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CLINICAL AND BIOCHEMICAL MARKERS AS PREDICTORS OF OUTCOME IN ACUTE EXACERBATIONS OF COPD IN A TERTIARY CARE CENTRE

Respiratory Medicine

Dr. Arif Qureshi PGJR 3, Department- Respiratory Medicine

Dr G.N Srivastava Professor Head Of Department Respiratory Medicine

Dr Vinod Kumar Assistant Professor, Respiratory Medicine

ABSTRACT

Background: Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) significantly contribute to disease progression, hospital admissions, and mortality. Clinical and biochemical markers may aid in early risk stratification but are underutilized in routine tertiary care settings. **Objectives:** To assess the prognostic value of clinical, electrocardiographic, echocardiographic, and biochemical markers in predicting outcomes among hospitalized AECOPD patients. **Methods:** This cross-sectional study included 100 patients with AECOPD admitted to a tertiary care hospital over 18 months. Data on demographic, clinical, ECG, echocardiographic, and biochemical parameters such as NT-proBNP, CRP, NLR, and eosinophil count were collected and analyzed. Outcomes were measured as recovery or in-hospital mortality. **Results:** The mean age was 61.6 ± 13.3 years; 57% were males. NT-proBNP elevation (55% mortality), eosinophilia (53.8%), and P-pulmonale (52.9%) were significantly associated with mortality ($p<0.001$). Dyspnea severity, comorbid hypertension and diabetes, and prolonged hospital stay also showed strong correlations with adverse outcomes. CRP and NLR showed moderate associations. **Conclusion:** Clinical severity, cardiovascular comorbidities, and specific biochemical markers can independently predict mortality in AECOPD. Comprehensive evaluation improves triage and management in tertiary settings.

KEYWORDS

COPD; Acute Disease; NT-proBNP; Biomarkers; Mortality; Exacerbation.

INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a major global health concern and a leading cause of chronic respiratory morbidity and mortality. As defined by GOLD 2024, it is a progressive, heterogeneous disease marked by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities (1). Key contributing factors include tobacco use, environmental pollutants, occupational exposures, and socio-economic status (2,3). Acute exacerbations of COPD (AECOPD)—sudden worsening of respiratory symptoms within 14 days—accelerate disease progression and significantly increase hospitalizations and mortality (4). These events are commonly triggered by infections and environmental pollutants, with peak incidence during colder seasons (4). Emerging evidence highlights the prognostic value of markers such as NT-proBNP and troponin, which reflect cardiac stress and are linked to poorer outcomes (5). Inflammatory markers like CRP, neutrophil-to-lymphocyte ratio (NLR), and red cell distribution width (RDW) also indicate disease burden (5). Elevated eosinophil counts (>300/μL) have been associated with a 1.32-fold increased risk of exacerbation (6). Despite their potential, these markers are underutilized in routine tertiary care. This study evaluates selected clinical and biochemical predictors to enhance risk stratification and management in hospitalized AECOPD patients.

MATERIAL AND METHODS

A hospital-based cross-sectional study was conducted over 18 months (July 2023–January 2025) in the Department of Respiratory Medicine, Heritage Institute of Medical Sciences, Varanasi, to assess clinical and biochemical markers predicting outcomes in AECOPD.

Study Population And Criteria:

A total of 100 AECOPD patients presenting to the emergency or inpatient department were enrolled after obtaining written informed consent. Inclusion criteria were age >40 years and a confirmed COPD diagnosis—either through spirometry or clinical and radiographic evidence. Patients were excluded if they had asthma, bronchiectasis, significant systemic comorbidities (renal, hepatic, neurological), hemodynamic instability, recent myocardial infarction, ischemic heart disease, or declined consent.

Sample Size Calculation:

The required sample size was estimated using the formula:

$$n = [(Z\alpha/2 + Z\beta)^2 \times \sigma^2] / d^2,$$

with $Z\alpha/2 = 1.96$, $Z\beta = 0.84$, and an assumed effect size of 0.3, based on a prior study (Bhardwaj et al., 2021). This yielded a sample size of 87.11, which, after adjusting for a 10% dropout rate, was rounded to 100 patients.

Data Collection And Investigations:

Each patient underwent a detailed clinical evaluation, and data were recorded using a structured proforma. Clinical history, demographic details, symptomatology, and exacerbation patterns were thoroughly assessed. Investigations included:

- **Hematological Tests:** Complete blood count, total and differential leukocyte counts, eosinophil count, CRP, and neutrophil-to-lymphocyte ratio.
- **Cardiac Biomarkers:** NT-proBNP and troponin I levels.
- **Radiological Evaluation:** Chest X-ray (PA view).
- **Pulmonary Function Testing:** Spirometry using RMS Helios 702 machine, with both pre- and post-bronchodilator measurements. Post-bronchodilator FEV1/FVC <0.70 confirmed COPD diagnosis. Severity was graded per GOLD guidelines.

Ethical Approval:

Ethics clearance was granted by the Institutional Ethics Committee (HIMS/IEC/222, dated 12/03/2025).

Statistical Analysis:

SPSS v26.0 was used. Continuous variables were reported as mean ± SD; categorical data as frequencies (%). Chi-square test was used for comparisons. A p-value <0.05 was considered significant.

RESULTS

Among 100 AECOPD patients (mean age 61.6 ± 13.3 years), 57% were male and 96% were smokers. Most had grade 4 dyspnea (78%), which was associated with higher mortality (17.9%) than grade 3 (9.1%).

Table 1: Distribution of Fever, Chest Pain, and Length of Hospital Stay with Mortality in AECOPD Patients

Parameter		Deceased	Recovered	Total	Mortality (%)
Fever	(Yes)	12	28	40	30.0%
	(No)	4	56	60	6.66%
Chest Pain	(Yes)	10	14	24	41.6%
	(No)	6	70	76	7.9%
Hospital Stay	<5 days	1	15	16	6.2%
	5–10 days	5	51	56	8.9%
	>10 days	10	18	28	35.7%

Table 2: Distribution of Comorbidities and ECG Findings with Mortality in AECOPD Patients

Parameter		Deceased	Recovered	Total	Mortality (%)
Hypertension	(Yes)	11	24	35	31.4%
	(No)	5	60	65	7.7%
T2DM	(Yes)	8	10	18	44.4%

	(No)	8	74	82	9.7%
Sinus Tachycardia	(Yes)	15	80	95	15.8%
	(No)	1	4	5	20.0%
P-Pulmonale	(Yes)	9	8	17	52.9%
	(No)	7	76	83	8.4%

Table 3: Distribution of Cardiac Findings and Respiratory Failure Type with Mortality in AECOPD Patients

Parameter		Deceased	Recovered	Total	Mortality (%)
Arrhythmias	(Yes)	2	0	2	100.0%
	(No)	14	84	98	14.2%
TR	Mild TR (Yes)	11	12	23	47.8%
	TR Normal	5	72	77	6.4%
PAH	Mild PAH (Yes)	12	42	54	22.2%
	PAH Normal	4	42	46	8.7%
Respiratory Failure	Type 1	2	27	29	6.9%
	Type 2	14	57	71	19.7%

Table 4: Distribution of Biochemical Markers and COPD Severity with Mortality in AECOPD Patients

Parameter		Deceased	Recovered	Total	Mortality (%)
NT-proBNP	Elevated	11	9	20	55.0%
	Normal	5	75	80	6.2%
CRP	Elevated	15	68	83	18.1%
	Normal	1	16	17	5.9%
NLR	Elevated	14	58	72	19.4%
	Normal	2	26	28	7.2%
Eosinophil Count	Elevated	7	6	13	53.8%
	Normal	9	78	87	10.3%
COPD	Moderate (FEV1 50–79%)	0	25	25	0.0%
	Severe (FEV1 30–49%)	7	54	61	11.5%
	Very Severe (FEV1 <30%)	9	5	14	64.3%

DISCUSSION

In this study of 100 AECOPD patients, the mean age was 61.6 ± 13.3 years, with the highest prevalence among those aged 60–69. Similar age trends were observed by Kuwal et al. and Rahet et al. (7,8). Males predominated slightly (57%), though increasing COPD incidence in females may reflect rising exposure to indoor pollution and tobacco.

Clinically, dyspnea was universal, with 78% in MMRC Grade 4. Cough (85%) and expectoration (78%) were frequent. Fever (40%) and chest pain (24%) showed significant associations with mortality (p=0.002 and p=0.000), supporting prior findings by Ma et al. and McManus et al. (9). Longer hospital stay was associated with poorer outcomes (p=0.003), echoing studies by Seemungal et al. and others (10).

Tobacco use was reported in 96% of patients, reinforcing its role in COPD pathogenesis, as shown in studies by Sharma et al. and B. Thomas et al. (11,12). However, smoking history alone was not significantly linked to mortality in our cohort. Hypertension and type 2 diabetes were observed in 35% and 18% respectively, both significantly increasing mortality risk (p=0.002), aligning with findings from Wang et al. (13).

ECG abnormalities such as sinus tachycardia (95%), P-pulmonale (17%), and arrhythmias (2%) were common. P-pulmonale (p=0.000) and arrhythmias (p=0.001) were significantly associated with mortality, in line with studies by Kanawade et al. (14). Mild TR and mild PAH on echocardiography also correlated with increased mortality (p<0.001), emphasizing the prognostic role of cardiac dysfunction.

Among biochemical markers, elevated NT-proBNP was significantly associated with mortality (55%, p=0.000), supporting the findings of Xiaojie et al. (15). Raised CRP (83% of patients) and elevated NLR (72%) were associated with increased mortality, though not statistically significant. Eosinophilia (13%) was significantly associated with higher mortality (53.8%, p=0.000), contrasting with some literature that suggests better short-term outcomes in eosinophilic exacerbations (16).

Finally, disease severity strongly predicted mortality, with very severe COPD cases showing a 64.3% death rate. This confirms prior evidence from Thorax and BMJ Open linking exacerbation frequency and severity to poorer outcomes (17,18).

CONCLUSION

Clinical markers like dyspnea severity, NT-proBNP, eosinophil count, and NLR were strong predictors of poor outcomes in AECOPD. Hypertension, diabetes, and cardiac abnormalities also increased mortality risk, underscoring the need for comprehensive risk assessment and early intervention.

Limitations

Limitations include the single-center design, small sample size, lack of long-term follow-up, and single-time biomarker measurement. Pulmonary function tests were not feasible in all cases, and confounders like medication history and socioeconomic status were not fully controlled.

Strengths

The study's strength lies in its comprehensive evaluation of clinical, ECG, echocardiographic, and biochemical markers in a well-defined AECOPD cohort, providing reliable insights into mortality risk and supporting integrated marker-based assessment.

Conflict Of Interest: None.
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Ethical Approval: Obtained.
Consent: Written consent secured.

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