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ORIGINAL: Evaluation of the Diagnostic Value of Procalcitonin in Acute Pyelonephritis Indices in Patients Referred to the Hospital

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ABSTRACT

Introduction: Uncomplicated urinary tract infection (UTI) is a widespread global ailment. The aim of this investigation was to evaluate the diagnostic efficacy of procalcitonin (PCT) in discriminating acute pyelonephritis from other lower urinary tract infections.

Material and Methods: This applied research concentrated on patients with acute pyelonephritis who were referred to Hazrat Valiasr Qaemshahr Hospital. A straightforward (random) sampling technique was implemented. Leukocyte count, ESR, serum CRP, and PCT measurements were obtained from all patients.

Results: Procalcitonin demonstrated positive results in 98.5% of pyelonephritis cases and 5% of cystitis cases, signifying a statistically significant differentiation (P=0.001). The diagnostic accuracy of procalcitonin was 97.7%, while its sensitivity and specificity were 98.5% and 95%, respectively. A notable correlation between serum PCT and CRP levels was observed in patients with acute pyelonephritis (P=0.038). The serum level of PCT in patients with acute pyelonephritis did not manifest any statistically significant variances based on age, gender, or history of urinary tract infection (P > 0.05).

Conclusion: Based on the findings of this study and comparisons with existing research, it can be deduced that procalcitonin functions as a dependable indicator for distinguishing acute pyelonephritis from other urinary tract infections. Consequently, its utilization for this purpose is recommended. Ultimately, conducting further studies with a larger sample size and in a multicenter manner is advised to validate the findings obtained in this study.

Introduction

Uncomplicated urinary tract infection is a prevalent condition that is widely observed across the globe. Currently, urinary tract infection (UTI) is a frequently encountered issue in the field of clinical medicine, with various clinical departments dealing with infected patients who suffer from this ailment. In the majority of cases, community-acquired and uncomplicated urinary infections are caused by common

Escherichia species, although other enterobacterias such as Klebsiella and Proteus can also be responsible(1-5). A feverish urinary infection is a prevalent issue characterized by the growth of bacteria in the urine. At present, the DMSA method is the standard diagnostic tool for acute pyelonephritis and the evaluation of kidney parenchymal damage. However, the limited availability of this method in all healthcare centers, the necessity of subjecting patients to radiation, and the associated costs pose as constraints for this procedure(1-2) Since 1993, proclexitonin (PCT) has been proposed as a valuable criterion for the diagnosis of bacterial infections in numerous studies (3). In healthy individuals, PCT levels are very low and typically less than 1/0 ng/ml. In viral infections and other inflammatory conditions, its level increases mildly to about 5/1 ng/ml but in severe bacterial infections its level reaches ng/ml 200-20.(1-2). Since 1993, proclexitonin (PCT) has been proposed as a valuable criterion for the diagnosis of bacterial infections in numerous studies (3). In healthy individuals, PCT levels are very low and typically less than 1/0 ng/ml. In viral infections and other inflammatory conditions, its level increases mildly to about ng/ml 5/1 but in severe bacterial infections its level reaches ng/ml 200-20.

This significant change in procalcitonin concentration has made it a beneficial marker in the diagnosis and possibly in the prognosis of microbial infections (4). PCT is a 116-amino-acid peptide, produced under normal conditions by C cells of the thyroid gland as a precursor to the hormone calcitonin, which after fracturing in the lung and pancreatic tissues leads to the production of calcitonin and two other molecules (5,6). Although the physiological function of PCT is still uncertain, microbial infections appear to cause the release of the prokelsitonin precursor from the majority of body tissues by stimulating the expression of the calci gene. Other characteristics of PCT include its association with the severity of the underlying disease. Serum levels of PCT increase much faster than CRP within approximately 2 hours after endotoxin enters the blood, while CRP takes about 12 hours. PCT returns to normal levels after 2 to 3 days and CRP returns to normal levels after 3 to 7 days (7-9).

CRP and PCT serve as valuable laboratory criteria for distinguishing acute pyelonephritis from inferior urinary infections. Nevertheless, while CRP boasts a sensitivity of 100% in diagnosing acute pyelonephritis, its normality implies the absence of this condition, thus rendering further examinations such as DMSA and injectable antibiotics unnecessary. This drawback significantly hampers its utility. In contrast, PCT, with its high specificity (6/82 %), appropriate sensitivity (3/70 %), and ease of use, has been considered a more valuable criterion than CRP for diagnosing acute pyelonephritis. Therefore, low PCT levels in patients suspected of acute pyelonephritis, even when clinical signs are present, indicate a low risk of kidney damage. Numerous studies support the high characteristics and sensitivity of PCT in distinguishing acute pyelonephritis from lower urinary tract infection. Furthermore, given the limited characteristics of CRP and the number of white blood cells in diagnosing acute pyelonephritis, measuring PCT can be introduced as a practical and useful criterion for its diagnosis (10).

Early identification of infections, particularly pyelonephritis, is crucial for the prevention of renal damage because prompt detection and appropriate administration of antibiotics can avert harm to the patient and the unnecessary use of antibiotics, as well as the subsequent development of antibiotic resistance. The assessment of procalcitonin (PCT) levels may be introduced as a valuable and practical criterion in diagnosing acute pyelonephritis, taking into account the limited diagnostic utility of C-reactive protein (CRP) and the number of white blood cells (WBC).

However, due to conflicting findings from previous studies regarding the diagnostic value of PCT, the objective of this study is to validate or refute its diagnostic significance in differentiating acute pyelonephritis from lower urinary tract infections. Therefore, definitive conclusions cannot be drawn based

on existing research, and further investigation by authoritative researchers is warranted. Lastly, considering the disparate outcomes reported in past reviews and studies on the diagnostic value of PCT(11,12), our study aimed to ascertain the diagnostic utility of PCT in distinguishing acute pyelonephritis from other inferior urinary tract infections.

Methods

The current study constitutes a pragmatic investigation that is grounded in both nature and methodology within the realm of prospective research. The targeted population for analysis consisted of patients who sought medical attention for acute pyelonephritis at Hazrat Valiasr hospital in Qaemshahr city. The sampling technique employed was simple random sampling. Inclusion criteria encompassed patients aged 15 to 60 years who had not received broad-spectrum antibiotics within the past six months, and who did not have gastrointestinal malignancies. Exclusion criteria included patient dissatisfaction with urinary catheter installation, absence of a catheter for any reason, pregnancy, history of kidney or liver transplants, immunodeficiency, treatment with immunosuppressive drugs, and acute kidney damage.

How to study

The methodology employed in this study involved the evaluation of all patients who had been clinically and lab-diagnosed with urinary tract infections and satisfied the inclusion criteria. To enhance the diagnostic accuracy of the tests, urine samples were collected using urinary catheters. For patients with pre-existing catheters, these were utilized for sampling purposes. A urinary infection was defined as a urine culture with more than 105 colonies of a pathogen or more than 104 colonies in symptomatic individuals. In the case of urine bag samples, a positive urine decomposition in symptomatic individuals, combined with a culture of more than 105 colonies of a pathogen, indicated a urinary infection. Leukocyte counts, ESR, Serum CRP, and PCT were measured in all patients.

Additionally, radioisotope scans were conducted for all patients presenting with febrile urinary tract infections. In the event of parenchymal damage observed in the scan, patients were diagnosed with acute pyelonephritis. Patients without fever and normal radioisotope scans were classified as having lower urinary tract infections. Laboratory parameter measurements were obtained prior to the initiation of antibiotic treatment.

Sample size

p:prevalence of pyelonephritis disease (0/004) and confidence percentage: 95% and accuracy: 4%

N= Z1-α/2 P(1-P) d2

So the number of samples needed to do this study was 67.

Analysis of the data

Finally, after collecting the information needed from all the subjects, we analyzed the data, which we used the SPSS statistical software version 25. The statistical tests used in this study for comparisons were independent Fisher and T and Kay Square, and the meaningful level was considered to be five hundred.

Results

According to the results of ***Table 1*** in pyelonephritis at 98/5% and in cystitis at 5% of cases prokelsitonin was positive, which showed a significant statistical difference (P=0.001) and its diagnostic accuracy was 97/7% and its sensitivity and characteristics were 98/5 and 95% respectively.

Serum PCT levels in patients with acute pyelonephritis were significantly associated with Serum CRP levels (P=0.038) (***Table 2***) (Serum PCT levels in patients with acute pyelonephritis did not differ statistically significantly based on age and gender (P > 0.05).

Serum PCT levels in patients with acute pyelonephritis did not differ statistically significantly based on the history of urinary

tract infections (P > 0.05) (***Table 3***). Leukocytosis (100%) and high ESR (100%) were observed in all patients with acute pyelonephritis.

Table 1 .diagnostic value of proclecitonin in acute pyelonephritis indicators.

		Proclecitonin		Total
		Pos	Neg	
Group	Pyelonephritis	66 98.5%	1 1.5%	67 100.0%
	Cystitis	1 5.0%	19 95.0%	20 100.0%
	Total	67 77.0%	20 23.0%	87 100.0%

Table 2-comparison of serum PCT levels in patients with acute pyelonephritis with Serum CRP levels.

		Proclecitonin		Total
		Pos	Neg	
CRP	1+	8 88.9%	1 11.1%	9 100.0%
	2+	52 100.0%	0 0%	52 100.0%
	3+	6 100.0%	0 0%	6 100.0%
	Total	66 98.5%	1 1.5%	67 100.0%

Table 3. serum PCT levels based on history of urinary infection.

		Proclecitonin		Total
		Pos	Neg	
History	Pos	62 98.4%	1 1.6%	63 100.0%
	Neg	4 100.0%	0 0%	4 100.0%
	Total	66 98.5%	1 1.5%	67 100.0%

Discussion

The objective of this study was to assess the diagnostic significance of procalcitonin (PCT) in distinguishing between acute pyelonephritis and inferior duct infection. However, previous studies have not provided conclusive evidence, and further investigation by authoritative research is necessary in order to form an opinion on this matter. Consequently, our study aimed to determine the diagnostic value of PCT in differentiating acute pyelonephritis from other inferior urinary tract infections(11,12). The results of our study indicated that PCT was positive in 98.5% of cases with pyelonephritis and in 5% of cases with cystitis, demonstrating a statistically significant difference (P=0.001).

The diagnostic accuracy of PCT was found to be 97.7%, with a sensitivity of 98.5% and specificity of 95%. In a study conducted by Saleh and colleagues, 100 patients were included, with 47 diagnosed with acute pyelonephritis and 53 with cystitis. The number of white blood cells (WBC) and erythrocyte sedimentation rate (ESR) differed significantly between the two groups, with higher averages observed in the acute pyelonephritis group. However, the average levels of procalcitonin did not show a significant difference between the two groups(13). In our study, we examined a larger sample size and found that WBC and ESR were not effective in differentiating between the two conditions, but a significant difference was observed in procalcitonin levels. In another study by Mahyar and colleagues, 70 children with urinary tract infections were

assessed, and the sensitivity and specificity of serum procalcitonin and interleukin 1-beta (IL-1ß) for diagnosing acute pyelonephritis were found to be 31.84% and 27.2% and 90%, respectively.

However, the sensitivity of procalcitonin and IL-1ß for diagnosing acute pyelonephritis was lower compared to conventional markers such as ESR and C-reactive protein (CRP). The study concluded that inflammatory markers like ESR and CRP, in addition to clinical findings, are reliable for diagnosing acute pyelonephritis in children(14). In our research, leucocytosis and elevated ESR were present in all cases, and although no significant relationship was found with these markers, CRP showed a meaningful correlation with procalcitonin. In a study by Chen and colleagues, which examined the diagnostic value of PCT in children with pyelonephritis, 136 children were included, with 87 diagnosed with pyelonephritis and 49 with urinary tract infections. The multivariate regression analysis identified procalcitonin and CRP as important predictors of pyelonephritis, indicating that PCT had a higher diagnostic value compared to WBC and CRP for both pyelonephritis and urinary tract infections(15). Similarly, our research revealed a significant association between CRP and pyelonephritis in addition to the observed correlation with procalcitonin.

In the study conducted by Rui-Ying and colleagues, the objective was to determine the serum levels of proxylatonin and CRP for the diagnosis of urinary tract infections. The results showed that PCT and CRP were notably elevated in children with pyelonephritis compared to children with UTI. Additionally, PCT values were found to be correlated with kidney involvement, whereas CRP values were not. The sensitivity of PCT in predicting nephropathy was reported to be 90.4% with a specificity of 88%. Similarly(16), in our research, the sensitivity and specificity were found to be 98.5% and 95% respectively.

Another study conducted by Saeedinejad and colleagues focused on the association between serum PCT levels and treatment response in patients with acute pyelonephritis. The study included 30 patients over the age of 30 with a positive inflammatory index. Prior to antibiotic treatment, serum PCT levels were measured, and the mean and standard deviation of PCT after treatment were reported to be 10.97 ± 1.46 and 0.54 ± 0.08 respectively in pyelonephritis with complications. The findings from this study support the use of PCT as an evaluation indicator for diagnosis and treatment response(17). In a retrospective study conducted by El-Said et al. in the United States, involving 437 patients, it was observed that prokelsitonin with a cutoff of 0.5 had a sensitivity of 80% and a specificity of 35% for diagnosing bacterial infections. However, it was concluded that prokelsitonin did not exhibit suitable sensitivity and specificity for diagnosing bacterial infections in individuals with renal failure undergoing hemodialysis. In contrast, our research reported higher sensitivity and specificity values(18). Finally, in a cross-sectional analysis study by Lee et al. in South Korea, published in 2015, it was found that serum proclexitonin levels were significantly higher in patients with chronic kidney failure who had infections. The sensitivity and specificity for detecting infections in these patients were reported to be 76.2% and 80% respectively, with lower percentages observed due to the smaller sample size(19).

In a comparative study conducted by Herget et al. in Germany, the findings of which were published in 2001, a total of 68 patients exhibited a tenderness incision point of 0/5 along with characteristics of 89% and 81% respectively. These results demonstrated a higher diagnostic efficiency in patients compared to the values of 89% and 48% obtained from CRP (20), thereby aligning with the outcomes of our own research. Similarly, an analytical study carried out by Steinbach and colleagues in Germany, which was published in 2004, identified that both procalcitonin and CRP levels increased in cases of hemodialysis with bacterial infection among 85 patients. However, the effectiveness of procalcitonin was found to be significantly inferior to CRP due to the elevated levels of

CRP in other inflammatory conditions (21), which is consistent with our research findings. Moreover, a cross-sectional study conducted by Dumea and colleagues in Romania and published in 2014 examined 82 patients, out of which 58 had a bacterial infection. The study revealed a significantly higher level of procalcitonin in patients with an infection, and the sensitivity and specificity were found to be 93% and 79%, respectively, using the specified cut-offs (22), thereby corroborating our study results. Furthermore, a cross-sectional study carried out by Fadel and colleagues in Egypt and published in 2016 investigated 102 patients, of whom 34 had a bacterial infection. The study observed a significantly elevated level of procalcitonin in the infection group, and with a cut-off value of 0.5%, the sensitivity and specificity were found to be 94% and 88%, respectively (23), which corresponds to the findings of our research.

Conclusion

Overall, based on the results of this study and their comparison with other studies, it can be deduced that procalcitonin is a reliable indicator for distinguishing pyelonephritis from other types of urinary infections, thus recommending its use for this purpose. Finally, it is advisable to conduct further studies with larger sample sizes and in a multicenter manner to confirm the findings of this study.

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Conflicts of interest

The authors declare no conflict of interest.

Authors' contributions

All authors were involved in the conception and design, analysis and interpretation of the data, drafting of the manuscript and revising it critically for intellectual content, approved the final version for submission, and agreed to be accountable for all aspects of the work.

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