



## Original Article

# Utility of Procalcitonin and C-reactive protein in diagnosing patients with urinary tract infections

Authors

**Dr Virendrasinh Bhati<sup>1</sup>, Dr Smita Patil<sup>2\*</sup>**

<sup>1</sup>Junior Resident, <sup>2</sup>Head of Unit

<sup>1,2</sup>Dept of General Medicine, D Y Patil University School of Medicine, Nerul, Navi Mumbai-400706, India

\*Corresponding Author

**Dr Smita Patil**

Dept of General Medicine, D Y Patil University School of Medicine, Nerul, Navi Mumbai-400706, India

## Abstract

**Introduction:** Urinary tract infection (UTI) is the inflammatory response of urothelium to bacterial invasion, is one of the most common infections in all ages of life. In this study, we aim to compare the levels of biomarkers among patients positive for UTI against those without UTI.

**Methodology:** This single centre, retrospective study included patients aged 18 years or above, who presented to the Emergency Department of DY Patil Hospital, Navi Mumbai and was tested with urinalysis and had urine culture, blood cultures, and samples for blood test were taken within 24 hours from which biomarkers like procalcitonin (PCT) and C-reactive protein (CRP) were evaluated. PCT was measured by quantitative electrochemiluminescence immunoassay with a sensitivity of 0.02 ng/ml and CRP was determined by quantitative enzyme immunoassay with a sensitivity of 1mg/l. All statistical tests were 2-tailed and a  $p < 0.05$  met statistical significance.

**Results:** During the study period 247 patients were included, of which 62 patients were positive for UTI. We observed a significantly higher proportion of patients with previous history of UTI, urinary stones, fever and systolic blood pressure less than 90 mm of Hg among patients who were positive for UTI. We found higher PCT and CRP levels among patients with UTI ( $0.82 \pm 0.15$  ng/ml and  $110.4 \pm 12.8$  mg/L respectively) as compared to those negative for UTI ( $0.11 \pm 0.20$  and  $27.7 \pm 8.16$  respectively).

**Conclusions:** Serum procalcitonin and blood CRP measurements are non-invasive tests which can diagnose UTI in patients.

**Keywords:** Procalcitonin; C-reactive protein; Biomarkers; Urinary tract infection.

## Introduction

Urinary tract infection (UTI) is the inflammatory response of urothelium to bacterial invasion, is one of the most common infections in all ages of life.<sup>1</sup> Upper UTIs (ie, acute pyelonephritis) may lead to renal scarring, hypertension, and end-stage

renal disease. There is scarce data on the prevalence of UTIs, but it is known that approximately half of all women will experience UTI once in their lives and one fifth of these will become complicated.<sup>2</sup> Majority of cases are treated in the outpatient clinic, but a few have to

be triaged at home so as to identify those patients who would need hospitalization. Also emergency physician has to identify those patients with UTI who meet the criteria for severe sepsis, or septic shock, where the prompt recognition of accompanying bacteremia would need early administration of antibiotic therapy along with performing early urinary diversion in cases of complicated UTI, key aspects in the emergency treatment of these patients.<sup>3</sup>

Patients with associated bacteremia, especially in immunocompromised patients, the elderly, diabetic and those with many other risk factors have been found to have increased mortality.<sup>4</sup> Evaluating patients with UTI and waiting for culture reports constitutes a diagnostic challenge. Clinical manifestations are non-specific and more so in patients with multiple risk factors, which make such patients even more susceptible to complications. This is why physicians need useful and immediate tools to suspect and diagnose cases of UTI reliably. In this study, we aim to compare the levels of biomarkers among patients positive for UTI against those without UTI.

## Methodology

### Study design and sampling

This single centre, retrospective study included patients aged 18 years or above, who presented to the Emergency Department of DY Patil Hospital, Navi Mumbai and was tested with urinalysis and had urine culture, blood cultures, and samples for blood test were taken within 24 hours from which biomarkers like procalcitonin and C-reactive protein were evaluated. Patients who were pregnant, had a primary infection other than a UTI, past medical history of a thyroid disorder, spinal cord injury resulting in paralysis, immunocompromised condition, or kidney transplantation were excluded from the study. In patients who had a history of more than one episode of UTI during the study period, only the first episode was included. Medical records of patients fulfilling the inclusion criteria were reviewed in detail to determine whether the

patients had UTI or not. A positive diagnosis of UTI was defined as patients who were symptomatic and had a positive result on urine culture. Signs and symptoms of UTI were an acute onset of any of dysuria, hematuria, frequency, urgency, urinary retention, suprapubic pain. Positive urine culture in non-catheterized patients was defined as a single, clean-catch, voided urine specimen with one bacterial species isolated in a quantitative count  $\geq 10^5$  colony forming unit (cfu)/mL.<sup>5</sup> A positive urine culture in catheterized patients was defined as a single catheterized urine specimen with one bacterial species isolated in a quantitative count of  $\geq 10^3$  cfu/ML.<sup>5</sup> Patients were labeled as negative for UTI if they were asymptomatic or had negative urine cultures test. This study was approved by the institutional review board, and the need for informed consent was waived.

### Data Collection and Data Analysis

Patient related information was extracted from their medical records. Demographic information of the patients was recorded in a pre-designed case report form. Past medical history and clinical features at the time of admission in the emergency department were noted as well. Results of various haematological tests and urinalysis were noted. PCT was measured by quantitative electrochemiluminescence immunoassay with a sensitivity of 0.02 ng/ml and CRP was determined by quantitative enzyme immunoassay with a sensitivity of 1mg/l. Data were coded and analysed using SPSS version 25.0 (IBM Corp, 2017). Quantitative data were expressed as mean and standard deviation and qualitative by frequency and percentages. For comparison of patient variables in the positive UTI and negative UTI group, Chi-square or Fisher exact, Student's "t", and Mann-Whitney U tests were used as applicable. All statistical tests were 2-tailed and a  $p < 0.05$  met statistical significance.

### Results

During the study period 247 patients met the inclusion criteria for the study. Of these, 62

patients were positive for UTI. Table 1 describes the baseline demographic and clinical characteristics of the patients included in the study. The age and gender in both the groups of patients were similar. We observed a significantly higher proportion of patients with previous history of UTI, urinary stones, fever and systolic blood pressure less than 90 mm of Hg among patients who were positive for UTI. Frequency of patients with urinary catheterization, liver diseases, diabetes mellitus and heart diseases was higher among patients who were positive for UTI, however the difference from patients who were negative with UTI was not statistically significant. Table 2 describes the comparison of findings of

laboratory tests ordered for the patients. Proportion of patients with leucocytosis and thrombocytopenia was higher among those who were positive with UTI as compared to those without UTI. Similarly, urinalysis results revealed that frequency of patients with pyuria and positive nitrite test was significantly higher among patients with positive UTI. On comparing the means of biomarkers among the two patient groups (Table 3), it was found that procalcitonin and C-reactive protein levels were higher among patients with UTI ( $0.82 \pm 0.15$  ng/ml and  $110.4 \pm 12.8$  mg/L respectively) as compared to those negative for UTI ( $0.11 \pm 0.20$  and  $27.7 \pm 8.16$  respectively).

**Table 1** Distribution of patients according to their demographic and clinical characteristics

Variables	Positive urinary tract infection (n=62)	Negative urinary tract infection (n=185)	p value
Age (in years)	48.44 $\pm$ 10.5	52.19 $\pm$ 11.47	0.10
Female gender	37 (60%)	115 (62%)	0.81
Co-morbidities			
Previous urinary tract infection episodes	22 (35%)	39 (21%)	0.04
Urinary stones	07 (12%)	08 (04%)	0.03
Urinary catheterization	02 (03%)	02 (01%)	0.100
Liver diseases	07 (12%)	13 (07%)	0.91
Diabetes mellitus	13 (21%)	35 (19%)	0.08
Heart disease	11 (18%)	30 (16%)	0.08
Clinical characteristics			
Fever (higher than 38 degrees)	47 (76%)	94 (51%)	0.04
Systolic blood pressure less than 90 mm Hg	30 (49%)	30 (16%)	0.03

Numbers are either mean and standard deviation or frequency and percentages

**Table 2** Laboratory findings of patients included in the study

	Positive urinary tract infection (n=62)	Negative urinary tract infection (n=185)	p value
<b>Hematological tests</b>			
Leucocytosis ( $>12,000/\text{mm}^3$ )	38 (62%)	72 (39%)	0.04
Thrombocytosis ( $<1,00,000/\text{mm}^3$ )	37 (60%)	15 (08%)	0.02
<b>Urinalysis</b>			
Pyuria ( $\geq 6/\text{high power field}$ )	50 (81%)	63 (34%)	0.02
Positive nitrite	28 (45%)	22 (12%)	0.03

**Table 3** Average levels of biomarkers tested in the patients included in the study

Biomarkers*	Positive urinary tract infection (n=62)	Negative urinary tract infection (n=185)	p value
Procalcitonin (ng/ml)	$0.82 \pm 0.15$	$0.11 \pm 0.20$	0.02
C-reactive protein (mg/L)	$110.4 \pm 12.8$	$27.7 \pm 8.16$	0.03

\*all number are mean and standard deviation

## Discussion

Patients who were positive with UTI had a significantly higher PCT and CRP levels. Immune response to UTI depends on numerous factors which also include the microbiological strain and expression of virulence factor.<sup>6</sup> It is due to this variability that biomarkers like PCT and CRP are sometimes not able to predict UTI consistently. de Jong et al demonstrated that PCT can thus be used to reduce the duration of antibiotic treatment rather than deciding if and when to start them.<sup>7</sup> For hospital acquired pneumonia, the Infectious Disease Society of America (IDSA) recommends using PCT along with the clinical criteria for stopping antibiotic coverage.<sup>8</sup> Additionally, guidelines by the Surviving Sepsis Campaign suggests that PCT levels can guide the physicians to discontinue antibiotic coverage in patients who have limited evidence of infection.<sup>9</sup> Furthermore, PCT has a very high predictability of diagnosing bacteremia by identifying possible cases of UTI in the emergency department.<sup>10</sup> This measuring PCT in emergency department may guide the doctor on deciding whether to discharge or to admit the patient, whether to request for urine and blood cultures, thus avoiding overloading the laboratory services. Such decisions are vital to the prognosis and evolution in the most severe patients.<sup>11</sup> Pediatric studies have demonstrated a similar sensitivity but higher specificity for PCT levels than CRP for predicting pyelonephritis.<sup>12</sup> Additionally, PCT levels have been found to correlate well with the extent of renal involvement and with renal scarring. Previously, a number of observational studies have successfully investigated the diagnostic potential of PCT in different types of infections. Problem with such conclusions is that a reliable PCT threshold is difficult to propose. For instance, circulating PCT levels were elevated among patients with infectious endocarditis as compared to non-infected patients.<sup>13</sup> Moreover, subclinical forms of various infectious diseases may be missed at a particular PCT cut-off point. For guiding antibiotic therapy in UTI, only one randomized

trial has tested the utility of PCT.<sup>14</sup> The algorithm devised for this trial recommended ceasing the use of antibiotics when PCT levels fell below 0.25 mg/ml or decreased by  $\geq 80\%$  of peak value and pyuria normalized. Patients who received PCT based algorithm had a significantly shorter antibiotic exposure by 3 days ( $p=0.011$ ).

Our current study has a few limitations. First, because this is a retrospective study, which potentially introduces bias due to missing patient information in the medical record. For instance, a positive UTI was based on the presence of positive urine culture and presence of symptoms suggestive of UTI. Completeness of the physician's note, which cannot be changed now, might have inaccurately labelled some patients as without UTI. Secondly, although only those patients were included in the study in which blood for PCT estimation was drawn within 24 hours of hospital presentation, prior antibiotic administration might have affected PCT levels in some patients. Lastly, clinical outcome of the patient at the time of discharge was not noted from the medical records and thus not analysed in this study.

## Conclusion

Serum procalcitonin and blood CRP measurements are non-invasive tests which can diagnose UTI in patients. PCT has already been validated in other infectious diseases like severe pneumonia and septic shock<sup>15</sup>, the results of our study highlight the effectiveness of using PCT as a diagnostic or prognostic tool in patients with UTI as well. Further, multicentric, randomized controlled trials are required to support our findings.

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**Conflict of interest:** None

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