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Original Article

The Effect of Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection

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ABSTRACT

Background: Lower respiratory tract infections are a major cause of hospitalization and antibiotic exposure, and procalcitonin-guided strategies have been proposed to reduce unnecessary antibiotic use by improving discrimination between bacterial and non-bacterial respiratory illness. Objective: To compare procalcitonin-guided antibiotic therapy with standard clinician-directed care in terms of antibiotic-use duration and hospital length of stay among patients with lower respiratory tract infection. Methods: This comparative observational study was conducted at the Department of Medicine, Combined Military Hospital, Quetta, A total of 190 patients with clinically or radiologically diagnosed lower respiratory tract infection were included and divided equally into a procalcitonin-guided group and a standard-care group. The primary outcome was duration of antibiotic use, while the secondary outcome was hospital length of stay. Continuous variables were summarized as median with interquartile range and compared using non-parametric methods, while categorical variables were compared using the chi-square test. Results: The median age of participants was 52.50 years, and 75.79% were male. ICU admission was significantly more frequent in the procalcitonin-guided group than in standard care (27.37% vs 10.53%, p=0.003). Median hospital stay was longer in the procalcitonin-guided group (8.00 vs 6.00 days, p<0.001). Although the median antibiotic duration was 7 days in both groups, the antibiotic-use distribution was significantly shifted upward in the procalcitonin-guided group (IQR 6.00-12.00 vs 5.00-9.00 days, p=0.012). Conclusion: Procalcitonin-guided care was associated with longer hospital stay and greater overall treatment burden in this cohort; however, the markedly higher ICU burden in the procalcitonin-guided group suggests that baseline severity imbalance likely influenced these findings. Keywords: procalcitonin; lower respiratory tract infection; antibiotics; length of stay; biomarker-guided therapy; antimicrobial stewardship.

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INTRODUCTION

Lower respiratory tract infections (LRTIs) remain a major cause of morbidity, hospitalization, and antibiotic consumption worldwide, particularly in adults presenting with acute bronchitis, community-acquired pneumonia, and infective exacerbations of chronic airway disease. Although antibiotics are frequently prescribed in these conditions, distinguishing bacterial from viral or non-infectious etiologies remains difficult in routine clinical practice, contributing to avoidable antibiotic exposure, antimicrobial resistance, adverse drug effects, and unnecessary healthcare utilization (1-3). This diagnostic uncertainty is especially important in hospital-based settings, where early empiric treatment decisions are often made before microbiological confirmation and where stewardship-oriented biomarkers may help refine antibiotic initiation and discontinuation (4).

Procalcitonin (PCT), a precursor peptide of calcitonin, has emerged as a clinically useful biomarker because its serum concentration typically rises in systemic bacterial infection while remaining relatively low in most viral infections and non-bacterial inflammatory states. Owing to this biological behavior, PCT-guided algorithms have been proposed to support antibiotic stewardship by discouraging antibiotic use at low biomarker thresholds and encouraging treatment when the likelihood of bacterial infection is higher (4,5). Several studies have reported that PCT-guided therapy can reduce antibiotic initiation,

shorten antibiotic exposure, and maintain safety across selected respiratory infections without increasing adverse clinical outcomes (6,7). A large randomized trial, however, found no meaningful reduction in antibiotic duration despite implementation of PCT-guided care, suggesting that biomarker-guided decision-making may not uniformly translate into shorter treatment courses across all settings and patient populations (8). Moreover, concerns remain regarding the interpretive limitations of PCT, particularly because elevated levels may not perfectly discriminate bacterial from viral etiologies in every clinical context and may also be influenced by disease severity and comorbid conditions (9).

The broader evidence base therefore remains heterogeneous. Pragmatic trials, systematic reviews, and implementation studies have shown variable effects of PCT-guided strategies on antibiotic use, mortality, and length of stay, with differences often attributable to clinical setting, patient acuity, adherence to stopping algorithms, and local prescribing behavior (10-18). Importantly, most of the available literature originates from high-resource settings with stronger antimicrobial stewardship infrastructure, while evidence from resource-constrained tertiary care environments remains limited. In Pakistan and similar healthcare systems, where prescribing practices, patient severity at presentation, and institutional pathways may differ substantially from those in trial-intensive regions, the real-world performance of PCT-guided therapy in hospitalized patients with LRTI has not been adequately characterized. This represents a clinically relevant knowledge gap because external validity of international findings cannot be assumed without contextual evaluation (10).

The present study was therefore conducted to compare procalcitonin-guided antibiotic therapy with standard clinician-directed care among patients presenting with lower respiratory tract infection at a tertiary care hospital. The primary objective was to determine whether PCT-guided management influenced the duration of antibiotic use, while the secondary objective was to compare hospital length of stay between the two groups. We hypothesized that incorporation of PCT-guided decision-making would optimize antibiotic use and improve short-term clinical efficiency in patients with LRTI.

MATERIALS AND METHODS

This comparative observational study was conducted in the Department of Medicine, Combined Military Hospital, Quetta, Pakistan, after approval from the institutional Ethical Review Board. The study was designed to evaluate the effect of procalcitonin-guided antibiotic therapy on antibiotic utilization and short-term hospital outcomes among patients presenting with lower respiratory tract infection. Participants were recruited from both the indoor and outpatient departments using a non-probability purposive sampling approach based on predefined clinical eligibility criteria. Written informed consent was obtained from all participants prior to enrolment, and confidentiality of patient information was maintained throughout the study in accordance with institutional ethical standards. Participants were informed of their right to withdraw at any stage without effect on clinical care.

Patients were eligible if they had a clinical diagnosis of lower respiratory tract infection, including symptoms such as fever and sputum production, and/or radiological evidence of infection involving the bronchi or lung parenchyma. Patients were excluded if they had severe immunosuppression, active tuberculosis, recent surgery or trauma within the preceding two weeks, sepsis, infection at a site other than the lungs, recent antibiotic exposure, pregnancy, or any non-respiratory condition known to elevate procalcitonin levels. Patients already receiving antibiotics before PCT testing were also excluded in order to minimize distortion of biomarker-guided treatment decisions and to improve comparability between management groups.

After eligibility screening, baseline assessment was performed at presentation and included demographic profile, relevant comorbidities, clinical examination findings, and laboratory evaluation. Serum procalcitonin was measured at the time of admission for patients managed under the biomarker-guided pathway. Participants were then managed in one of two care pathways: the procalcitonin-guided group and the standard care group. In the procalcitonin-guided group, antibiotic prescribing decisions

were aligned with predefined PCT thresholds, whereby antibiotic use was strongly discouraged at PCT levels below 0.1 ng/mL, discouraged at 0.1-0.25 ng/mL, encouraged at 0.25-0.50 ng/mL, and strongly encouraged at levels above 0.50 ng/mL. In this group, antibiotics were discontinued when serum PCT fell below 0.25 ng/mL or decreased by more than 80% from baseline. In the standard care group, antibiotic initiation and discontinuation were based on the treating clinician's routine assessment of clinical status, with discontinuation generally occurring after clinical recovery, defined by resolution of fever, improvement in respiratory symptoms, and hemodynamic stability.

The primary outcome was duration of antibiotic use, measured in days from initiation to discontinuation during the treatment course. The secondary outcome was length of hospital stay, measured in days from admission to discharge. Additional baseline clinical variables included age, sex, diabetes mellitus, hypertension, ischemic heart disease, smoking status, chronic obstructive pulmonary disease, and intensive care unit admission. These variables were recorded to characterize the sample and to assess group comparability, particularly because non-randomized allocation could introduce baseline differences in severity and comorbidity burden. Standardized data collection procedures were used throughout the study to support completeness and internal consistency of the dataset.

Data were entered and analyzed using Statistical Package for the Social Sciences version 25.0. Distribution of continuous variables was assessed with the Shapiro-Wilk test, and because continuous variables were not normally distributed, they were summarized as median with interquartile range. Categorical variables were expressed as frequency and percentage. Between-group comparisons for categorical variables were performed using the chi-square test or Fisher's exact test where appropriate, while non-normally distributed continuous variables were compared using the Mann-Whitney U test. A two-sided p-value of 0.05 or less was considered statistically significant. All analyses were conducted using the same predefined outcome definitions and uniform reporting rules to preserve reproducibility and data integrity.

RESULTS

A total of 190 patients were analyzed, with 95 patients in the procalcitonin-guided group and 95 in the standard-care group. The overall median age was 52.50 years (IQR 39.75-64.25), and males constituted 75.79% of the study population. Most baseline comorbidities were broadly comparable between groups, although the procalcitonin-guided group showed a statistically significant difference in age distribution relative to standard care. More importantly, ICU admission was substantially more frequent in the procalcitonin-guided group, indicating a clinically more severe case mix in that arm.

Table 1. Baseline Characteristics of the Study Population

Characteristic	Total (n=190)	PCT Group (n=95)	Standard Care Group (n=95)	Effect Estimate*	p-value
Age, years, median (IQR)	52.50 (39.75-64.25)	56.00 (42.00-66.00)	61.00 (35.00-61.00)	Median difference: -5.00 years	0.033
Female, n (%)	46 (24.21)	21 (22.11)	25 (26.32)	OR 0.79 (95% CI 0.41-1.55)	0.498
Male, n (%)	144 (75.79)	74 (77.89)	70 (73.68)	—	—
Diabetes mellitus, n (%)	72 (37.89)	33 (34.74)	39 (41.05)	OR 0.76 (95% CI 0.42-1.38)	0.370
Hypertension, n (%)	34 (17.89)	16 (16.84)	18 (18.95)	OR 0.87 (95% CI 0.41-1.82)	0.705
Ischemic heart disease, n (%)	34 (17.89)	18 (18.95)	16 (16.84)	OR 1.15 (95% CI 0.55-2.43)	0.705
Smoking, n (%)	73 (38.42)	40 (42.11)	33 (34.74)	OR 1.37 (95% CI 0.76-2.46)	0.296
COPD, n (%)	57 (30.00)	31 (32.63)	26 (27.37)	OR 1.29 (95% CI 0.69-2.40)	0.429

Baseline comparison showed no statistically significant between-group difference for sex, diabetes, hypertension, ischemic heart disease, smoking, or COPD, with all p-values above 0.05. The observed odds ratios for these baseline variables remained close to unity, supporting approximate demographic and comorbidity comparability. However, age differed significantly between groups (p=0.033), and this imbalance, together with the later ICU imbalance, should be considered when interpreting outcome differences.

Table 2. Clinical Outcomes by Study Group

Outcome	Total (n=190)	PCT Group (n=95)	Standard Care Group (n=95)	Effect Estimate	p-value
ICU admission, n (%)	36 (18.95)	26 (27.37)	10 (10.53)	OR 3.20 (95% CI 1.45-7.10)	0.003
Length of stay, days, median (IQR)	7.00 (5.00-10.00)	8.00 (6.00-12.00)	6.00 (5.00-8.00)	Median difference: +2.00 days	<0.001
Duration of antibiotic use, days, median (IQR)	7.00 (5.00-10.00)	7.00 (6.00-12.00)	7.00 (5.00-9.00)	Median difference: 0.00 days; upper-quartile difference: +3.00 days	0.012

The outcome analysis demonstrated a substantially higher acute-care burden in the procalcitonin-guided arm. ICU admission occurred in 27.37% of patients in the PCT group compared with 10.53% in the standard-care group, corresponding to more than threefold higher odds of ICU use (OR 3.20, 95% CI 1.45-7.10; p=0.003). Median hospital stay was also longer in the PCT group, increasing from 6.00 days in standard care to 8.00 days with PCT-guided management, an absolute difference of 2.00 days (p<0.001). Although the median duration of antibiotic therapy was 7.00 days in both groups, the distribution was shifted upward in the PCT group, as reflected by a higher lower quartile (6 vs 5 days) and higher upper quartile (12 vs 9 days), with the between-group comparison remaining statistically significant (p=0.012). This pattern suggests that the observed antibiotic burden difference was driven not by central tendency alone but by a heavier upper-end treatment duration in the PCT-guided cohort.

Table 3. Derived Comparative Burden Indicators for Clinical Interpretation

Derived Indicator	PCT Group	Standard Care Group	Relative Burden of PCT Group
ICU admission rate (%)	27.37	10.53	2.60-fold
Median LOS (days)	8.00	6.00	1.33-fold
Upper-quartile LOS (days)	12.00	8.00	1.50-fold
Median antibiotic duration (days)	7.00	7.00	1.00-fold
Upper-quartile antibiotic duration (days)	12.00	9.00	1.33-fold

Derived comparative indicators further clarified the direction of effect. Relative to standard care, the PCT-guided group demonstrated a 2.60-fold higher ICU admission rate, a 1.33-fold higher median hospital stay, a 1.50-fold higher upper-quartile hospital stay, and a 1.33-fold higher upper-quartile antibiotic duration. These derived gradients show that the between-group difference was clinically concentrated among patients at the more severe end of care utilization and treatment exposure, rather than being limited to a simple median shift.

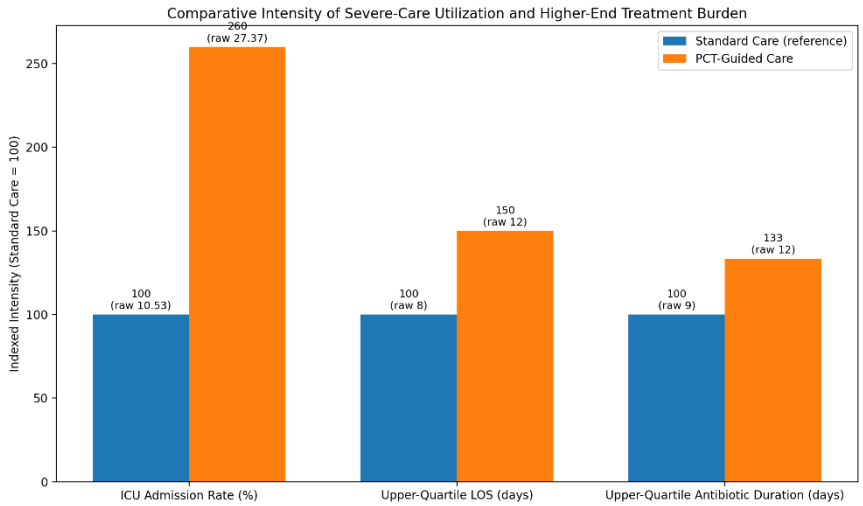

Figure 1 Comparative Intensity of Severe-Care Utilization and Higher-End Treatment Burden

The procalcitonin-guided group showed a markedly higher severe-care and higher-end treatment burden than standard care, with ICU admission intensity reaching 260% of the standard-care reference (27.37% vs 10.53%), upper-quartile length of stay rising to 150% of the reference (12 vs 8 days), and upper-quartile antibiotic duration increasing to 133% of the reference (12 vs 9 days). This pattern indicates that the excess burden associated with the PCT-guided cohort was most pronounced in the more severe and resource-intensive segment of the population, supporting the interpretation that case

severity imbalance likely contributed materially to the longer hospitalization and extended antibiotic exposure observed in that group.

DISCUSSION

The present study evaluated whether procalcitonin-guided antibiotic therapy influenced antibiotic exposure and short-term hospital outcomes among patients with lower respiratory tract infection in a tertiary care setting. Contrary to the original expected stewardship benefit, patients managed in the procalcitonin-guided arm demonstrated significantly greater healthcare utilization, with higher ICU admission frequency, longer hospital stay, and a statistically significant upward shift in antibiotic-duration distribution compared with standard care. These findings require careful interpretation because the procalcitonin-guided group also appeared to have a clinically more severe baseline profile, most notably reflected by the markedly higher ICU admission rate of 27.37% compared with 10.53% in the standard-care group. This difference strongly suggests that the observed prolongation in hospital stay and antibiotic exposure may have been driven, at least in part, by greater illness severity rather than by a harmful effect of procalcitonin-guided decision-making itself.

The broader literature on procalcitonin-guided therapy in respiratory infection has remained heterogeneous. Several studies have reported that biomarker-guided algorithms reduce antibiotic initiation or shorten treatment duration without compromising safety, particularly when used within structured stewardship frameworks and in clinically stable patients with acute respiratory tract infections (6,7,12,13). Townsend et al. observed reduced antibiotic exposure in lower respiratory tract infection with implementation of a procalcitonin-guided strategy, while meta-analytic evidence has also supported fewer antibiotic days and lower initiation rates in selected populations (6,7). Similarly, patient-level pooled analyses have suggested that procalcitonin-guided management may reduce mortality in acute respiratory infections when embedded in protocols with high clinician adherence (13). However, these beneficial findings have not been universal. Huang et al. reported no meaningful difference in antibiotic duration between procalcitonin-guided and usual care groups, despite a large randomized design, and other implementation studies have shown variable or attenuated benefit depending on treatment setting and uptake of the algorithm (8,11). The inconsistency across studies indicates that procalcitonin is not a self-executing intervention; its effectiveness depends substantially on contextual factors such as severity distribution, clinician confidence in the assay, timing of repeat testing, threshold adherence, and the surrounding antimicrobial stewardship culture (5,10,11,17,18).

The findings of the present study align more closely with reports showing limited or even paradoxical benefit from procalcitonin-based management under real-world conditions. In this dataset, the median antibiotic duration was numerically identical between groups at 7 days, but the interquartile distribution was shifted upward in the procalcitonin-guided arm, with the upper quartile extending to 12 days compared with 9 days in standard care. This suggests that the excess antibiotic burden was concentrated among patients with more prolonged or complex clinical courses rather than being uniformly distributed across the cohort. A similar pattern was observed for hospital stay, where the median length of stay was 8 days in the procalcitonin-guided group versus 6 days in standard care, with the upper quartile extending to 12 versus 8 days. These findings indicate that the procalcitonin-guided cohort contained a greater proportion of high-resource, prolonged-care cases, further reinforcing the possibility of residual confounding by disease severity. In pragmatic hospital settings, clinicians may also be reluctant to discontinue antibiotics solely on the basis of biomarker decline when patients are clinically unstable, have extensive radiographic involvement, or require critical care support. Under such circumstances, procalcitonin may serve more as an adjunctive marker than as a decisive stewardship tool (4,5,9,18).

Another important explanation for the divergent findings may lie in operational implementation. Procalcitonin-guided therapy is most effective when linked to prespecified initiation and discontinuation

thresholds, repeated measurements at clinically appropriate intervals, and strong adherence by treating physicians. Even where a protocol exists, real-time clinical judgment often overrides biomarker guidance, especially in tertiary hospitals managing referred or unstable patients. The present study was conducted at a military tertiary care institution, where case acuity may have been higher than in community-based respiratory infection cohorts. This is supported by the ICU imbalance observed between study arms. Hospital-level factors, including disease severity mix, referral pathways, clinician prescribing norms, and local thresholds for admission or ICU transfer, may therefore have materially influenced the apparent association between procalcitonin-guided care and worse short-term outcomes (14,15). In this context, procalcitonin may have been preferentially applied in patients who were already perceived to be more clinically concerning, which would bias group comparisons in the absence of randomization or statistical adjustment.

The study adds useful local evidence because data from Pakistan on biomarker-guided antibiotic stewardship in lower respiratory tract infection remain sparse. This is important because evidence generated in high-resource settings cannot automatically be generalized to hospitals operating under different patient volumes, referral burdens, diagnostic turnaround times, and prescribing cultures. The present results therefore contribute a contextually relevant signal: procalcitonin-guided management in routine tertiary care did not demonstrate the expected reduction in antibiotic burden and was associated with longer hospital stay within this observational comparison. However, the interpretation must remain circumspect. Since the groups were not randomized and no adjusted multivariable model was reported, the findings should not be taken to mean that procalcitonin-guided therapy intrinsically prolongs treatment. Rather, the results suggest that in this setting, implementation of procalcitonin guidance did not overcome the clinical realities of a more severe patient subset and may have been confounded by selective use in sicker individuals.

Several limitations should be emphasized. First, the observational, non-randomized design limits causal inference. Second, purposive sampling and clinician-directed allocation to treatment pathways increase the possibility of selection bias. Third, the marked difference in ICU admission frequency between groups indicates probable baseline severity imbalance that may have confounded both length of stay and antibiotic duration. Fourth, no pathogen-specific or etiologic stratification was presented, although the diagnostic performance and stewardship utility of procalcitonin may differ across bacterial pneumonia, viral infection, and acute exacerbations of chronic obstructive pulmonary disease (9). Fifth, the analysis was based primarily on unadjusted group comparisons, so residual confounding from age, comorbidity burden, and disease severity cannot be excluded. Finally, the study was performed at a single center with a modest sample size, which may limit generalizability. Despite these constraints, the study highlights an important implementation gap and supports the need for larger multicenter randomized or analytically adjusted prospective studies in comparable low- and middle-income healthcare settings. Such work should incorporate standardized severity indices, serial procalcitonin adherence metrics, and regression-based adjustment to distinguish the effect of the biomarker-guided strategy from the effect of underlying disease acuity.

CONCLUSION

In this tertiary-care observational cohort of patients with lower respiratory tract infection, procalcitonin-guided antibiotic management was associated with higher ICU admission frequency, longer hospital stay, and a statistically significant shift toward longer antibiotic exposure compared with standard clinician-directed care; however, these findings should be interpreted cautiously because the procalcitonin-guided group appeared to include a more clinically severe case mix, making residual confounding a likely contributor to the observed differences. Rather than demonstrating a definitive disadvantage of procalcitonin-guided therapy, the study suggests that its real-world effectiveness in resource-constrained hospital settings may depend heavily on baseline patient severity, protocol

adherence, and local stewardship practices, warranting larger multicenter studies with stronger control of confounding.

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