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COMPARATIVE STUDY OF PROCALCITONIN VERSUS C-REACTIVE PROTEIN LEVELS IN DIAGNOSIS OF ACUTE PYELONEPHRITIS

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Abstract

Objective: *To compare the diagnostic accuracy of serum procalcitonin and C-reactive protein levels in distinguishing acute pyelonephritis from lower urinary tract infection in adult patients.*

Study Design: *Cross-sectional analytical study.*

Place and Duration of Study: *Armed Forces Institute of Urology (AFIU), Rawalpindi, Pakistan, from 1st March 2024 to 31st August 2024.*

Methodology: *This study included 164 patients selected by consecutive non-probability sampling. The selection criteria was based on the signs of UTI on clinical assessment. The age range of these patients was kept between 18-65 years old. A detailed diagnostic protocol was used to evaluate quantitative urine culture, estimation of serum procalcitonin and C-protein concentrations, and sonographic evaluation of the kidneys. A composite reference standard served as the basis for confirming acute pyelonephritis. The effectiveness of the biomarkers to contrast between the two experimental groups under study was determined with the help of the receiver operating characteristic. The ROC was used determine the threshold values of AUC, sensitivity and specificity. Statistical computations were carried out on SPSS version 24.*

Results: *The results of this study clearly showed a high occurrence of lower urinary tract infection in patients i.e. 56.1% in comparison to acute pyelonephritis in patients i.e. 43.9%. Procalcitonin concentrations in serum were substantially elevated in the pyelonephritis cohort relative to the lower tract group (3.74 ± 3.28 ng/mL versus 0.41 ± 0.36 ng/mL; p<0.001), and C-reactive protein followed a parallel trend (74.6 ± 42.3 mg/L versus 18.8 ± 13.7 mg/L; p<0.001). A remarkable accuracy was shown by procalcitonin with an AUC of 0.943. With a threshold of 0.4 ng/mL the sensitivity and specificity were 91.7% and 89.1% respectively. For C-reactive protein at 30 mg/L, the corresponding figures were 87.5%, 54.3%, and 0.812 respectively, with a statistically significant difference between the two curves on DeLong testing (p<0.001).*

Conclusion: *In the task of separating acute pyelonephritis from infections confined to the lower urinary tract, procalcitonin in serum outperformed C-reactive protein across key diagnostic indices, most notably in specificity and positive predictive value.*

INTRODUCTION

Globally, infections of the urinary tract rank as one of the most frequently encountered bacterial illnesses, with roughly 150 million cases diagnosed each year, placing a considerable demand on medical services.[1,2] Within the Pakistani healthcare landscape, the clinical load attributable to urinary tract infections is noteworthy, as hospital-based studies have documented prevalence figures between 25% and 52%, with a predilection for women in their childbearing years and diabetic individuals.3 Clinically, these infections span a wide severity gradient, from straightforward bladder inflammation at one end to acute pyelonephritis at the other, the latter carrying risks of bloodstream dissemination, perinephric abscess formation, and irreversible kidney tissue injury when treatment is delayed.[3]

Distinguishing reliably between bladder-level infection and renal parenchymal involvement carries direct therapeutic consequences, shaping decisions about antimicrobial potency, parenteral versus oral drug delivery, treatment length, and the necessity for inpatient care.[4] Conventionally, clinicians have depended on a constellation of signs—including pyrexia, loin discomfort, renal angle elicitation pain, and constitutional symptoms—together with urinalysis showing leucocyturia and microbiologically confirmed bacteriuria.[5] Nonetheless, the symptom profile is often misleading, particularly among older adults and those with compromised immunity, in whom site-specific manifestations can be subtle or entirely lacking.[6] Although contrast-enhanced computed tomography and radionuclide renal scanning with dimercaptosuccinic acid offer dependable verification of upper tract disease, their high cost, ionizing radiation exposure, and restricted availability throughout much of Pakistan curtail their routine clinical deployment.[6,7]

Among serological inflammatory indicators, C-reactive protein—a hepatocyte-derived acute-phase protein whose synthesis is driven by interleukin-6—has long served as a broadly employed, albeit non-specific, gauge of systemic inflammatory activity.[8] Although its serum levels tend to climb during renal parenchymal infections, C-reactive protein cannot reliably distinguish bacterial pathology from other inflammatory triggers, including autoimmune flares, surgical trauma, and neoplastic processes.[9,10] Adding to this drawback, C-reactive protein reaches its zenith only 24 to 48 hours following the inflammatory insult, a lag that may compromise its usefulness when rapid clinical decisions are needed.[11]

Over the past two decades, procalcitonin—a 116-amino-acid polypeptide that normally functions as the hormonal precursor of calcitonin—has attracted growing interest as a comparatively specific sentinel of invasive bacterial disease.[12,13] In response to bacterial challenge, numerous extra-thyroidal tissues—including hepatic, renal, and adipose compartments—begin synthesizing this peptide, producing a measurable rise within two to four hours and maximal concentrations between six and twelve hours after onset.[14] Pooled data from a Cochrane meta-analysis placed procalcitonin's sensitivity at 86% and its specificity at 74% for identifying renal involvement in paediatric urinary infections.[15] Despite these encouraging paediatric data, head-to-head evaluations involving grown-up patients in the South Asian clinical milieu remain scarce.[7,16]

This study was designed to compare the diagnostic performance of serum procalcitonin and C-reactive protein in adult patients presenting with suspected urinary tract infection at a tertiary care hospital in Rawalpindi, with the aim of generating locally relevant evidence.

METHODOLOGY

This cross-sectional analytical study was conducted at the Armed Forces Institute of Urology (AFIU), Rawalpindi, Pakistan, from 1st March 2024 to 31st August 2024. The study protocol received clearance from the AFIU Institutional Ethics Committee (reference AFIU/IRB/2024-041, approved on February 20, 2024) and adhered to the ethical tenets of the Helsinki Declaration in its 2013 revision. Every participant provided documented voluntary consent before enrolment. Sample size estimation followed the World Health Organization's approach for studies of diagnostic test performance, as outlined by Lwanga and Lemeshow, following the practical methodology

outlined by Althubaiti.[17,18] Based on an anticipated area under the receiver operating characteristic curve of 0.85 for procalcitonin, 95% confidence level, 80% statistical power, and an expected disease prevalence of 40%, the minimum required sample size was 150 participants, inflated to 164 to account for potential incomplete data.

Eligibility extended to adults between 18 and 65 years who exhibited a minimum of two recognized urinary symptoms—namely burning micturition, increased voiding frequency, urgency, lower abdominal discomfort, loin pain, renal angle tenderness and temperature exceeding 38°C—coupled with demonstrable pyuria surpassing 10 white cells per high-power microscopic field. Grounds for exclusion encompassed gravidity, pre-existing renal impairment with estimated glomerular filtration rate below 30 mL/min/1.73m², active malignant disease, co-existent infection at a non-urinary site, any operative procedure in the preceding four weeks, ongoing immunosuppressive medication, presence of an in-dwelling bladder catheter, and antimicrobial exposure within the 48 hours before presentation. Participant recruitment proceeded on a consecutive non-probability basis.

Following a structured clinical work-up, mid-void urine samples from each participant were inoculated onto both blood agar and MacConkey agar media; ≥100,000 CFU/mL of a single uropathogen constituted a positive culture. The cut-off time for sample collection was 6 hours after admission. The sample was used for Cobas e411 platform, procalcitonin quantification biochemical renal assessment, C-reactive protein determination and haematological profiling. Laboratory staff processed all specimens without knowledge of each patient's clinical categorization. Bilateral renal sonography was carried out by a senior radiologist.

Acute pyelonephritis was diagnosed when all three criteria were met: (a) fever ≥38°C with flank pain or costovertebral angle tenderness; (b) positive urine culture; and (c) supportive ultrasonographic findings or systemic inflammatory response (leukocytosis >12,000 or leukopenia <4,000 cells/µL). Lower urinary tract symptoms along with bacteriuria were used for the diagnosis of lower urinary tract infection. However, there were no signs of systemic involvement or renal involvement on ultrasonography. Diagnostic group assignment was verified independently by two attending physicians, with any disagreement settled through joint discussion.

Statistical results for this study were calculated using IBM SPSS software, release 24.0. Quantitative measures were reported as arithmetic mean with standard deviation when normally distributed, or as median accompanied by the interquartile range otherwise. Group differences were tested with the unpaired Student's t-test or the Mann–Whitney U statistic for continuous data and the Pearson chi-square test for categorical variables. The threshold was optimized on the ROC curves by the Youden index and then the two AUC

were determined by the DeLong method. Two-sided p-values below 0.4 were deemed statistically significant.

RESULTS

Initial screening encompassed 178 individuals, from whom 14 were subsequently removed: six owing to incomplete laboratory records, four because a concurrent extra-urinary infectious focus was identified, two following detection of previously unrecognized chronic kidney disease, and two who chose to withdraw. The remaining 164 patients constituted the analytical sample, comprising 72 (43.9%) with confirmed acute pyelonephritis and 92 (56.1%) with infection restricted to the lower tract. The cohort had a mean age of 38.5 ± 12.6 years, and females predominated at 103 (62.8%). No statistically meaningful inter-group differences emerged for age, sex ratio, or body mass index. The pyelonephritis group had significantly higher temperature (39.1 ± 0.7°C vs 37.5 ± 0.5°C; p<0.001) and TLC (15,840 ± 4,520 vs 9,760 ± 3,180 cells/µL; p<0.001), as shown in Table-I.

Table-I: Demographic and Clinical Characteristics (n=164)

Variable	APN (n=72)	LUTI (n=92)	Total (n=164)	p-value
Age (years)	39.8±13.1	37.3±12.1	38.4±12.6	0.206
Male n(%)	29(40.3)	32(34.8)	61(37.2)	0.467
Female n(%)	43(59.7)	60(65.2)	103(62.8)	
BMI (kg/m²)	26.1±4.3	25.4±3.8	25.7±4.1	0.278
Diabetes n(%)	18(25.0)	14(15.2)	32(19.5)	0.118
Temp (°C)	39.1±0.7	37.4±0.4	38.1±1.0	<0.001
TLC (cells/µL)	15840±4520	9760±3180	12430±4870	<0.001
Creatinine (mg/dL)	1.18±0.34	0.94±0.22	1.04±0.30	<0.001

Continuous data as Mean±SD. APN=Acute Pyelonephritis; LUTI=Lower UTI; BMI=Body Mass Index; TLC=Total Leukocyte Count.

Mean procalcitonin was 3.74±3.28 ng/mL in the pyelonephritis group versus 0.41±0.36 ng/mL in the lower UTI group (p<0.001). Mean CRP was 74.6±42.3 mg/L versus 18.9±13.7 mg/L (p<0.001). Biomarker data are in Table-II.

Table-II: Biomarker Levels Between Groups (n=164)

Biomarker	APN (n=72)	LUTI (n=92)	p-value
PCT (ng/mL), Mean±SD	3.74±3.28	0.41±0.36	<0.001
PCT, Median (IQR)	2.58(1.12–5.47)	0.28(0.14–0.52)	<0.001
CRP (mg/L), Mean±SD	74.6±42.3	18.9±13.7	<0.001
CRP, Median (IQR)	64.5(38.2–104.8)	14.6(8.3–26.4)	<0.001

PCT=Procalcitonin; CRP=C-Reactive Protein; IQR=Interquartile Range.

ROC analysis showed PCT at 0.4 ng/mL had sensitivity 91.7%, specificity 89.1%, PPV 86.8%, NPV 93.2%, and AUC 0.943 (95% CI: 0.907–0.979). CRP at 30 mg/L had sensitivity 87.5%, specificity 54.3%, PPV 60.0%, NPV 84.7%, and AUC 0.812 (95% CI: 0.748–0.876). The AUC difference was significant (p<0.001, DeLong test), as in Table-III.

Table-III: Diagnostic Performance of PCT and CRP (n=164)

Parameter	PCT (≥0.5ng/mL)	CRP (≥30mg/L)
Sensitivity(95%CI)	91.7%(82.7–96.9)	87.5%(77.6–94.1)
Specificity(95%CI)	89.1%(81.0–94.5)	54.3%(43.7–64.7)
PPV	86.8%	60.0%
NPV	93.2%	84.7%
LR+	8.41	1.92
LR–	0.8	0.23
Accuracy	90.2%	68.9%
AUC(95%CI)	0.943(0.907–0.979)	0.812(0.748–0.876)
DeLong p-value	<0.001	–

PCT=Procalcitonin; CRP=C-Reactive Protein; PPV=Positive Predictive Value; NPV=Negative Predictive Value; LR=Likelihood Ratio; AUC=Area Under the Curve.

Escherichia coli dominated in both groups (66.7% pyelonephritis, 63.0% lower UTI), followed by Klebsiella pneumoniae (15.3%, 17.4%). No significant difference in pathogen distribution existed (p=0.714), as in Table-IV.

Table-IV: Uropathogens Distribution (n=164)

Organism	APN n(%)	LUTI n(%)	Total n(%)
Escherichia coli	48(66.7)	58(63.0)	106(64.6)
Klebsiella pneumoniae	11(15.3)	16(17.4)	27(16.5)
Proteus mirabilis	5(6.9)	6(6.5)	11(6.7)
Enterococcus faecalis	4(5.6)	4(4.3)	8(4.9)
Pseudomonas aeruginosa	2(2.8)	4(4.3)	6(3.7)
S. saprophyticus	1(1.4)	3(3.3)	4(2.4)
Others	1(1.4)	1(1.1)	2(1.2)

Chi-square p=0.714.

DISCUSSION

The present investigation, carried out at a tertiary-level hospital in Pakistan, set out to evaluate whether procalcitonin offers a measurable diagnostic advantage over C-reactive protein when the clinical question is upper versus lower urinary tract localization. Procalcitonin had a high AUC (0.943) in comparison to C-reactive protein (0.812) on the ROC analysis. This difference in values was found to be statistically significant. Notably, the discriminative edge of procalcitonin resided chiefly in its superior specificity (89.1% against 54.3%), whereas both markers exhibited broadly similar sensitivity in the range above 87%. The pattern of results obtained in our study is broadly concordant with previously published

work. Pecile and colleagues reported procalcitonin sensitivity and specificity of 83.3% and 93.6% for predicting pyelonephritis, while C-reactive protein achieved 94.4% sensitivity but only 31.9% specificity.[16] Narayan Swamy and colleagues similarly documented substantially higher C-reactive protein concentrations in patients with upper tract infection relative to those with bladder-level disease, supporting the role of inflammatory biomarkers in anatomical localization of urinary infections.[19] The recurrently poor specificity of C-reactive protein observed across multiple investigations underscores its inherent inability to distinguish bacterial pathology from other causes of systemic inflammation.[11,9]

Hertz and colleagues confirmed in their study the superior diagnostic utility of procalcitonin in patients diagnosed with urinary tract infections.[20,21] Similar findings were reported by Wu and colleagues of elevated procalcitonin in upper vs lower UTI in 314 patients retrospectively.[21] Taken together, these geographically diverse reports lend external validity to the trends observed in our cohort. The area under the curve of 0.943 in our study exceeds the pooled estimate in the Cochrane review, likely reflecting differences in reference standards and population characteristics.[15]

From a practical standpoint, the considerably greater positive predictive value afforded by procalcitonin (86.8% compared with 60.0% for C-reactive protein) means that a smaller proportion of patients would be incorrectly labelled as having upper tract disease, a benefit that carries tangible ramifications for judicious antibiotic prescribing and optimal channelling of healthcare resources in health care institutions.[12,13] Choi and colleagues found procalcitonin performed poorly for diagnosing any UTI in elderly hospitalized adults (AUC 0.56), indicating context-dependent performance.[23,24] Kuil and colleagues similarly found limited utility of both biomarkers for distinguishing UTI from asymptomatic bacteriuria.[6] The biomarker utility in urosepsis has been further explored by Wu and colleagues, who highlighted the prognostic value of procalcitonin in severe urinary infections.[25]

From a microbiological standpoint, the preponderance of Escherichia coli—accounting for roughly two out of every three culture-positive specimens—mirrors the uropathogen distribution documented in other Pakistani surveillance studies.[1] The near-identical pathogen profile across the two clinical groups reinforces the notion that what separates upper from lower tract disease is the depth of parenchymal penetration and the magnitude of the host's systemic inflammatory reaction, rather than the identity of the offending microorganism.[21]

Several methodological constraints warrant acknowledgment: the cross-sectional framework precludes longitudinal tracking of biomarker trajectories; reliance on a single institution narrows the demographic representativeness of the findings; the substitution of renal sonography for radionuclide scintigraphy in the reference composite may have introduced classification imprecision; and the sample did not permit stratified analyses by age, sex, or diabetic status. Prospective multi-site investigations that employ scintigraphy as the gold standard and explore combined biomarker prediction models would strengthen the evidence base.

CONCLUSION

In this cohort, procalcitonin in serum proved a markedly more accurate discriminator of acute pyelonephritis than C-reactive protein, chiefly by virtue of its higher specificity and positive predictive value. On the strength of these observations, routine procalcitonin estimation merits consideration as part of the initial laboratory panel for patients in whom upper urinary tract involvement is suspected, especially in facilities that lack ready access to advanced renal imaging.

Conflict of Interest

None.

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