European Journal of Molecular & Clinical Medicine

ISSN 2515-8260 Volume 9, Issue 3, Winter 2022

The procalcitonin albumin ratio as an early diagnostic predictor in discriminating urosepsis from patients with febrile urinary tract infection

[1]B Akhil Reddy, [2]Shubhransu Patro, [3]Sujit Kumar Pradhan, [4]Nikunj Kishore Rout

[1]Post Graduate Resident, [2]Professor Department of General Medicine, Kalinga Institute of Medical Sciences, Bhubaneswar, Odisha, India

[3]Associate Professor, Critical Care Medicine, KalingaInstitute of Medical Sciences, Bhubaneswar, India

[4]Assistant Professor, Department of Nephrology, Kalinga Institute of Medical Sciences, Odisha, India

Correspondence:

Nikunj Kishore Rout

Assistant Professor, Department of Nephrology, Kalinga Institute of Medical Sciences, Odisha, India

ABSTRACT

Distinguishing urosepsis from febrile urinary tract infections is critical in therapeutic decision-making to identify appropriate treatments to avoid sepsis-related organ failure. Accurate diagnosis takes time and is prone to false-positive outcomes. Furthermore, patient reactions to urosepsis are complex and variable. As a result, the goal of this study was to create a new, early diagnostic predictor that might distinguish between patients with urosepsis and those with febrile urinary tract infections by combining initial procalcitonin and albumin levels.A retrospective analysis of 200 patients with febrile urinary tract infections during an eighteen-month period. The independent risk variables for distinguishing urosepsis from febrile urinary tract infection were identified using univariate and multivariate logistic models. To examine the prediction accuracy of the procalcitonin/albumin ratio, a receiver operating characteristic (ROC) curve analysis was performed. Procalcitonin/albumin ratios were greater in the urosepsis group than in the febrile urinary tract infection group [2.254 (0.978, 6.299) vs 0.021 (0.004, 0.095); P<.001].

According to multivariate logistic analysis, the procalcitonin/albumin ratio [adjusted odds ratio (OR) 1.029, 95 percent confidence interval (CI) 1.013-1.045, P<.001] was an independent predictor of urosepsis, allowing patients with febrile urinary tract infections to be distinguished. The procalcitonin/albumin ratio had an area under the ROC curve (AUC) of 0.937 (95 percent CI, 0.894-0.980); P.001. The procalcitonin/albumin ratio cut-off values (>0.44) had a sensitivity of 84.62 percent and a specificity of 96.00 percent, respectively.Furthermore, in a sample of 65 patients with urosepsis, the procalcitonin/albumin ratio in the uroseptic shock group was greater than in the non-uroseptic shock group [5.46 (1.43, 6.58) vs 1.24 (0.63, 4.38); P =.009]. The procalcitonin/albumin ratio is an early diagnostic predictor that can distinguish between urosepsis and febrile urinary tract infection, according to our findings. Furthermore, patients with urosepsis who had greater procalcitonin/albumin ratios were more likely to develop uroseptic shock. Our findings indicate that the procalcitonin/albumin ratio is a quick and low-cost biomarker that can be employed in clinical practise.

Key Words: Bacteriuria, Procalcitonin/albumin ratio, Urosepsis, Febrile urinary tract infection

INTRODUCTION

The presence of bacteria or other organisms in typically sterile urine or genitourinary tissues is known as urinary tract infection (UTI). Bacteriuria is defined as any bacterium that can be discovered in the urine. A urinary tract infection (UTI) is a collection of clinical symptoms that includes asymptomatic bacteriuria (ABU), prostatitis, cystitis, and pyelonephritis [1].

The manifestation of UTI is more variable in the older generation. In community settings, a larger share (95 percent) life alone. Others, on the other hand, reside in LTC facilities (5 percent). These two groups' characteristics have an impact on epidemiology, diagnosis, risk factors, and UTI management [2, 3]. UTI accounts for 24 percent of all reported infections in a population environment, followed by RTI. Incontinence (33–50%), cystoceles, urinary diverticula, an increased amount of leftover urine, and recent surgery were all linked to an increased risk of infection in elderly women [4].

The most prevalent risk factors for UTI in humans include chronic urine retention associated with BPH, bacterial prostatitis, and incontinence. Despite the fact that the majority of older persons live in the community, the majority of research has been entirely on LTC residents [5]. UTI is the most prevalent illness recorded in long-term care settings, accounting for 25 to 30 percent of all bacterial infections [6]. In this context, both silent and symptomatic infections were related with the use of indwelling catheters (for around 5 to 10% of institutionalised patients), bowel and bladder incontinence, co-morbidities, and the risk of uropathogen transmission.As a result, the frailer or weakened the individual, the greater the likelihood of a symptomatic or asymptomatic UTI [7]. It is also worth mentioning that, like with the overall population, women over the age of 65 are more likely than men to develop symptomatic UTI [8].

Microbial infections that enter the urinary tract generate UTIs, which can result in a variety of clinical signs and symptoms as well as mortality. To circumvent the time-consuming, traditional culture process, healthcare practises must implement quick screening processes. Urine test strips use biomarkers such as nitrite and LE to detect UTIs quickly [9, 10]. Despite this, there are considerable differences in experiment performance.

To diagnose UTIs, the results of a quick diagnostic nitrite strip test that detects the presence of bacteria and a semi-quantitative assessment of the leukocyte count in the urine are combined with the results of a symptomatic approach [11, 12, 13]. However, as compared to the gold standard of urine culture, the primary diagnosis has a substantially higher rate of mistake. This frequently leads to unnecessary antibiotic prescriptions, unpleasant reactions, and the emergence of drug resistance [14, 15]. As a result, we conducted study at our tertiary care centre employing procalcitonin and albumin ratio (PAR) to increase the diagnostic accuracy of predicting sepsis in patients presenting with UTI.

METHODOLOGY

The prospective observational study was carried out in the Department of General Medicine our tertiary care centre, Kalinga Institute of Medical Sciences and Pradyumna Bal Memorial Hospital, Bhubaneswar, on patients attending OPD/IPD after receiving permission from the institutional ethics committee and review board and obtaining written informed consent from the patients.

Once the Institutional Ethics Committee authorised it, a valid permission was obtained. Once the patient agreed to participate in the study, a complete history and physical examination were undertaken in accordance with the protocol. A documented informed consent form was signed by the patients or their attendants.

All patients who visited the medicine OPD and were admitted to the ward throughout the study period and met the inclusion criteria were included in the study. Detailed demographic data, as well as symptoms at the time of admission, were documented in a pre-tested organised format

after admission. Urine routine microscopy, urine culture, and blood culture were submitted to determine a positive diagnosis of UTI.
Blood samples were collected within 24 hours of admission to determine serum procalcitonin and serum albumin levels. The enhanced chemiluminescence approach was used to calculate the level of procalcitonin. The dye binding approach was used to estimate the albumin level. Other regular tests, such as a CBC, LFT, RFT, chest XRAY, and USG abdomen pelvis, were performed and documented. Patients were thoroughly assessed to rule out any other possible primary source of illness. All patients were kept under observation and were closely monitored for the onset of Sepsis using the SOFA score and clinical symptoms.

STATISTICAL ANALYSIS

Quantitative evidence is supplied using the mean and standard deviation. An unpaired t-test is used to compare the sample groups based on the results of the normality test. Qualitative data is displayed using a frequency and percentage chart. The Fisher test, student 't' test, and Chi-Square test are used to examine the relationship between the sample groups. A 'p' value of less than 0.05 is considered significant.

RESULTS

DISTRIBUTION OF PATIENTS ACCORDING TO AGE

The majority of patients (30%) were between the ages of 61 and 70, followed by 51-60 years (21%), 71-80 years (20%), 41-50 years (11%), 81-90 years (10%), 21-30 years (4.5%), and 31-40 years (3.5 percent). The patients' average age was 62.44 ± 14.54 years.

Table 1: Distribution of patients according to Age

Age (years)	N	%
21-30 years	9	4.5%
31-40 years	7	3.5%
41-50 years	22	11%
51-60 years	42	21%
61-70 years	60	30%
71-80 years	40	20%
81-90 years	20	10%
Total	200	100%
Mean ± SD	62.44±14.54	

DISTRIBUTION OF PATIENTS ACCORDING TO SEX

In our study, 115 (57%) of the patients were male, whereas 85 (43%) were female. There was a male predominance, with a M:F ratio of 1.35:1.

Table 2: Distribution of patients according to Sex

Sex	N	%
Male	115	57%
Female	85	43%
Total	200	100%
M:F Ratio	1:35:1	

DISTRIBUTION OF PATIENTS ACCORDING TO CO-MORBIDITIES

Diabetes affected 105 (53%) of the patients, while hypertension affected 104 (52%) of the patients.

Table 3: Distribution of patients according to Co-morbidities

Co-morbidites	N	%
Diabetes	105	53%
Hypertension	104	52%

ROC ANALYSIS OF PAR, PROCALCITONIN, ALBUMIN AS DIAGNOSTIC INDICATOR OF UROSEPSIS

According to ROC analysis, with a cut off value of 0.4, PAR has a sensitivity of 84.8 percent and a specificity of 77.3 percent in predicting sepsis in UTI patients. This is comparable to the use of Procalcitonin alone.

Figure 1: ROC analysis of PAR, Procalcitonin, Albumin as an indicator of urosepsis

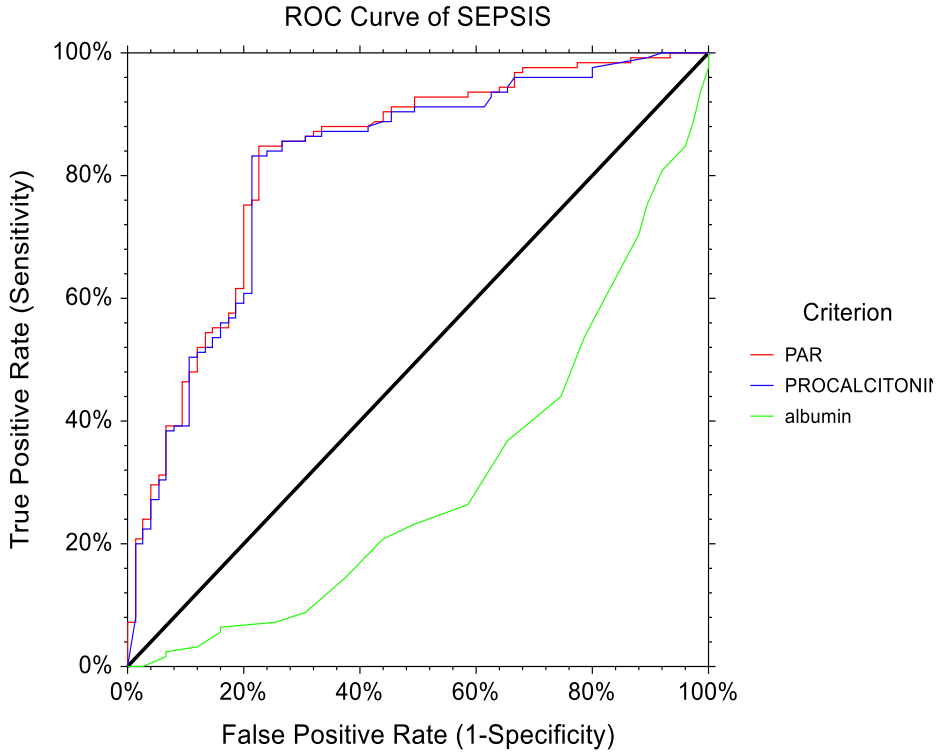

Table 4: AUC and other findings of Variables

Variable	AUC	SE	Z value to Test AUC >0.5	p-value	95%CI	
					Lower	Upper
PAR	0.8273	0.0311	10.506	0.000	0.7556	0.8793
Procalcitonin	0.8171	0.0321	5.876	0.000	0.7437	0.8710
Albumin	0.3048	0.0385	-5.070	1.000	0.2276	0.3782

ROC analysis of our study variables showed that

1. PAR has an AUC of 0.8273, a standard deviation of 0.0311, and a Z value of 10.506. A p-value of 0.000 indicates that the result is statistically significant.
2. Procalcitonin has a Z value of 5.876 and an AUC of 0.8171 with a standard error of 0.0321. A p-value of 0.000 indicates that the result is statistically significant.
3. PAR has a Youden index of 0.6213 with cut-off of ≥0.4, with a distance to the corner of 0.2729 and a PPV of 86.1 percent, NPV of 75.3 percent, sensitivity of 84.8 percent, and specificity of 77.3 percent.
4. Procalcitonin has a Youden index of 0.6187 with a cut-off of ≥ 1.42, a distance to the corner of 0.2715, a PPV of 86.6 percent, a sensitivity of 83.2 percent, and a specificity of 78.6 percent with a cut-off of 1.42.

Albumin has an AUC of 0.3048, a standard deviation of 0.0385, and a Z value of –5.070.

DISCUSSION

A hospital-based study with 200 patients demonstrated that an initial PAR aids in the early diagnosis of sepsis in patients presenting with UTI, allowing appropriate actions to be implemented to prevent further deterioration.

PCT is described as a peptide precursor that contains 116 amino acids, prohormones, and calcitonin. In the natural condition of the body, it is generated by thyroid gland C-cells and, less crucially, neuro-endocrine lung and small intestine cells. Serum concentrations in healthy people are exceedingly low, less than 0.05 ng/ml, or even undetectable [16]. It is synthesised in a variety of organs and tissues (including the lung, kidney, liver, and adipose tissue) and released into the circulation when there is systemic inflammation, particularly in bacterial infections, as a result of inflammatory cytokines and bacterial endotoxin, where its level can increase by 1000 folds [16, 17].The first quantifiable values are detected 2 to 4 hours after infection, with a maximum of 6 to 24 hours following bacterial tissue invasion.

The host's immune response to UTI is complicated. It is determined by a number of parameters, including the source of infection, strain type, and virulence factor expression [18]. These variances in the host's response limit the ability of diagnostic biomarkers like PCT to reliably predict positive infections.

According to Sastre et al. [18], PCT is not trustworthy as a standalone marker of sepsis and should be included as part of a comprehensive sepsis evaluation. Deng et al. discovered that the albumin:PCT ratio can be used as an early diagnostic predictor for nosocomial BSI in ICH patients. As a result, we used PAR to assess the accuracy of early detection of sepsis in UTI patients because it is a low-cost and quick method in practise.

Urinalysis has been the most commonly used screening tool for predicting UTI. This test looks for the presence of urine biomarkers like nitrite and LE, as well as urinary sediment, to determine if you have an upper or lower UTI [19]. The advantages include low processing costs and a quick turnaround time. However, several experiments call the test's reliability into question. Positive nitrite reactions with a demonstrated specificity of 75% to 98.5% are very specific to the presence of a positive UTI diagnosis [20]. However, the absence of a positive nitrite reaction cannot rule out UTI due to its low sensitivity (36–57%) and negative predictive potential.LE has a higher sensitivity of 72 percent to 94 percent for identifying UTIs, but only a 9 percent to 83 percent specificity because other illnesses can cause pyuria, resulting in false-positive leukocyte esterase. When positive nitrite or leukocyte esterase responses are combined with positive urine leukocytes, the test's sensitivity and specificity are increased. Even if both symptoms are negative, UTI cannot be completely ruled out.

Drozdov et al. [20] discovered that a PCT-based and quantitative pyuria algorithm reduces antibiotic exposure by 9 (15 percent) in the PCT-pyuria group and 19 (30 percent) in the control group; 84 (67 percent) had a febrile UTI, and 95 (76 percent) of the 125 patients were female patients. The median age was 73 years (19 to 96 years), and 35 individuals were considered outpatients (28 percent).

In our investigation, E. coli was the most prevalent bacteria recovered from urine culture, which is consistent with Allan Ronald's findings. According to Allan Ronald's study on the pathogenesis of UTI [21], E. coli is responsible for 80 percent of urinary tract infections. In our investigation, a PAR Cut-off value of 0.40 exhibited an 84.8 percent sensitivity and a 77.3 percent specificity in predicting urosepsis, which is equivalent to a study by Luo X et al.

CONCLUSION

The PCT is a sensitive predictor that aids in the earlier detection and evaluation of the severity and prognosis of bacterial infections. However, specificity is low, and some studies suggest that PCT should not be used alone to diagnose sepsis, but rather in conjunction with other indicators to increase diagnostic accuracy. Furthermore, symptoms in UTI patients vary

depending on the site of infection, making it more difficult to distinguish a case of sepsis from a typical UTI infection. As a result, we conducted a study in which we used PCT and albumin levels, as well as PAR, to help detect sepsis in patients with UTI.The study found that a PAR of ≥0.4 can aid in the early diagnosis of Urosepsis, allowing for improved antibiotic prescriptions and other supportive measures to assist relieve the patient's economic and disease burden.

REFERENCES

1. Dreger NM, Degener S, Ahmad-Nejad P, Wöbker G, Roth S. Urosepsis - Ursache, diagnose und therapie. DtschArztebl Int. 2015 Dec 4;112(49):837–47.
2. Foxman B. The epidemiology of urinary tract infection. Nat Rev Urol. 2010 Dec;7(12):653–60.
3. CC B, MK H, A Q, CA M. Incidence, severity, help seeking, and management of uncomplicated urinary tract infection: a population-based survey. Br J Gen Pract. 2015 Oct 1;65(639):e702–7.
4. Butler CC, Francis N, Thomas-Jones E, Llor C, Bongard E, Moore M, et al. Variations in presentation, management, and patient outcomes of urinary tract infection: a prospective four-country primary care observational cohort study. Br J Gen Pract. 2017 Dec 1;67(665):e830–41.
5. B F, R B, H D, B G, JD S. Urinary tract infection: self-reported incidence and associated costs. Ann Epidemiol. 2000;10(8):509–15.
6. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay A. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. BMJ. 2010 May 19;340(7756):c2096.
7. Hillier S, Roberts Z, Dunstan F, Butler C, Howard A, Palmer S. Prior antibiotics and risk of antibiotic-resistant community-acquired urinary tract infection: a case–control study. J AntimicrobChemother. 2007 Jul 1;60(1):92–9.
8. Jim O'Neill. The Review on Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations Wellcome Trust (London, England); Dec 2014 Available from: https://wellcomecollection.org/works/rdpck35v/ .
9. TA H, B L. The diagnostic accuracy of rapid dipstick tests to predict urinary tract infection. Am J Clin Pathol. 1991;96(5):582–8.
10. Knottnerus BJ, Geerlings SE, Charante EPM van, Riet G ter. Toward A Simple Diagnostic Index for Acute Uncomplicated Urinary Tract Infections. Ann Fam Med. 2013 Sep 1;11(5):442–51.
11. DL P. “Collateral damage” from cephalosporin or quinolone antibiotic therapy. Clin Infect Dis. 2004 May 15;38 Suppl 4(S341-s45).
12. Gillings MR. Evolutionary consequences of antibiotic use for the resistome, mobilome and microbial pangenome. Front Microbiol. 2013JAN 22; 4:4.
13. Urinary tract infections: Sobel, J. D.,Kaya D MG. Douglas and Bennett’s Principal and Practice of Infectious Diseases. 5th ed. Philadelphia,PA,USA; 2000. 773–805 p.
14. M A, D G, H C, J R, J G, C B. High serum procalcitonin concentrations in patients with sepsis and infection. Lancet (London, England). 1993 Feb 27;341(8844):515–8.
15. Becker KL, Nylén ES, White JC, Müller B, Snider RH. Procalcitonin and the Calcitonin Gene Family of Peptides in Inflammation, Infection, and Sepsis: A Journey from Calcitonin Back to Its Precursors. J Clin Endocrinol Metab. 2004 Apr 1;89(4):1512–25.
16. S L, A G. Procalcitonin: a key marker in children with urinary tract infection. Adv Urol. 2011 Jan 17; 2011:397618–397618.
17. Zaffanello M, Brugnara M, Franchini M, Fanos V. Is serum procalcitonin able to predict long-term kidney morbidity from urinary tract infections in children? Clin Chem Lab Med.

2008 Oct 1;46(10):1358–63.

18. Sastre JB, Solís DP, Serradilla VR, Colomer BF, Cotallo GD, Vidal XK, López EN, del Río MG, Luna MS, Cueto AB, Serrano MM. Procalcitonin is not sufficiently reliable to be the sole marker of neonatal sepsis of nosocomial origin. BMC pediatrics. 2006 Dec;6(1):1-7.
19. DengShuixiang, GaoJiamin, ZhaoZhiyong, TianMi, LiYuming, GongYe. Albumin/Procalcitonin Ratio Is a Sensitive Early Marker of Nosocomial Blood Stream Infection in Patients with Intra-Cerebral Hemorrhage. https://home.liebertpub.com/sur. 2019 Nov 13;20(8):643–9.
20. Drozdov D, Schwarz S, Kutz A, Grolimund E, Rast AC, Steiner D, et al. Procalcitonin and pyuria-based algorithm reduces antibiotic use in urinary tract infections: a randomized controlled trial. BMC Med 2015 131. 2015 May 1;13(1):1–13.
21. X L, X Y, J L, G Z, Y L, G Q, et al. The procalcitonin/albumin ratio as an early diagnostic predictor in discriminating urosepsis from patients with febrile urinary tract infection. Medicine (Baltimore). 2018 Jul 1;97(28).