors had significantly higher TLC (14,200±2,800 vs. 10,900±2,900 cells/mm³; p=0.002) and ESR (58.3±15.6 vs. 38.1±16.2 mm/hour; p=0.001), and a higher prevalence of hypoxia (83.3% vs. 37.5%; p=0.003). The combined presence of elevated TLC, ESR, and hypoxia was associated with the highest mortality (50%; p<0.001). ROC analysis demonstrated improved predictive accuracy for the combined model (AUC 0.89) compared to TLC (AUC 0.78) and ESR (AUC 0.81) individually. On multivariable analysis, ESR (OR 2.6; p=0.006) and hypoxia (OR 3.4; p=0.003) were independent predictors of mortality. **Conclusions:** The combined assessment of TLC, ESR, and hypoxia at admission provides a simple, cost-effective and robust tool for early prediction of in hospital mortality in Acute Exacerbations Of COPD.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide and is characterized by progressive airflow limitation with recurrent exacerbations that contribute to increased hospitalizations and mortality.[1] Early risk stratification during acute exacerbations remains essential for optimizing management and improving outcomes.

COPD is now recognized as a systemic inflammatory disorder, with elevated levels of circulating inflammatory markers such as total leukocyte count (TLC), erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP), particularly during exacerbations.[2,3] These markers correlate with disease severity and adverse clinical outcomes. Among them, TLC and ESR are inexpensive, widely available, and routinely used in clinical practice, making them attractive candidates for prognostic assessment.[2] Serial changes in

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inflammatory markers have also been shown to reflect disease activity and response to therapy.[4]
Hypoxia, reflecting impaired gas exchange, is a key indicator of disease severity and has been associated with increased risk of respiratory failure and mortality during exacerbations.[5]
In this context, we evaluated whether elevated TLC and ESR at admission, when combined with hypoxia, can serve as a simple and early prognostic marker for mortality risk stratification in patients with COPD.

Aim

To determine the predictive value of total leukocyte count (TLC) and erythrocyte sedimentation rate (ESR) and hypoxia at admission for in hospital mortality in patients with acute exacerbations of chronic obstructive pulmonary disease (COPD).

Objectives

- To assess the association of TLC, ESR, and hypoxia with in-hospital mortality.
- To determine the predictive value of their combined use.
- To correlate these parameters with disease severity and clinical outcomes.
- To determine their utility as simple, cost-effective tools for early risk stratification

MATERIALS AND METHODS

Study Design and Oversight

We conducted a hospital-based prospective observational study at **Basaveshwara Medical College and Hospital** over an 18-month period from **April 2024 to September 2025**. The study protocol was approved by the Institutional Ethics Committee, and informed consent was obtained in accordance with institutional guidelines.

Inclusion

- Age >18 years.
- Clinical diagnosis of COPD as per GOLD criteria.
- Admitted with acute exacerbation of COPD.
- Provided informed consent.

Exclusion

- Patients with acute infections (e.g.. pneumonia, sepsis) at admission.
- Hematologic disorders (e.g.. leukemia, anemia, thrombocytopenia).
- Malignancy.
- Autoimmune or other systemic inflammatory diseases.
- Recent surgery or major trauma.
- Patients on systemic steroids or immunosuppressive therapy prior to admission

Clinical and Laboratory Assessment

Baseline demographic and clinical data were recorded at admission. Oxygen saturation was measured using pulse oximetry. Blood samples obtained at admission were analyzed for total leukocyte count (TLC) and ESR using standard automated laboratory methods.

Definition of Hypoxia

Hypoxia was defined as peripheral oxygen saturation (SpO_2) <90% on room air at presentation, measured by pulse oximetry, corresponding to significant hypoxemia (arterial PaO_2 <60 mmHg) on the oxyhemoglobin dissociation curve.

Outcomes

The primary outcome was in-hospital mortality. Secondary outcomes included requirement for intensive care unit admission, need for ventilatory support, and duration of hospitalization.

Statistical Analysis

Continuous variables are presented as means ± standard deviation, and categorical variables as frequencies and percentages. Group comparisons were performed using the Student's t-test or Mann–Whitney U test for continuous variables and the chi-square or Fisher's exact test for categorical variables, as appropriate. Multivariable logistic regression analysis was used to identify independent predictors of mortality. The predictive performance of TLC, ESR, and hypoxia, individually and in combination, was evaluated using receiver operating characteristic (ROC) curves and the area under the curve (AUC). A two-sided p-value of less than 0.05 was considered to indicate statistical significance. Statistical analyses were performed using **Statistical Package for the Social Sciences (SPSS) software, version 25.0 (IBM Corp., Armonk, NY, USA).**

RESULTS

Baseline Characteristics

A total of 60 patients were included in the study. The mean age was 64.3±9.8 years, and 42 patients (70%) were male. Hypoxia at admission (SpO_2 <90%) was present in 28 patients (46.7%). The mean total leukocyte count (TLC) was 11,800±3,200 cells/mm^3, and the mean erythrocyte sedimentation rate (ESR) was 42.6±18.4 mm/hour. The baseline characteristics of the study population are shown in Table 1.

Table 1: A total of 60 patients were included in the study. The baseline characteristics of the study population are shown

Variable	Overall (N=60)
Age — yr (mean ± SD)	64.3 ± 9.8
Male sex — no. (%)	42 (70.0)
Hypoxia (SpO_2 <90%) — no. (%)	28 (46.7)
TLC — cells/mm^3 (mean ± SD)	11,800 ± 3,200
ESR — mm/hr (mean ± SD)	42.6 ± 18.4
ICU admission — no. (%)	18 (30.0)

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Ventilatory support — no. (%)	15 (25.0)
In-hospital mortality — no. (%)	12 (20.0)

Clinical Outcomes

In-hospital mortality occurred in 12 patients (20%). A total of 18 patients (30%) required intensive care unit admission, and 15 patients (25%) required ventilatory support.

Association of TLC, ESR, and Hypoxia with Mortality

Patients who died had significantly higher mean TLC (14,200±2,800 vs. 10,900±2,900 cells/mm³; p=0.002) and ESR (58.3±15.6 vs. 38.1±16.2 mm/hour; p=0.001) compared to survivors. Hypoxia was more frequent among non-survivors (83.3% vs. 37.5%; p=0.003). These comparisons between survivors and non-survivors are shown in Table 2.

Table 2: TLC denotes total leukocyte count, and ESR erythrocyte sedimentation rate. Values are expressed as mean ± standard deviation or number (percentage)

Variable	Survivors (n=48)	Non-Survivors (n=12)	P Value
TLC — cells/mm³ (mean ± SD)	10,900 ± 2,900	14,200 ± 2,800	0.002
ESR — mm/hr (mean ± SD)	38.1 ± 16.2	58.3 ± 15.6	0.001
Hypoxia — no. (%)	18 (37.5)	10 (83.3)	0.003

Combined Marker Analysis

Patients with elevated TLC, elevated ESR, and hypoxia had the highest mortality rate (50%) compared to those with one or no risk factors (8.3%; p<0.001), indicating a strong association between combined markers and adverse outcomes. Patients were further stratified into four risk categories based on admission total leukocyte count (TLC), erythrocyte sedimentation rate (ESR), and oxygen saturation levels (Table 4).

Table 3: TLC denotes total leukocyte count, ESR erythrocyte sedimentation rate, and SpO_2 peripheral oxygen saturation. Elevated TLC was defined as >11,000 cells/mm³, and elevated ESR as >30 mm/hour. Hypoxia was defined as SpO_2 <90%. Risk categories were defined based on admission parameters

Risk Category	TLC	ESR	SpO_2 (%)	Clinical Interpretation
Low Risk	Normal	Normal	≥92	Mild inflammation, stable status
Moderate Risk	↑ TLC *or* ↑ ESR	One elevated	88–91	Moderate inflammation or early hypoxia
High Risk	↑ TLC + ↑ ESR	Both elevated	<90	Significant inflammation with hypoxia
Very High Risk	Markedly ↑ TLC + ESR	Both markedly elevated	<85	Severe systemic inflammation with hypoxia

Predictive Performance

Receiver operating characteristic (ROC) analysis demonstrated moderate predictive value for TLC (AUC 0.78) and ESR (AUC 0.81) individually. The combination of TLC, ESR, and hypoxia improved predictive accuracy (AUC 0.89). The predictive performance of these parameters is shown in Figure 1.

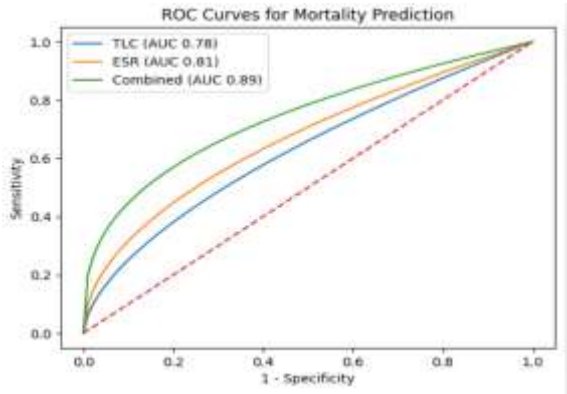

Figure 1. Predictive Performance of TLC, ESR, and Combined Model for Mortality.

ROC curves show the predictive value of TLC (AUC 0.78), ESR (AUC 0.81), and the combined model (AUC 0.89) for in-hospital mortality.

Multivariable Analysis

On multivariable logistic regression analysis, elevated ESR (OR 2.6; 95% CI, 1.3–5.2; p=0.006) and hypoxia (OR 3.4; 95% CI, 1.5–7.8; p=0.003) were independent predictors of mortality, while TLC showed a strong but borderline association (OR 1.9; p=0.058). The results of multivariable analysis are presented in Table 4.

Table 4: Odds ratios are adjusted for variables included in the multivariable model. TLC denotes total leukocyte count, and ESR erythrocyte sedimentation rate

Variable	Odds Ratio (OR)	95% Confidence Interval	P Value
Elevated ESR	2.6	1.3 – 5.2	0.006
Hypoxia	3.4	1.5 – 7.8	0.003
Elevated TLC	1.9	—	0.058

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Table 4: Odds ratios are adjusted for variables included in the multivariable model. TLC denotes total leukocyte count, and ESR erythrocyte sedimentation rate.

DISCUSSION

6.1 Key Findings of the Study

The present study shows that elevated total leukocyte count (TLC) and erythrocyte sedimentation rate (ESR) at admission, when combined with hypoxia, are associated with adverse outcomes in patients with COPD. This combination of simple clinical and laboratory parameters appears to provide a practical approach for early mortality risk stratification.

6.2 Role of Inflammatory Markers in COPD Severity

Systemic inflammation is a key component of COPD and contributes to both disease progression and exacerbations. Elevated TLC and ESR reflect this inflammatory burden and have been shown to correlate with worsening clinical status and disease severity.[2,3] Leukocytosis represents activation of the innate immune response, whereas an elevated ESR reflects ongoing inflammatory activity. Together, these findings support the clinical relevance of basic hematological markers as indicators of systemic inflammation in COPD.

6.3 Comparison with Existing Biomarkers

C-reactive protein (CRP) remains one of the most widely studied biomarkers in COPD and has been shown to correlate with exacerbation severity and response to treatment.[4] However, emerging biomarkers such as interleukins, tumor necrosis factor-α, and procalcitonin, although promising, are not routinely available in many clinical settings.[3]

In contrast, TLC and ESR are inexpensive, universally available, and easy to interpret, making them more suitable for routine use, particularly in resource-constrained environments.

6.4 Importance of Hypoxia in Prognosis

Hypoxia is a well-established marker of disease severity in COPD and reflects impaired gas exchange. It has consistently been associated with an increased risk of respiratory failure, need for ventilatory support, and mortality.[5] The present findings suggest that when hypoxia is assessed alongside inflammatory markers, the ability to identify high-risk patients is improved, emphasizing its importance in early prognostic evaluation.

6.5 Clinical Implications

From a clinical standpoint, the combined use of TLC, ESR, and hypoxia at admission may facilitate early risk stratification and triage. This approach can assist in identifying patients who require closer monitoring, early escalation of care, or intensive care unit admission. Its simplicity and low cost make it particularly applicable in busy clinical settings and in regions where access to advanced investigations is limited.

6.6 Strengths of the Study

The primary strength of this study lies in the use of simple, widely available, and cost-effective parameters that can be easily integrated into routine clinical practice. Additionally, the combined evaluation of inflammatory markers with hypoxia provides a clinically relevant and pragmatic model for early risk assessment.

6.7 Limitations

This study has several limitations. The relatively small sample size and single-center design may limit the generalizability of the findings. Furthermore, advanced inflammatory biomarkers were not included for comparison, which may have provided additional insight into prognostic performance.

6.8 Future Directions

Further multicenter studies with larger sample sizes are required to validate these findings. Incorporation of these parameters into existing prognostic scoring systems may enhance their clinical utility. Future research should also explore combining basic hematological markers with advanced biomarkers to improve accuracy in risk stratification.

These findings suggest that the combined assessment of TLC, ESR, and hypoxia at admission may assist in early risk stratification and clinical decision making in patients with COPD, particularly in settings where advanced biomarkers are not readily available. However, these observations require validation in larger, multicenter cohorts before routine clinical implementation.

CONCLUSION

The combined assessment of total leukocyte count, erythrocyte sedimentation rate, and hypoxia at admission provides a simple, cost-effective, and clinically robust tool for early prediction of in-hospital mortality in patients with acute exacerbations of COPD. This approach may facilitate timely risk stratification and guide clinical decision-making, particularly in resource-limited settings.

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