
ORIGINAL ARTICLE**A study of serum procalcitonin albumin ratio in predicting urosepsis from febrile urinary tract infection***Juhi R^{*}, Rajathy Fathima S¹, Navin Kumar B K¹, Velammal P¹, Sujaya Menon¹**¹Department of General Medicine, PSG Institute of Medical Sciences and Research, Coimbatore-641004 (Tamil Nadu) India*

Abstract

Background: Urinary Tract Infection (UTI) is a common clinical entity and may progress to urosepsis with poor outcomes. Reliable biomarkers are essential for identifying high risk patients. *Aim and Objectives:* To determine the efficacy of the serum procalcitonin to albumin ratio as a predictor of urosepsis in patients with febrile urinary tract infection. *Material and Methods:* This one-year cross-sectional study at a tertiary healthcare institution in Tamil Nadu included 84 adults (≥ 18 years) with febrile UTI. Serum procalcitonin and albumin levels were measured, and their ratio calculated. SPSS v24 software was used to analyse the data, with $p < 0.05$ considered significant. Continuous data were summarised using Mean \pm SD and categorical variables as frequencies and percentages. Receiver Operating Characteristic (ROC) curve analyzed the predictive value. *Results:* Urosepsis was observed in 41% cases with mean age of 61.7 ± 18.3 years. Hypotension, elevated serum urea, creatinine, procalcitonin, procalcitonin/albumin ratio, and leukocyte count ($p < 0.05$) were significantly associated with urosepsis. ROC analysis showed excellent discrimination for procalcitonin and procalcitonin/albumin ratio, with area under the curve of 0.914 and 0.915, respectively ($p < 0.001$). The procalcitonin/albumin cut-off of 0.405 yielded 67.8% sensitivity and 96.2% specificity, highlighting it as a novel marker. *Conclusion:* The pro-calcitonin/albumin ratio shows strong potential as a marker for distinguishing febrile urinary tract infections from urosepsis. Incorporating this can enhance diagnostic accuracy.

Keywords: Biomarkers, procalcitonin, procalcitonin-to-albumin ratio, serum albumin, septic shock, urinary tract infections, complications

Introduction

Urinary Tract Infection (UTI) has a wide clinical spectrum that may lead to infections from the urethra to the kidneys. Clinical presentations [1-2] like fever, rigors, chills, nausea, vomiting, and renal angle tenderness, along with laboratory evidence of urine culture, blood tests substantiate UTI diagnosis. Febrile UTI (fUTI) [3-4] refers specifically to infections accompanied by fever [5], indicating more severe forms such as acute pyelonephritis or acute prostatitis. Acute Pyelonephritis (AP) is a condition where a UTI involves the kidney [6-7] whereas, urosepsis [6] is a sepsis in the urinary tract, which is a serious organ dysfunction resulting due

to inappropriate host immune responses to infections. As the pathogens causing AP are increasingly becoming resistant to current therapies, there is a growing need for clinical trials and epidemiological studies to evaluate the risk factors linked with resistant strains and to develop effective prevention strategies-particularly among individuals with a history of AP [8-13]. The prognosis of septic syndromes is influenced by the underlying diseases and severity of inflammatory response, reflected in the extent of organ dysfunction [14].

The prevalence of sepsis among Intensive Care Unit (ICU) patients [15] is significantly high, with

the majority presenting clinically or microbiologically documented infections, although certain subgroups may present without identifiable sources. Previous researches have implied 2 blood cultures detect approximately 80% of bloodstream infections, while three blood cultures detected 96% of episodes [16]. However, as the cultures take a longer time to report, new biomarkers [17] were essential for improving sepsis management. Procalcitonin was first reported to be elevated in infections [18-21] and a reliable predictor of bloodstream infections. Procalcitonin and C-Reactive Protein (CRP) [22] used in clinical practice have limited ability to differentiate bacterial sepsis from other inflammatory conditions. Serum albumin reduces during acute-phase infections, making it a marker of sepsis [23-24]. Patients with sepsis or severe bacterial or fungal infections have high procalcitonin levels. However, procalcitonin levels can vary in the initial course of the disease. However, researchers have suggested that the predictive performance of the test becomes relevant only when the illness advances [18]. To strengthen the diagnostic work-up, the procalcitonin-to-albumin ratio has been investigated as a potential early and reliable biomarker. According to a study by Luo et al. [25], this ratio can serve as a promising marker in discriminating fUTIs and urosepsis. Furthermore, elevated procalcitonin/albumin ratios could indicate an increased risk of progression to uroseptic shock and can reflect the severity. Early differentiation between them is crucial to prevent organ failure and reduce mortality. The study aimed to evaluate the effectiveness of procalcitonin-to-albumin ratio as a promising biomarker for discriminating fUTIs and urosepsis.

Material and Methods

The present study adopted a cross-sectional observational methodology over one year at a specialised care center in Tamil Nadu, India. This study enrolled 84 adult patients diagnosed with fUTI. fUTI was defined as an infection of the upper or lower urinary tract accompanied by fever and chills. Patients who met the inclusion criteria were consecutively recruited from both outpatient and inpatient departments. Individuals aged 18 years or older who presented with fever and had a UTI confirmed by urine culture were eligible for inclusion. Patients younger than 18 years, as well as those with decompensated chronic liver disease or chronic kidney disease, were excluded from the study. Individuals with fUTI was diagnosed to have urosepsis when Quick Sequential Organ Failure Assessment (qSOFA) score was ≥ 2 [26].

Ethical approval for the study was secured from the Institutional Ethics Committee (Reference Number 23/304) prior to commencement. All study participants gave a written informed consent. Comprehensive history elicitation, physical examination, and laboratory investigations were performed. Serum procalcitonin and albumin levels were measured, and the procalcitonin-to-albumin ratio was computed. Efforts were made to reduce bias by careful sample selection and by considering potential confounders such as age, comorbidities, lactate levels, and qSOFA scores. The formula $n = 4pq/d^2$ was used to calculate the required sample size assuming a sensitivity of 84% for the procalcitonin-to-albumin ratio in predicting urosepsis and expecting 10% non-response, the final sample size consisted of 84 patients. Descriptive statistical analysis was employed to describe patient characteristics and laboratory values. Continuous parameters were summarised as means along with

Standard Deviation (SD), and categorical variables as frequency and percentages. Quantitative data were expressed as median or mean along with standard deviations depending on their distribution. Data were tabulated in Microsoft Excel and analyzed using the Statistical Package for the Social Sciences version 24. Receiver Operating Curve (ROC) analysis was performed to assess the predictive validity of the procalcitonin-to-albumin ratio. Statistically significant p-value was <0.05 .

Results

The study included 90 cases of UTI, of which 37 were diagnosed with urosepsis and 53 with fUTI. Clinical profile and baseline characteristics are detailed in Table 1 including laboratory test results, and clinical presentations. It also presents the overall mean \pm SD values of serum procalcitonin, albumin, and their ratio across the study population. Among the clinical presentations, most of them exhibited common UTI symptoms, such as fever (74.4%) and burning micturition (71.1%). Laboratory parameters, including serum urea, creatinine, procalcitonin, procalcitonin/albumin ratio, and

leukocyte count, demonstrated higher mean values in urosepsis patients. The baseline characteristics indicate that predominant proportion belonged to the geriatric age group, with a slightly higher proportion of female participants. Collectively, the study findings highlight the role of laboratory markers in distinguishing fUTI from urosepsis, with fever and burning micturition being the commonly reported clinical features at presentation. The study participants were evaluated using the qSOFA score (≥ 2), 29% were diagnosed with urosepsis while 71% had fUTI as depicted in Figure 1.

Based on sepsis cut-off values for various laboratory parameters, Table 2 summarizes the distribution of patients with values in normal and sepsis-related ranges. Elevated serum procalcitonin levels (> 0.5 ng/mL) were observed in 41.1% of patients, which is suggestive of a systemic inflammatory response. Low serum albumin levels (≤ 2.45 g/dL) were noted in only 2.2% of patients. A notable proportion of patients (80%) demonstrated urine pus cells greater than $11/\mu\text{L}$, indicating inflammatory response. Additionally, 30% of

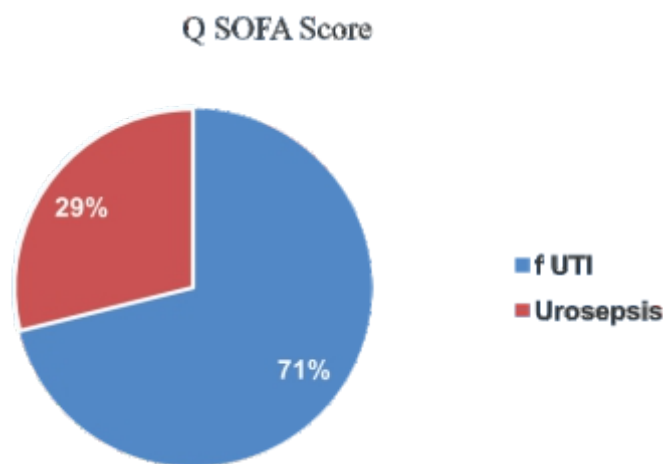


Figure 1: Distribution of study patients based on quick SOFA Score (n=90)

qSOFA – Quick sepsis related organ failure assessment; fUTI – febrile urinary tract infection

Table 1 : Clinico-laboratory profile of study participants (n=90)

Characteristics	fUTI n = 53	Urosepsis n = 37	Total n = 90
Age (Mean ± SD)	60.5 ± 20.2	63.4 ± 15.3	61.7 ± 18.3
Male [n (%)]	26 (49.1)	17 (45.9)	43 (47.8)
Female [n (%)]	27 (50.9)	20 (54.1)	47 (52.2)
Laboratory tests (Mean ± SD)			
Urea (mg/dL)	27.6 ± 13.2	46.1 ± 19.8	35.1 ± 18.5
Creatinine (mg/dL)	1.1 ± 0.4	1.56 ± 0.5	1.36 ± 0.82
Albumin (g/dL)	3.7 ± 0.5	3.2 ± 0.4	3.51 ± 0.54
Procalcitonin (ng/mL)	0.3 ± 0.42	13.9 ± 33.6	5.94 ± 22.4
Procalcitonin/albumin ratio	0.09 ± 0.12	4.6 ± 10.8	1.95 ± 7.27
Leucocyte count ($\times 10^3/\mu\text{L}$)	11.7 ± 4.3	16 ± 6.2	13.5 ± 5.6
Clinical presentations [n (%)]			
Fever	53 (100)	31 (83.8)	67 (74.4)
Burning micturition	42 (79.2)	22 (59.5)	64 (71.1)
Vomiting	19 (35.8)	15 (40.5)	34 (37.8)
Lower Quadrant pain	17 (32.1)	26 (70.3)	43 (47.7)
Abdominal signs	19 (35.8)	26 (70.3)	45 (50)

Values are expressed as Mean ± standard deviation (SD)

fUTI – Febrile urinary tract infection

patients exhibited an elevated procalcitonin -to-albumin ratio (> 0.44), supporting its potential role as a useful biomarker in diagnosing urosepsis. These laboratory cut-offs may aid in early risk stratification and clinical decision-making in patients with suspected urosepsis.

A univariate analysis of different clinical and laboratory variables is summarized in Table 3. It demonstrates that variables including hypotension, serum urea, creatinine, procalcitonin, the procalci-

tonin/albumin ratio, leukocyte count, and organ dysfunction were significantly associated with urosepsis ($p < 0.05$) and hence may be considered as important indicators of urosepsis. In contrast, gender, high blood pressure, serum albumin levels, and urine routine showed no statistical significance. The diagnostic performance of various clinical and laboratory parameters in predicting urosepsis among fUTI participants have been tabulated in Table 4.

On ROC curve analysis, procalcitonin (AUC = 0.914, 95% CI: 0.839–0.988) and the procalcitonin/albumin ratio (AUC = 0.915, 95% CI: 0.842–0.988) showed excellent diagnostic performance in predicting urosepsis among fUTI patients. Both markers demonstrated high specificity (94.3%)

Table 2 : Laboratory parameters (n=90)

Laboratory tests	Sepsis cutoff values	Normal level n (%)	Sepsis level n (%)
Serum Procalcitonin (ng/ml)	> 0.5	53 (58.9)	37 (41.1)
Serum Albumin (g/dL)	≤ 2.45	88 (97.8)	2 (2.2)
Serum Procalcitonin /Albumin ratio	> 0.44	63 (70)	27 (30)
Urine – pus cells(µl)	> 11	18 (20)	72 (80)

Table 3: Univariate analysis for discriminating urosepsis from fUTI (n=90)

Variables	Univariate OR with 95% CI	p
Gender	0.8 (0.38 – 2.04)	0.770
Hypotension < 90/60 mmHg	67.8 (3.8 – 1191.9)	<0.001***
Hypertension > 140/90 mmHg	1.18 (0.3 – 4.4)	0.801
Urea (mg/dL)	11.5 (3.9–33.6)	<0.001***
Creatinine (mg/dL)	8.6 (3.1 – 24.1)	<0.001***
Procalcitonin (ng/mL)	61.4 (16.4 – 229.5)	<0.001***
Albumin (g/dL)	1.44 (0.8 – 23.8)	0.796
Procalcitonin/Albumin ratio	53.1(11.03 –255.7)	<0.001***
Leucocyte count (×10 ^{3/µL})	3.3 (1.2 – 8.8)	0.015*
Urine – pus cells	2.96 (0.88 – 9.87)	0.069
Organ dysfunction	41.9 (8.8 – 119.6)	<0.001***

*p < 0.05, ** p < 0.01, ***p < 0.001

Table 4 : Various characteristics in predicting urosepsis in febrile UTI patients (n=90)

Characteristics	AUC (95% CI)	<i>p</i>	Cut off	Sensitivity	Specificity
Temperature	0.638 (0.519 - 0.757)	0.026*	99.9	54.1 %	68.9 %
Pulse Rate	0.666 (0.550 - 0.783)	0.007**	99	56.8 %	73.6 %
Leucocyte count ($\times 10^3/\mu\text{L}$)	0.732 (0.626 - 0.837)	<0.001***	11.05	81.1 %	47.2 %
Urea (mg/dL)	0.796 (0.695 - 0.897)	<0.001***	40.5	59.5 %	90.6 %
Creatinine (mg/dL)	0.768 (0.657 - 0.879)	<0.001***	1.14	78.4 %	69.8 %
Procalcitonin (ng/mL)	0.914 (0.839 - 0.988)	<0.001***	1.07	75.7 %	94.3 %
Albumin (g/dl)	0.189 (0.099 - 0.280)	<0.001***	3.15	59.5 %	13.2 %
Procalcitonin /Albumin ratio	0.915 (0.842 - 0.988)	<0.001***	0.405	67.8 %	96.2 %

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

and 96.2% respectively), with procalcitonin showing higher sensitivity (75.7%). Among other parameters, serum creatinine (AUC = 0.768) and urea (AUC = 0.796) also exhibited good predictive value, while leucocyte count had higher sensitivity (81.1%) but lower specificity (47.2%). In contrast, albumin alone had poor discriminatory power (AUC=0.189) but with low specificity (13.2%).

Temperature and pulse rate provided limited discrimination (AUC 0.638 and 0.666) respectively. Overall, procalcitonin and the procalcitonin/albumin ratio were accurate and reliable markers for identifying urosepsis in this study. The clinical parameters along with laboratory predictors were analysed by ROC and illustrated in Figure 2, where pulse rate, temperature, leukocyte count, serum urea, creatinine, procalcitonin, albumin, and the procalcitonin/albumin ratio revealed statistically significant predictive ability ($p < 0.05$) for urosepsis among fUTI patients, however only procalcitonin and procalcitonin/albumin ratio showed excellent diagnostic performance. Overall, these findings highlight the procalcitonin/albumin ratio as a novel and highly effective predictor of

urosepsis in this population. Patient outcome studied where majority of patients (72.2%) were discharged after recovery, while 26.7% required ICU discharge for procedures such as stenting or dialysis. Only one death (1.1%) was observed, and the serum procalcitonin/albumin ratio in this patient was 12.7.

Discussion

By using procalcitonin and albumin ratio, the study aimed to develop an early diagnostic predictor which discriminates patients with fUTI and those with urosepsis. Conventional diagnostic methods like inflammatory markers and blood cultures are restricted by some limitations. The prolonged turnaround time for obtaining results [27–28] limits timely initial treatment decisions, highlighting the need for a reliable biomarker. The demographic characteristics of the participants predominantly belong to the geriatric population, with 52.2% females and 47.8% males. Fever was the most common clinical presentation in UTI cases. Similar findings were reported by Luo et al. (2018) [25], where the mean age was 58.47 ± 16.99 years, 32.86% were males, and 72.86% presented with

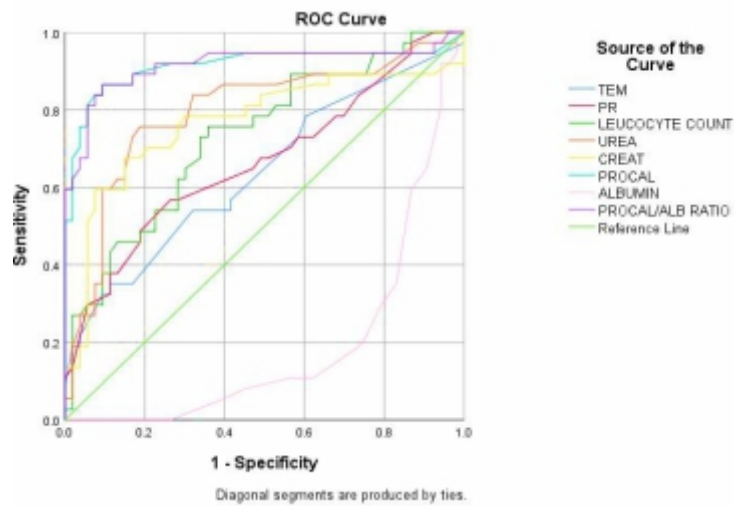


Figure 2: ROC curve of variables in predicting urosepsis in febrile UTI patients

fever or chills. Additionally, 84.29% had flank pain or dysuria, and 21.43% had hypotension.

In contrast, Sahin *et al.* (2023) [29] reported a male predominance (53.85% males, 46.15% females), as did Rout *et al.* (2022) [30] with 57% males and 43% females, yielding a male-to-female ratio of 1.35:1. The sepsis incidence in our study was 41%, lower than the 62.5% reported by Rout *et al.* (2022) [30]. However, their findings on procalcitonin levels and serum albumin were consistent with our observations. The qSOFA score was used as an initial screening tool to identify high risk patients. It takes into account altered mental activity, a systolic blood pressure of 100mmHg or less and respiratory rate > 22/min or greater. A score of more than or equal to two of these three clinical conditions indicates urosepsis in fUTI patients. Similar scoring tool was utilized in our study to indicate urosepsis among the study patients.

In the study conducted by Rout *et al.* (2022) [30], the AUC for the procalcitonin/albumin ratio at admission was 84.62% and 96.00%, respectively. CRP demonstrated a sensitivity of 87.50% and a specificity of 50.77%, whereas leukocyte count cut-

off values were less specific, with a sensitivity of 64.62% and a specificity of 74.32%. Comparable results were observed in the present study, where the serum procalcitonin/albumin ratio showed a sensitivity of 67.8% and a specificity of 96.2%. In contrast, the leukocyte count cut-off value demonstrated a sensitivity of 81% and a specificity of 47.2%.

In our study, serum albumin demonstrated poor specificity (13.2%) for predicting urosepsis among patients with fUTI probably because sepsis could have caused increased breakdown or loss of albumin from kidney or gastrointestinal tract. However, newer evidence links hypoalbuminemia to severity of the disease and mortality, making it a biomarker rather than a specific diagnostic marker. In contrast, procalcitonin reliably reflects bacterial infection and burden. The combined procalcitonin /albumin ratio improved diagnostic accuracy, with a cutoff value > 0.44 effectively differentiating urosepsis from fUTI. Similar to previous studies, CRP and leukocyte count at admission were associated with urosepsis[25] significantly.

Overall, this study highlights the procalcitonin/albumin ratio for early identification and risk stratification of urosepsis in fUTI patients. Elevated procalcitonin, low albumin, and a high procalcitonin/albumin ratio alongside significant pyuria form a critical diagnostic panel for sepsis. Incorporating these parameters into clinical assessments forms may facilitate diagnosis, guide timely interventions, and ultimately reduce urosepsis-related mortality.

In this study, urosepsis constituted a substantial proportion of fUTI case, predominantly affecting elderly population. Parameters like hypotension, leukocyte count, renal dysfunction, procalcitonin, and the procalcitonin/albumin ratio demonstrated an association that was significant. Among these, the procalcitonin-to-albumin ratio demonstrated strong discriminatory performance, with a cutoff value of 0.405 showing high specificity for urosepsis. A procalcitonin/albumin ratio greater than 0.44

effectively differentiated urosepsis from fUTI and appeared to outperform conventional inflammatory markers such as CRP and leukocyte count.

Conclusion

Given its rapid availability and cost-effectiveness, the procalcitonin/albumin ratio may serve as a valuable adjunctive tool for early identification of urosepsis, facilitating timely clinical decision-making and potentially improving patient outcomes.

Recommendations

A serum procalcitonin/albumin ratio ≥ 0.405 on day 1 of admission, with 67.8% sensitivity and 96.2% specificity, may serve as a promising marker in diagnosing urosepsis in fUTI patients. Incorporation of this marker into early clinical assessment may potentially help with prompt diagnosis and treatment, thereby reducing the mortality.

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