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Original Research Article

C-Reactive Protein Testing to Guide Antibiotic Prescribing for COPD Exacerbations

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Abstract: *Acute exacerbations of chronic obstructive pulmonary disease (AECOPD) are commonly treated with antibiotics, although bacterial infection is not present in all cases. Overprescription contributes to antimicrobial resistance and unnecessary healthcare costs. Biomarkers such as C-reactive protein (CRP) may help clinicians guide more appropriate antibiotic use.* ***Objective:*** *To determine whether C-reactive protein (CRP)–guided antibiotic prescribing reduces antibiotic use in patients with acute exacerbations of chronic obstructive pulmonary disease.* ***Methods****: A randomized controlled trial was conducted at Benazir Bhutto Hospital in Rawalpindi from 11 June 2025 to 11 November 2025. A total of 174 patients aged ≥40 years with confirmed COPD presenting with AECOPD were enrolled and randomly allocated into two groups (87 patients each). The intervention group received CRP-guided care in which point-of-care CRP testing was performed, and antibiotics were prescribed only when CRP levels exceeded 20 mg/L. The control group received standard care based on clinical assessment and physician judgment without CRP testing. Patients were followed for four weeks to evaluate antibiotic prescription rates. Data were analyzed using SPSS version 25.0. Categorical variables were compared using the Chi-square test and continuous variables using the Student's t-test. A p-value <0.05 was considered statistically significant.* ***Results:*** *Baseline demographic and clinical characteristics were comparable between the two groups. At the initial consultation, antibiotics were prescribed to 36.7% of patients in the CRP-guided group compared with 77% in the standard care group (χ^2=28, p<0.0001). At four-week follow-up, antibiotic prescription rates were 10.3% in the CRP-guided group and 89.6% in the standard care group (χ^2=109, p<0.0001), demonstrating a marked reduction in antibiotic utilization in the intervention group.* ***Conclusion****: CRP-guided antibiotic prescribing significantly reduces antibiotic utilization among patients with acute exacerbations of COPD compared with standard clinical judgment alone. Incorporating CRP testing into routine clinical practice may help promote rational antibiotic use in the management of AECOPD.*

Keywords: Chronic obstructive pulmonary disease, C-reactive protein, acute exacerbation, antibiotic prescribing, antimicrobial stewardship, point-of-care testing.

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Introduction

Globally, family physicians prescribe a substantial proportion of antibiotics, a considerable number of which are potentially avoidable(1). Inappropriate and excessive antibiotic use represents a major driver of antimicrobial resistance (AMR), contributes to unnecessary healthcare expenditures, and is associated with adverse effects, including disruption of the host microbiome(2).In response, industry-sponsored clinical trials and government awareness initiatives have promoted the implementation of point-of-care tests (POCTs) for diagnosing acute infections. These strategies aim to optimize antibiotic prescribing, mitigate the development of AMR, and ultimately improve patient outcomes(3). However, the existing literature on POCTs for acute infections has predominantly focused on analytical performance characteristics, such as sensitivity and specificity. In contrast, relatively few studies have rigorously evaluated their impact on clinical decision-making and patient-centered outcomes(4).

Nearly half of individuals diagnosed with chronic obstructive pulmonary disease (COPD) experience at least one acute exacerbation each year, often requiring management with systemic corticosteroids, antibiotics, or a combination of both, and occasionally resulting in hospital admission(5). Moreover, approximately 25% of patients experience two or more exacerbations per year (6). Globally, antibiotics are prescribed in more than 80% of COPD exacerbations. Although these treatments provide symptomatic relief for many patients, not all individuals derive clinical benefit. Non-infectious etiologies are estimated to account for approximately 20% of COPD exacerbations; nevertheless, current clinical guidelines continue to recommend antibiotic therapy for patients presenting with moderate-to-severe symptoms, particularly in the presence of increased dyspnea, cough, and purulent sputum (7). In primary care settings, antibiotic prescribing decisions are commonly guided by clinical criteria, such as the Anthonisen criteria. However, reliance on these symptom-based criteria is challenging, as they are inherently subjective and demonstrate limited diagnostic accuracy in distinguishing patients who can safely recover without antibiotic therapy (8).

C-reactive protein (CRP), an acute-phase protein, is a well-defined biomarker of systemic inflammation, including acute exacerbations of COPD (AECOPD) (9). A previously conducted research study on patients with acute COPD exacerbations and CRP levels below 40 mg/L demonstrated no significant difference in clinical outcomes between those treated with antibiotics and those receiving a placebo. Findings from such studies indicate that point-of-care CRP testing may support more targeted antibiotic prescribing decisions in COPD exacerbations(10, 11). Although available data suggest that CRP-based point-of-care testing may assist in treatment decision-making, there is still a lack of strong evidence assessing its impact on meaningful clinical and patient-centered outcomes. This study aims to evaluate whether incorporating point-of-care CRP testing into the clinical assessment of acute COPD exacerbations in primary care can safely and effectively reduce antibiotic prescribing among these patients.

Methodology

We conducted this randomized controlled trial (RCT) at Benazir Bhutto Hospital, Rawalpindi. The institutional ethics review board approved the

study. The study was completed from 11th June 2025 to 11th November 2025, following ethical approval. The sample size was estimated using the WHO sample size calculator, based on parameters from Butler et al., assuming antibiotic prescribing rates of 57% in the intervention group and 77.4% in the standard care group (12). With 80% power and a two-sided α of 0.05, a total sample of 174 patients (87 per group) was required. Men and women aged 40 years or older with a confirmed diagnosis of COPD presenting with AECOPD were eligible. Acute exacerbation of COPD (AECOPD) was characterized by the occurrence of at least one of the following clinical features: worsening breathlessness, increased sputum production, or greater sputum purulence. Patients with suspected pneumonia or a respiratory rate >30 breaths/min were included. Exclusion criteria comprised need for urgent hospitalization, concurrent infections, prior antibiotic use for the current episode, current antibiotic therapy, history of respiratory failure or mechanical ventilation, cystic fibrosis, bronchiectasis, tracheostomy, immunocompromised state, or pregnancy. Informed written consent was obtained from all participants prior to enrollment in the study. Participants were randomized using sealed envelopes (lottery method) into two groups. Group A (CRP-guided care) underwent point-of-care C-reactive protein (CRP) testing at presentation, and antibiotics were prescribed if CRP levels exceeded 20 mg/L. Group B (standard care) received antibiotics at the clinician's discretion without CRP testing. Baseline data, including duration of illness and comorbidities, were recorded prior to randomization. Patients were followed for four weeks to assess additional antibiotic prescriptions; CRP testing was repeated in Group A if symptoms persisted.

Statistical analysis was performed using SPSS (version 25.0). Categorical data were described in terms of number and proportion (%) and evaluated using the Chi-square test. Quantitative variables were reported as mean with standard deviation and compared using the independent samples t-test. Statistical significance was determined using a two-tailed P-value threshold of 0.05

Results

A total of 174 patients with acute exacerbation of chronic obstructive pulmonary disease were enrolled and randomized equally into two groups: the CRP-guided group (n=87) and the standard care group (n=87). All participants completed the four-week follow-up and were included in the final analysis. The baseline demographic and clinical characteristics of the participants were comparable between the two groups. The mean age of participants was 61.3 ± 3.0 years in the CRP-guided group and 59.2 ± 5.0 years in the standard care group (p=0.412). The mean body mass index was similar between groups (27.0 ± 3.1 kg/m² in the CRP group vs 26.8 ± 3.2 kg/m² in the standard care group; p=0.638). The average duration of symptoms before presentation was also comparable (5.3 ± 1.9 days in the CRP group vs 5.8 ± 2.0 days in the standard care group; p=0.284). Gender distribution and comorbidities such as hypertension and asthma were evenly distributed across the two groups ($p > 0.05$), indicating adequate comparability at baseline (Table 1).

At the initial consultation, antibiotics were prescribed to 32 patients (36.7%) in the CRP-guided group compared with 67 patients (77.0%) in the standard care group. This difference was statistically significant ($\chi^2 = 28$, $p < 0.001$), indicating a substantial reduction in antibiotic prescribing when CRP testing was used to guide treatment decisions. During the four-week follow-up period, additional antibiotic prescriptions were required in 9 patients (10.3%) in the CRP-guided group compared with 78 patients (89.6%) in the standard care group. The difference remained highly significant ($\chi^2 = 109$, $p < 0.001$), indicating sustained lower antibiotic utilization among patients managed with CRP-guided therapy (Table 2).

These findings suggest that incorporation of point-of-care CRP testing into clinical assessment significantly reduces antibiotic prescribing in patients with acute exacerbations of COPD.

Table 1 Baseline Characteristics of Study Participants (n = 174)

Variable	CRP Group (n=87)	Standard Care (n=87)	p-value
Age (years)	61.3 ± 3.0	59.2 ± 5.0	0.412
BMI (kg/m²)	27.0 ± 3.1	26.8 ± 3.2	0.638
Duration of symptoms (days)	5.3 ± 1.9	5.8 ± 2.0	0.284
Male	56 (64.4%)	58 (66.7%)	0.761
Female	31 (35.6%)	29 (33.3%)	
Hypertension	28 (32.2%)	30 (34.5%)	0.694
Asthma	19 (21.8%)	17 (19.5%)	

Values are presented as mean ± standard deviation or frequency (%).

Table 2: Antibiotic Prescription Rates in Both Groups

Time Point	CRP Group (n=87)	Standard Care (n=87)	χ^2	p-value
Initial consultation	32 (36.7%)	67 (77.0%)	28	<0.001
4-week follow-up	9 (10.3%)	78 (89.6%)	109	<0.001

Values are presented as a number (%).

Discussion

This randomized controlled trial demonstrates that CRP-guided antibiotic prescribing significantly reduces antibiotic use in patients with AECOPD compared with antibiotic use based solely on clinical judgment. At baseline, antibiotic prescribing was reduced by approximately 40 percentage points in the CRP group, with an even greater divergence observed at four-week follow-up.

Our findings are consistent with the landmark PACE trial, which demonstrated that CRP-guided management significantly reduced antibiotic prescribing in primary care patients with COPD exacerbations without compromising clinical recovery(12). Similarly, a Dutch hospital-based randomized trial reported reduced antibiotic exposure in patients with AECOPD managed using CRP thresholds, without increased treatment failure. These results collectively support CRP as a reliable biomarker to guide antibiotic decisions(13).

Evidence from a systematic review and meta-analysis of biomarkers in AECOPD further indicates that elevated CRP levels are moderately associated with bacterial infections, reinforcing its diagnostic value(14). Additional studies evaluating respiratory viral panels have also shown that objective diagnostic tools reduce unnecessary antibiotic prescribing in respiratory conditions(15).

The CRP threshold used in our study (20 mg/L) is supported by previous international research. However, some evidence suggests that higher thresholds (e.g., 40 mg/L) may better distinguish bacterial from non-bacterial exacerbations, and a tiered approach to CRP interpretation has been proposed. Nonetheless, purulent sputum combined with elevated CRP appears to be a stronger predictor of bacterial infection than symptom-based criteria alone(15).

In Pakistan, antimicrobial resistance remains a major public health challenge. A recent national scoping review identified widespread inappropriate prescribing practices and limited awareness of antimicrobial stewardship principles among healthcare providers(16). In this context, point-of-care CRP testing offers a practical and scalable intervention to improve prescribing behavior in primary care and hospital settings.

Qualitative research has also shown that CRP testing enhances clinician confidence, reduces diagnostic uncertainty, and facilitates shared decision-making with patients (17). The rapid turnaround time of point-of-care CRP testing enables real-time management decisions without delaying treatment in those who truly require antibiotics.

The strengths of this study include its randomized design, adequate sample size, and comparable baseline characteristics between groups. However, limitations must be acknowledged. Clinical outcomes such as hospitalization rates, treatment failure, and mortality were not assessed. Additionally, follow-up was limited to four weeks, and a single CRP threshold was used.

Overall, our findings support integrating CRP-guided antibiotic prescribing into the routine management of AECOPD as an effective antimicrobial stewardship strategy, particularly in resource-limited healthcare systems.

Conclusion

This study concludes that CRP-guided antibiotic prescribing significantly reduces antibiotic use in patients with AECOPD in a Pakistani hospital setting. Incorporating point-of-care CRP testing into routine clinical practice may support antimicrobial stewardship without compromising patient care.

Declarations

Data Availability statement
All data generated or analysed during the study are included in the manuscript.

Ethics approval and consent to participate
Approved by the department concerned. (IRBEC-BBHP-233-25)

Consent for publication
Approved

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Conflict of interest

The authors declared no conflict of interest.

Author Contribution

RF (Post Graduate Trainee)
Manuscript drafting, Study Design,
RM (SR)
Review of Literature, Data entry, Data analysis, and drafting articles.
SM (Professor)
Conception of Study, Development of Research Methodology Design

All authors reviewed the results and approved the final version of the manuscript. They are also accountable for the study's integrity.

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