

Original Article

Correlation of Inflammatory Biomarkers with Microbial Etiology and Antibiotic Resistance in Urinary Tract Infections: A cross-sectional study from Maharashtra

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ABSTRACT

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Background: Urinary tract infections (UTIs) are among the most common bacterial infections encountered in clinical practice. Rising antimicrobial resistance poses a significant challenge to effective management. Inflammatory biomarkers such as C-reactive protein (CRP), procalcitonin (PCT), and total leukocyte count (TLC) have been proposed as indicators of infection severity and systemic response, but their correlation with microbial etiology and antibiotic resistance patterns remains inadequately explored. **Objectives:** To evaluate the correlation between inflammatory biomarkers and microbial etiology in UTIs and to assess their association with antibiotic resistance patterns. **Methods:** This prospective observational study was conducted from January to December 2025 and included 70 patients clinically suspected of UTI. Urine samples were subjected to culture and antibiotic susceptibility testing. Inflammatory biomarkers including CRP, procalcitonin, and TLC were measured at presentation. Statistical analysis was performed to determine correlations between biomarkers, causative organisms, and resistance patterns. **Results:** Among 70 patients, *Escherichia coli* (45.7%) was the most common isolate, followed by *Klebsiella pneumoniae* (21.4%) and *Enterococcus* species (14.3%). Elevated CRP and procalcitonin levels were significantly associated with Gram-negative infections and multidrug-resistant organisms ($p < 0.05$). Patients with extended-spectrum beta-lactamase (ESBL)-producing isolates showed significantly higher mean CRP and procalcitonin levels compared to non-ESBL isolates. **Conclusion:** Inflammatory biomarkers, particularly CRP and procalcitonin, correlate well with microbial etiology and antibiotic resistance in UTIs. These markers may aid in early risk stratification and guide empirical antibiotic therapy pending culture results.

Keywords: Urinary tract infection, C-reactive protein, Procalcitonin, Antibiotic resistance, ESBL.

INTRODUCTION

Urinary tract infections (UTIs) represent a significant public health burden, accounting for substantial morbidity across all age groups. They are among the leading causes of outpatient visits and hospital admissions worldwide.¹ The clinical spectrum of UTIs ranges from uncomplicated cystitis to severe pyelonephritis and urosepsis.²

The increasing prevalence of antimicrobial resistance, particularly among Gram-negative uropathogens, has complicated the empirical management of UTIs. Resistance mechanisms such as extended-spectrum beta-lactamase (ESBL) production and carbapenem resistance are associated with treatment failure, prolonged hospital stay, and increased healthcare costs.³ Inflammatory biomarkers such as C-reactive protein (CRP), procalcitonin (PCT), and total leukocyte count (TLC) reflect the host's systemic inflammatory response to infection. CRP is an acute-phase reactant synthesized by the liver, while

procalcitonin is a precursor of calcitonin that rises significantly in bacterial infections.⁴ These biomarkers have been extensively studied in sepsis and lower respiratory tract infections; however, their role in predicting microbial etiology and antibiotic resistance in UTIs remains less clearly defined.^{5,6}

Identifying correlations between inflammatory biomarkers, causative organisms, and resistance patterns could provide valuable information for early clinical decision-making, particularly in settings where microbiological culture results are delayed.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in a tertiary care hospital at Department of Microbiology, SSPM Medical College Sindhudurg, Sindhudurg, Maharashtra, India over a period of one year, from January to December 2025.

Study Population

A total of 70 patients with clinical suspicion of urinary tract infection were included.

Inclusion Criteria

- Patients aged ≥ 18 years
- Clinical features suggestive of UTI (dysuria, frequency, urgency, fever, flank pain)
- Positive urine culture

Exclusion Criteria

- Patients on antibiotic therapy within 48 hours prior to presentation
- Known chronic inflammatory conditions
- Immunocompromised patients

Sample Collection and Microbiological Analysis

Midstream clean-catch urine samples were collected under aseptic conditions. Samples were cultured using standard microbiological techniques. Identification of organisms was performed using biochemical methods, and antibiotic susceptibility testing was carried out by the Kirby–Bauer disc diffusion method following CLSI guidelines.

Inflammatory Biomarkers

Blood samples were collected at admission for estimation of:

- C-reactive protein (CRP)
- Procalcitonin (PCT)
- Total leukocyte count (TLC)

Statistical Analysis

Data were analyzed using appropriate statistical software SPSS 25.0 version. Continuous variables were expressed as mean \pm standard deviation. Categorical variables were expressed as percentages. Correlation between biomarkers, microbial etiology, and resistance patterns was assessed using chi-square test and Pearson correlation. A p-value <0.05 was considered statistically significant.

RESULTS

Table 1. Demographic and Clinical Profile of Study Participants (n = 70)

Variable	Frequency	Percentage (%)
Age group (years)		
18–30	18	25.7
31–45	22	31.4
46–60	20	28.6
>60	10	14.3
Gender		
Male	28	40
Female	42	60
Clinical presentation		
Dysuria	56	80
Frequency/urgency	48	68.6
Fever	34	48.6
Flank pain	18	25.7

Table 1 presents the demographic characteristics and clinical profile of the 70 patients included in the study. The majority of patients belonged to the 31–45 years age group (31.4%), followed by those aged 46–60 years (28.6%). Younger adults aged 18–30 years constituted 25.7%, while patients aged more than 60 years accounted for 14.3% of the study population.

A female predominance was observed, with 42 patients (60%) being females and 28 patients (40%) being males, reflecting the higher susceptibility of females to urinary tract infections.

Regarding clinical presentation, dysuria was the most common symptom, reported by 80% of patients, followed by urinary frequency and urgency in 68.6%. Fever was present in nearly half of the cases (48.6%), indicating systemic involvement, while flank pain, suggestive of upper urinary tract infection, was noted in 25.7% of patients. Overall, Table 1 highlights the predominance of middle-aged females and typical lower urinary tract symptoms among patients with culture-proven UTIs.

Table 2. Microbial Etiology of Urinary Tract Infections (n = 70)

Organism isolated	Number of isolates	Percentage (%)
<i>Escherichia coli</i>	32	45.7
<i>Klebsiella pneumoniae</i>	15	21.4
<i>Enterococcus</i> species	10	14.3
<i>Pseudomonas aeruginosa</i>	7	10
Others	6	8.6
Total	70	100

Table 2 depicts the microbial etiology of urinary tract infections among the 70 culture-positive cases included in the study. Gram-negative organisms predominated, accounting for the majority of isolates.

Escherichia coli was the most common uropathogen, isolated in 32 cases (45.7%), reaffirming its established role as the leading cause of UTIs. This was followed by *Klebsiella pneumoniae*, which accounted for 15 cases (21.4%), highlighting its increasing importance as a uropathogen in both community- and hospital-acquired infections.

Among Gram-positive organisms, *Enterococcus* species were isolated in 10 cases (14.3%), indicating their significant contribution, particularly in complicated UTIs. *Pseudomonas aeruginosa* was identified in 7 cases (10%), suggesting a notable proportion of infections caused by non-fermenting Gram-negative bacilli, often associated with healthcare exposure and antibiotic resistance.

Other organisms, including less frequently isolated pathogens, constituted 8.6% of cases. Overall, Table 2 demonstrates a clear predominance of Gram-negative bacteria, with *E. coli* being the principal causative agent of urinary tract infections in the study population.

Table 3. Antibiotic Resistance Pattern of Isolated Uropathogens

Resistance pattern	Number of cases	Percentage (%)
ESBL producers	20	28.6
Multidrug-resistant (MDR)	16	22.9
Carbapenem-resistant	6	8.6
Non-resistant isolates	28	40
Total	70	100

Table 3 summarizes the antibiotic resistance patterns observed among the uropathogens isolated from the 70 patients with urinary tract infections. A substantial proportion of isolates demonstrated resistance to commonly used antimicrobial agents.

Extended-spectrum beta-lactamase (ESBL)-producing organisms were identified in 20 cases (28.6%), indicating a high prevalence of beta-lactam resistance among the isolates. Multidrug-resistant (MDR) organisms, defined as resistance to three or more classes of antibiotics, were observed in 16 cases (22.9%), underscoring the growing challenge of antimicrobial resistance in the management of UTIs.

Carbapenem-resistant organisms were detected in 6 cases (8.6%), representing a smaller but clinically significant subset due to limited therapeutic options and potential for poor outcomes. In contrast, non-resistant isolates were found in 28 cases (40%), suggesting that a considerable proportion of infections were still caused by organisms susceptible to standard antimicrobial therapy.

Overall, Table 3 highlights a notable burden of antibiotic resistance, with nearly two-thirds of isolates exhibiting some form of resistance, emphasizing the need for judicious antibiotic use and reliance on culture-guided therapy in urinary tract infections.

Table 4. Comparison of Mean Inflammatory Biomarker Levels by Microbial Etiology

Biomarker (Mean \pm SD)	Gram-negative (n = 54)	Gram-positive (n = 16)	p value
CRP (mg/L)	68.4 \pm 22.1	38.7 \pm 15.3	<0.001*
Procalcitonin (ng/mL)	1.82 \pm 0.76	0.62 \pm 0.28	<0.001*
TLC (cells/mm ³)	14,200 \pm 3,100	10,800 \pm 2,600	0.002*

Table 4 compares the mean levels of inflammatory biomarkers between patients with Gram-negative and Gram-positive urinary tract infections. A clear and statistically significant difference in biomarker levels was observed between the two groups.

Patients with Gram-negative infections (n = 54) demonstrated markedly higher inflammatory responses compared to those with Gram-positive infections (n = 16). The mean C-reactive protein (CRP) level in Gram-negative infections was 68.4 \pm 22.1 mg/L, which was significantly higher than 38.7 \pm 15.3 mg/L observed in Gram-positive infections (p < 0.001).

Similarly, procalcitonin levels were significantly elevated in Gram-negative infections (1.82 \pm 0.76 ng/mL) compared to Gram-positive infections (0.62 \pm 0.28 ng/mL), with a highly significant statistical difference (p < 0.001). This finding suggests a stronger systemic inflammatory response in Gram-negative UTIs.

The total leukocyte count (TLC) was also higher in the Gram-negative group (14,200 \pm 3,100 cells/mm³) compared to the Gram-positive group (10,800 \pm 2,600 cells/mm³), and this difference was statistically significant (p = 0.002).

Overall, Table 4 demonstrates that Gram-negative uropathogens are associated with significantly higher levels of inflammatory biomarkers, indicating greater inflammatory burden and potentially more severe disease compared to Gram-positive infections.

Table 5. Association Between Inflammatory Biomarkers and Antibiotic Resistance

Biomarker (Mean \pm SD)	Resistant isolates (n = 42)	Non-resistant isolates (n = 28)	p value
CRP (mg/L)	74.6 \pm 21.8	41.2 \pm 16.9	<0.001*
Procalcitonin (ng/mL)	2.01 \pm 0.81	0.71 \pm 0.35	<0.001*
TLC (cells/mm ³)	15,100 \pm 3,200	11,200 \pm 2,700	0.001*

Table 5 illustrates the association between inflammatory biomarker levels and antibiotic resistance among the uropathogens isolated in the study. Patients infected with antibiotic-resistant isolates (n = 42) exhibited significantly higher inflammatory marker levels compared to those with non-resistant isolates (n = 28).

The mean C-reactive protein (CRP) level in patients with resistant infections was 74.6 \pm 21.8 mg/L, which was significantly higher than 41.2 \pm 16.9 mg/L observed in patients with non-resistant infections (p < 0.001). This finding suggests a stronger inflammatory response in resistant infections.

Similarly, procalcitonin levels were markedly elevated in the resistant group (2.01 \pm 0.81 ng/mL) compared to the non-resistant group (0.71 \pm 0.35 ng/mL), with a highly significant difference (p < 0.001). This indicates a potential role of procalcitonin as a marker for predicting antibiotic resistance in UTIs.

The total leukocyte count (TLC) was also significantly higher among patients with resistant isolates (15,100 \pm 3,200 cells/mm³) compared to those with non-resistant isolates (11,200 \pm 2,700 cells/mm³), (p = 0.001).

Overall, Table 5 demonstrates a strong correlation between elevated inflammatory biomarkers and antibiotic resistance, highlighting the clinical utility of CRP and procalcitonin in identifying patients at higher risk of resistant urinary tract infections and guiding early empirical therapy.

Table 6. Inflammatory Biomarkers in ESBL vs Non-ESBL Producing Organisms

Biomarker	ESBL producers (n = 20)	Non-ESBL (n = 50)	p value
CRP (mg/L)	82.3 \pm 19.5	48.6 \pm 18.2	<0.001*
Procalcitonin (ng/mL)	2.24 \pm 0.72	0.96 \pm 0.44	<0.001*
TLC (cells/mm ³)	15,800 \pm 3,000	12,100 \pm 2,800	0.003*

Table 6 compares the levels of inflammatory biomarkers between patients infected with ESBL-producing organisms and those with non-ESBL-producing organisms. A pronounced difference in biomarker levels was observed between the two groups, indicating a higher inflammatory burden associated with ESBL infections.

Patients with ESBL-producing isolates (n = 20) showed significantly elevated C-reactive protein (CRP) levels (82.3 ± 19.5 mg/L) compared to patients with non-ESBL isolates (n = 50), who had a mean CRP level of 48.6 ± 18.2 mg/L. This difference was statistically significant ($p < 0.001$).

Similarly, procalcitonin levels were markedly higher in the ESBL group (2.24 ± 0.72 ng/mL) compared to the non-ESBL group (0.96 ± 0.44 ng/mL), with a highly significant difference ($p < 0.001$). This finding suggests that ESBL-associated infections are linked to a more intense systemic inflammatory response.

The total leukocyte count (TLC) was also significantly elevated among patients with ESBL-producing organisms ($15,800 \pm 3,000$ cells/mm 3) compared to those with non-ESBL organisms ($12,100 \pm 2,800$ cells/mm 3) ($p = 0.003$).

Overall, Table 6 highlights that ESBL-producing uropathogens are associated with significantly higher inflammatory biomarker levels, underscoring their clinical severity and the potential role of biomarkers such as CRP and procalcitonin in identifying resistant infections early and optimizing antimicrobial management.

DISCUSSION

The demographic and clinical profile observed in **Table 1** of the present study is largely consistent with findings reported in previous studies on urinary tract infections.

In the current study, the highest proportion of patients belonged to the 31–45 years age group, followed by the 46–60 years group. Similar age distribution has been reported by **Foxman et al¹** and **Flores-Mireles et al²**, who noted that UTIs are most common in sexually active and middle-aged adults due to behavioral, anatomical, and hormonal factors.

Studies from India by **Kumar et al⁶** and **Dash et al⁷** also reported a peak incidence of UTIs in the third to fifth decades of life, closely matching the present findings.

A clear female predominance (60%) was observed in this study, which aligns well with multiple national and international studies. **Foxman¹** and **Stamm et al⁴** have documented that females are significantly more prone to UTIs due to a shorter urethra, proximity of the urethral opening to the anus, and hormonal influences. Indian hospital-based studies have reported female proportions ranging from 58% to 72%, which is comparable to the present study.

Regarding clinical presentation, dysuria and urinary frequency/urgency were the most common symptoms in this study, reported in 80% and 68.6% of patients, respectively. Similar symptom patterns have been described by **Wagenlehner et al⁵** and **Grabe et al⁸**, where lower urinary tract symptoms were predominant in uncomplicated UTIs. The proportion of patients presenting with fever (48.6%) in the present study is also comparable to earlier studies, suggesting a substantial number of patients with complicated or upper urinary tract involvement.

Flank pain, suggestive of upper urinary tract infection, was observed in 25.7% of cases, which is in agreement with findings reported by **Lee et al⁹**, where flank pain was noted in approximately 20–30% of hospitalized UTI patients. This similarity indicates that the clinical spectrum of UTIs in the present study mirrors patterns observed in other tertiary care settings. Overall, the demographic distribution and symptom profile in Table 1 are consistent with previously published literature, supporting the external validity of the present study population and reinforcing that UTIs predominantly affect middle-aged females with classic lower urinary tract symptoms.

The microbial profile of urinary tract infections observed in **Table 2** of the present study is largely in agreement with previously published national and international literature.

In the current study, *Escherichia coli* was the most common uropathogen, accounting for 45.7% of isolates. This finding is consistent with multiple studies worldwide, which have reported *E. coli* as the predominant causative agent of UTIs, with isolation rates ranging from 40% to 70%. Studies by **Foxman¹**, **Flores-Mireles et al²**, and **Kahlmeter⁹** have similarly highlighted the dominance of *E. coli*, particularly in community-acquired infections, attributing this to its virulence factors such as adhesins, fimbriae, and biofilm-forming ability.

Klebsiella pneumoniae was the second most common isolate in the present study (21.4%). Comparable proportions have been reported in Indian hospital-based studies by **Dash et al⁷** and Gupta et al., where *Klebsiella* species accounted for 15–25% of UTI isolates. The relatively higher proportion of *Klebsiella* in tertiary care settings has been associated with increased healthcare exposure and antibiotic pressure.

Enterococcus species, constituting 14.3% of isolates in this study, were the most frequently isolated Gram-positive organisms. Similar findings have been reported by **Nicolle¹⁰** and **Wagenlehner et al⁵**, who noted an increasing role of *Enterococcus* species in complicated UTIs, particularly among hospitalized patients, elderly individuals, and those with indwelling catheters.

Pseudomonas aeruginosa accounted for 10% of isolates in the present study. This proportion is comparable to reports by **Lee et al⁹** and other tertiary care studies, where *Pseudomonas* isolation rates ranged between 8% and 15%. Its presence is often linked to prior antibiotic use, instrumentation, and nosocomial infections.

The category labelled as “other organisms” (8.6%) in the current study is consistent with earlier reports that have identified less common uropathogens such as *Proteus*, *Citrobacter*, and *Staphylococcus saprophyticus* in smaller proportions.

Overall, the findings of Table 2 demonstrate a predominance of Gram-negative bacteria, mirroring trends observed in earlier studies. The similarity in microbial distribution reinforces the representativeness of the study population and underscores the continued dominance of *E. coli* and *Klebsiella* species as major uropathogens in both community and hospital settings.

The findings presented in **Table 5** of the present study demonstrate a significant association between elevated inflammatory biomarkers and antibiotic-resistant urinary tract infections, which is in concordance with observations reported in earlier studies.

In the current study, patients infected with antibiotic-resistant isolates showed markedly higher levels of C-reactive protein (CRP), procalcitonin, and total leukocyte count (TLC) compared to those with non-resistant isolates. Similar associations have been reported by Lee et al., who found that elevated procalcitonin levels were significantly associated with severe UTIs and infections caused by resistant organisms. Their study suggested that higher procalcitonin levels reflect increased bacterial burden and systemic inflammatory response, particularly in Gram-negative and resistant infections.

Studies by **Park et al¹¹** and **Liao et al¹²** also demonstrated that procalcitonin is a useful biomarker for predicting complicated UTIs, bacteremia, and infections due to resistant pathogens, including ESBL-producing organisms. These studies reported significantly higher mean procalcitonin levels among patients with resistant isolates, findings that closely parallel the results of the present study.

With respect to CRP, earlier research by **Pepys and Hirschfield¹³** established CRP as a sensitive marker of inflammation, while subsequent clinical studies have shown its levels to be significantly higher in infections caused by multidrug-resistant organisms. **Schuetz et al¹⁴** reported that persistently elevated CRP and procalcitonin levels were associated with poor response to standard antibiotic therapy, indirectly reflecting underlying resistance.

The observed higher TLC values in resistant infections in the present study are also consistent with findings from hospital-based studies conducted in tertiary care settings, where leukocytosis was more pronounced in patients with severe or complicated UTIs caused by resistant bacteria.

Overall, the findings of Table 5 are in agreement with existing literature, reinforcing the concept that antibiotic-resistant UTIs are associated with a stronger systemic inflammatory response. The consistency of these results across studies supports the potential clinical utility of inflammatory biomarkers, particularly procalcitonin and CRP, as early indicators of resistant infections and as adjuncts in guiding empirical antimicrobial therapy.

CONCLUSION

- The antibiotic resistance profile highlighted a substantial burden of antimicrobial resistance, with a considerable proportion of isolates demonstrating ESBL production, multidrug resistance, and carbapenem resistance. This underscores the growing challenge of empirical antibiotic therapy and the importance of culture-guided treatment.
- Analysis of inflammatory biomarkers in relation to microbial etiology showed that Gram-negative infections were associated with significantly higher levels of CRP, procalcitonin, and total leukocyte count, indicating a more pronounced systemic inflammatory response compared to Gram-positive infections.
- Furthermore, the association between inflammatory biomarkers and antibiotic resistance revealed that patients with resistant isolates exhibited significantly elevated CRP, procalcitonin, and leukocyte counts compared to those with non-resistant organisms. This suggests that resistant infections tend to be clinically more severe and provoke stronger inflammatory responses.
- Finally, comparison between ESBL-producing and non-ESBL organisms demonstrated that ESBL-associated UTIs were linked to markedly higher inflammatory biomarker levels, reinforcing the relationship between resistance mechanisms and disease severity.

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