



## Original Article

## Usefulness of procalcitonin rapid test for the diagnosis of acute pyelonephritis in children in the emergency department

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**Abstract** *Background:* Urinary tract infection (UTI) is a common problem in children. The aim of this study was to determine the usefulness of the procalcitonin (PCT) rapid test in the diagnosis of renal involvement in children with urinary tract infection.

*Methods:* Through a case series study, PCT and C-reactive protein rapid tests were measured in children with proven UTI at the Tehran Children's Medical Center, Iran. One-hundred patients aged 1 month–14 years old (19 boys and 81 girls) with documented UTI were enrolled in the study.

*Results:* Of 100 children, 62 patients (62%) had renal involvement on the basis of abnormal Tc-dimercaptosuccinic acid scintigraphy and 38 patients (38%) had infection restricted to the lower urinary tract. There were no differences related to age or gender among the groups. The sensitivity and specificity of PCT were 77% and 89%, respectively, in prediction of renal involvement, whereas C-reactive protein had a sensitivity of 80% and a specificity of 65%.

*Conclusion:* We concluded that a rapid determination of PCT concentration could be useful for the management of children with febrile UTI in the emergency room.

**Key words** children, C-reactive protein, Iran, procalcitonin, urinary tract infection.

Urinary tract infection (UTI) is one of the most common problems among infants and children: its prevalence is 3–5% in girls and 1% in boys. Furthermore, UTI in childhood is 2–4 times more prevalent in girls than boys.<sup>1,2</sup>

The general entry route of this infection is ascending and the origin of pathogens is perineal flora. Such an infection can be restricted to the bladder or spread to the kidneys causing pyelonephritis. Signs and symptoms of UTI in infants and children are nonspecific; therefore, the clinical differentiation of acute pyelonephritis and lower UTI is difficult. Common laboratory tests, such as serum leukocyte counts, neutrophil counts, erythrocyte sedimentation rate, and C-reactive protein (CRP) value cannot reliably differentiate acute pyelonephritis from lower UTI.

Accurate diagnosis and early treatment of acute pyelonephritis are important because of the high risk of renal parenchymal damage and subsequent secondary hypertension and renal failure. Previous studies noted that even children with unilateral renal disease are at risk for long-term complications. Therefore accurate rapid diagnosis of acute pyelonephritis would be

valuable, because early aggressive treatment reduces the risk of renal scarring.<sup>3–5</sup>

It is well known that Tc-dimercaptosuccinic acid (DMSA) scintigraphy performed during the acute phase of infection is very sensitive in assessment of renal parenchymal involvement. It is considered the gold standard method for the diagnosis of acute pyelonephritis.<sup>5–7</sup>

When DMSA scintigraphy is available the identification of patients at risk should be carried out with this technique but it is not readily accessible in all centers, it exposes patients to radiation, and it is expensive.<sup>5</sup>

Procalcitonin (PCT) is a 116-amino acid propeptide of calcitonin, the concentration of which is low (<0.1 ng/mL) in healthy individuals. Plasma PCT concentration rises to high values in response to endotoxins, and appears to be related to the severity of infection, but it is normal in patients with noninfectious inflammatory conditions or viral infections.<sup>8,9</sup>

Recently, quantitative measurement of PCT has been described as a valuable marker for the diagnosis and management of urinary tract infection in children.<sup>10–15</sup>

A few studies have been reported on the usefulness of the semi-quantitative rapid PCT test for the diagnosis of urinary tract infection in children.<sup>11</sup>

The purpose of the following study was to determine the diagnostic value of the PCT semiquantitative test in comparison with CRP to predict renal involvement in children with febrile UTI.

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## Methods

All 1 month to 14 year old children who were admitted to the infectious and nephrology departments of the Tehran Children's Medical Center with fever (rectal temperature  $\geq 38^{\circ}\text{C}$ ), signs and symptoms suggestive of urinary tract infection and/or a positive dipstick urinalysis, were enrolled in the study after a written consent was obtained from their parents.

Inclusion in the study was confirmed by a diagnosis of UTI based on a positive urine culture (any growth of microorganisms in suprapubic aspiration and/or  $>10^5$  microorganism/ml in clean void catch or sterile collection bags).

On admission, and before initiation of intravenous antibiotic therapy, blood was obtained for routine laboratory investigations including leukocyte count, CRP and PCT. CRP was measured by a rapid immunometric semiquantitative method (Kimiapajooan, Tehran, Iran) following the instructions of the manufacturer. A value of  $>20$  mg/L was considered abnormal.

In order to measure PCT, clotted blood was centrifuged, serum was separated and frozen at  $-20^{\circ}\text{C}$ , and then PCT was determined by a rapid semiquantitative immunochromatographic test (Brahms PCT-Q). Then 200  $\mu\text{L}$  of serum was applied to the test strip. Additionally PCT in the sample was bound by mouse anti-calcitonin antibodies to form a sandwich complex that could be seen as a reddish band. The color intensity of the band was directly proportional to the PCT concentration of the sample. Values of PCT were displayed in four different ranges:  $<0.5$ ,  $0.5-2$ ,  $>2-10$  and  $>10$  ng/mL. A PCT value of  $>0.5$  ng/mL was considered abnormal.

In the first 5 days of admission, renal cortical scintigraphy (CS) was performed on every child with positive urine culture. CS was considered to be abnormal if a focal, or diffuse decreasing or the absence of 99 m Tc-dimercaptosuccinic acid (DMSA) uptake was noticed. All children received antibiotics intravenously until the results of renal cortical scintigraphy were obtained.

Demographic characteristics and laboratory values of children with UTI were compared using the  $\chi^2$ -test and Fisher's exact test, and the Z-test was defined as  $P \leq 0.01$ .

The sensitivity, specificity, positive predictive value and negative predictive value of CRP and PCT rapid tests and binominal exact 95% confidence intervals were calculated. The best cut-off points of both tests were determined with a receiver operating characteristics curve. The likelihood ratio for a positive PCT or CRP test to predict acute pyelonephritis was calculated.

## Results

One hundred children with documented urinary tract infection were analyzed: nineteen were boys and 81 were girls. *Escheri-*

*chia coli* was isolated from the urine samples of 87 children. The other microorganism was *klebsiella* in five cases, *enterococcus fecalis* in five cases, and *proteus* in three cases. Blood cultures were negative in all patients. Among these patients, 63 were diagnosed as having acute pyelonephritis on the basis of abnormal DMSA, while the other 37 patients were diagnosed as having a lower UTI.

A comparison of children with cystitis and those with pyelonephritis demonstrated no statistically significant difference in age ( $P = 0.50$ ), gender ( $P = 0.38$ ) or white blood cell count ( $P = 0.24$ ).

The median PCT and CRP levels were significantly higher in the acute pyelonephritis group than in the lower UTI group.

PCT had a sensitivity of 77% and a specificity of 89% in prediction of acute pyelonephritis.

The sensitivity and specificity of CRP were 80% and 65%, respectively (Table 1).

## Discussion

The distinction between lower and upper urinary tract infection is important, because renal involvement can induce permanent renal damage (scars), which may lead to arterial hypertension and chronic renal failure.<sup>1-4</sup>

In the present study, significant renal lesions were observed for 63% of children in the acute phase of febrile UTI. These results are in accordance with other studies in which 61-67% of children with symptomatic febrile UTI had renal involvement and they confirm that infection of the lower urinary tract spreads to the upper tract and kidneys more frequently than expected in children.<sup>10-12</sup>

The nonspecific nature of symptoms among febrile infants and small children makes the clinical differentiation of acute pyelonephritis and lower UTI difficult.

DMSA scintigraphy performed during the acute phase of infection is considered the gold standard for the diagnosis of renal parenchymal involvement. However, it is an expensive test that is not readily accessible in all centers, and it also exposes the patient to radiation.<sup>6,7</sup>

It is well known that the commonly used laboratory markers like leukocyte count cannot reliably indicate the diagnosis of acute pyelonephritis, especially among young children.

Since Assicot *et al.* first proposed PCT as an early accurate marker of bacterial infections that seems to be correlated with severity of microbial invasion, interesting studies among children have been published.<sup>8,9</sup>

Recently, a few studies evaluated the accuracy of PCT levels, compared with CRP levels, to predict renal involvement among children with febrile UTI. Those previous studies have shown

**Table 1** Sensitivity, specificity, positive (PPV) and negative predictive values (NPV) of procalcitonin (PCT) and C-reactive protein (CRP) in children with acute pyelonephritis

	Sensitivity	Specificity	NPV	PPV	Likelihood ratio
PCT( $\geq 0.5$ ng/mL) <sup>†</sup>	77% (65-87) <sup>‡</sup>	89% (75-97)	71% (56-83)	92% (81-98)	7
CRP( $\geq 20$ mg/L)	80% (68-89)	65% (48.9-80)	67% (50-82)	79% (67-88)	2.29

<sup>†</sup>Cutoff determined by receiver operating characteristics curve analysis. <sup>‡</sup>Numbers in parenthesis, 95% confidence interval.

that PCT, determined by either an immunoluminometric quantitative or a rapid semiquantitative test, diagnosed acute pyelonephritis with a sensitivity of 70.3% to 94.1% and a specificity of 82.65% and 89.7%.<sup>10–15</sup>

The PCT-*Q*-test has been validated in adults, and studies have been published on its utility in patients with severe acute pancreatitis and patients treated in intensive care units. The PCT-*Q*-test allows a rapid, simple and semiquantitative measurement of plasma PCT to be made. Meisner *et al.* concluded that the validity of the test results and its ease of use are sufficient to support acute diagnostic decisions.<sup>16,17</sup>

In pediatrics there is one reference to the semiquantitative rapid test for PCT in children with UTI. In this study, a positive PCT-*Q*-value predicted renal involvement in 87–92% of children with febrile UTI, compared with 44–83% using CRP values.<sup>11</sup>

In the present study, the sensitivity and specificity of PCT with rapid semiquantitative method were 77% and 89%, respectively, and these results are in accordance with the study by Geravix *et al.*

As in recent studies, a positive correlation between high levels of CRP and abnormal results of a DMSA scan was found in our study with a sensitivity of 80%. However, the elevated CRP levels have a low specificity (65%), which limits the clinical usefulness in current practice. In fact, a large number of children with elevated CRP levels exhibited no renal lesions and would have undergone unnecessary tests, treatment and follow-up monitoring.<sup>10–12</sup>

In conclusion, these data indicate that at admission, the PCT test has a high sensitivity and specificity for the differentiation of acute pyelonephritis from lower UTI in infants and children and the semiquantitative rapid tests for procalcitonin could be useful for the management of children with febrile UTI in the pediatric emergency department, which may not have the quantitative determination procedures of the marker available.

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