

Research Article

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## The sensitivity of ultrasonography in detecting renal cortical defects in pyelonephritic patients with or without vesicoureteral reflux

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**Introduction:** The presence of renal scarring has been documented in 5% to 15% of febrile urinary tract infections. The main aim of this study was to compare the value of renal ultrasonography and cortical scintigraphy with technetium-99m dimercaptosuccinic acid (DMSA) in detecting renal cortical defects in acute pyelonephritis.

**Materials and Methods:** Between June 2003 and February 2012 a prospective cohort study of patients aged 1 month to 14 years of age was conducted. Pediatric patients with documented urinary tract infections were evaluated with renal ultrasonography, voiding cystoureterography (VCUG) and DMSA scintigraphy. Statistical test was two-tailed and was considered significant when  $P \leq 0.05$ .

**Results:** The results of DMSA scans showed 70.2% of cases as being abnormal. Renal ultrasonographies were reported to be normal in 72.45 and showed mild hydronephrosis in 37.7% of cases, moderate to severe hydronephrosis in 40.62%, stone formation in 13.66% and scar formation or decreased cortical thickness in 8.2%. There was a significant difference in ultrasonography reports between patients with normal and abnormal DMSA scans ( $P < 0.012$ ) but there was no significant difference in detection of scar formation between DMSA scan results and those of ultrasonography in our patients. Among patients with severe abnormalities on DMSA scintigraphy the percent of cases with vesicoureteral reflux was significantly higher than those with normal scans or mild to moderate changes on DMSA scintigraphy. (46.3% vs 26.9%).

**Conclusions:** We concluded that ultrasonography is a sensitive method for detection of renal cortical defects and ultrasonography can also predict the presence of vesicoureteral reflux in pyelonephritic patients.

**Keywords:** Ultrasonography; Pyelonephritis; Pediatrics; Vesico-ureteral Reflux; Technetium Tc 99m dimercaptosuccinic acid; Radionuclide imaging

**Running Title:** Ultrasonography and renal cortical defects

### Introduction

The incidence of childhood urinary tract infection (UTI) is unknown. An average incidence of 1% for both sexes is reported [1].

As a matter of fact 8% of girls and 2% of boys are estimated to have at least one episode of UTI during childhood [2].

Renal scarring has been documented in 5% to 15% of the pediatric patients after the first febrile UTI [3-5]. In previous studies ultrasonography was found to be an inappropriate study in the detection of renal parenchymal scars [6-7] with an unacceptable risk of missing scarring [8]. Since the advantages of ultrasound include the lack of ionizing radiation, availability and acceptability, other studies detailing a systematic approach to ultrasound for the detection of renal scarring shows promise to improve ultrasound sensitivity [9].

The main aim of this cohort study was to evaluate the sensitivity of renal ultrasonography in detecting renal cortical defects in pyelonephritic patients and compare it to DMSA scintigraphy as a golden standard test.

### Materials and Methods

Between June 2003 and February 2012 a prospective cohort study of patients aged 1 month to 14 years of age was conducted. A database was constructed of the study group. The diagnosis of UTI was deemed certain in the following instances: positive urine culture or in patients with negative urine cultures, significant leukocyturia in febrile children with clinical ([fever, abdominal pain, anorexia, dysuria and vomiting) and paraclinical (leukocytosis more than 10000/hpf, increased ESR > 20 mm/hr, positive CRP $\geq$  1+) accompanying signs and symptoms.

The diagnosis of pyelonephritis was documented by DMSA scintigraphy in all of them. The exclusion criteria included any evidence of renal insufficiency, previous known urological problems or surgical intervention, hypertension, recent history of antibiotic taking, extra renal infections. Patients who met the excluding criteria were segregated from our study. All patients were evaluated with renal ultrasonography and voiding cystoureterography (VCUG) during admission time. The evaluations to be performed in our study group included a complete blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), measurement of serum blood urea nitrogen, creatinine, urinalysis, and urine culture. Depending on the patients' age, the sample for urine culture was collected by urine bags, suprapubic aspiration or clean catch method. DMSA scintigraphy studies were done in the same center and all were reported by the same scintigraphy specialist.

The ultrasonographic studies were done by ESAOTE Au4-Idea in the same center. Glomerular filtration rate was calculated according to Schwartz' formula and was in the normal range in the study group. The ethics committee of the Shahid Beheshti Medical University and Pediatric Infectious Research Center approved this study. Data were expressed as mean $\pm$ SD. Findings were compared using the Mann-Whitney U test and Pearson's correlation coefficient. Statistical test was two-tailed and was considered significant when P less than 0.05. The SPSS software was used for statistical analyses.

### Results

According to this study, among 2550 pyelonephritic patients 82% were female. The mean age of our patients was 36.17 $\pm$ 33.87 months and the mean body weight was 27.8 $\pm$ 24.7 kg. the presenting symptom of pyelonephritis was fever in 83%, dysuria in 15.4%, vomiting in 12% and abdominal pain in 8% of cases. DMSA scan results were normal in 29.8% and abnormal in 70.2% (showing mild decreased cortical uptake in 43.4%, moderate decreased cortical uptake in 24.9%, severe decreased cortical uptake in 22.8% and scar formation in 8.9%). Renal ultrasonographies were reported as normal in 72.4% and abnormal in 27.6% (showing mild hydronephrosis in 37.7%, moderate to severe hydronephrosis in 40.6%, stone formation in 13.6% and scar formation or decreased cortical thickness in 8.1%). There was a significant difference in ultrasonography results between patients with normal and abnormal DMSA scans (P=0.012). There was no significant difference in detection of scars between DMSA scans and ultrasonographies in our patients (P=0.5). The sensitivity (95% CI) and specificity (95% CI) of ultrasonography for prediction of renal cortical defect in our study group, with DMSA scintigraphy as golden standard test were 69.2 (62.1 to 72.6) and 89.3 (80.2 to 94.9) respectively. In addition, the positive predictive value (PPV) of ultrasonography for prediction of renal cortical defects was 65.6% (60.5–70.9) and its negative predictive value (NPV) was 81.5% (75.9–84.7). The VCUG results were reported normal in 75.3% and showed vesicoureteral reflux in 24.7% (grade I in 54.2%, Grade II in 24.8%, Grade III in 12.5%, Grade IV in 4.45% and Grade V in 4.05%). Frequency of scar formation was not significantly different in patients with or without reflux. Among patients with severe abnormalities on DMSA scintigraphy the frequency of

vesicoureteral reflux was significantly higher than those with normal DMSA scans or with mild to moderate changes on DMSA scintigraphies. (46.3% vs 26.9%) Severe abnormalities on DMSA scintigraphy can predict the presence of vesicoureteral reflux with a likelihood ratio of 1.06 (1-1.26). There was a significant correlation between changes on DMSA scintigraphy and the presence of vesicoureteral reflux ( $P < 0.015$ ).

## Discussion

Urinary tract infection (UTI) is by far the most common serious bacterial infection in febrile young infant. When studying a child with urinary tract infection it is important to detect and localize any renal scars. It is well known that DMSA scan is at present the most sensitive method to detect renal defects. According to our study renal ultrasonography can also be a sensitive method for detection of renal scar. There has been a difference of opinion about the sensitivity of ultrasonography in detection of renal scars among investigations. Our previous studies showed that kidney ultrasonography and DMSA scans should be performed before VCUG in children with UTI and VCUG is indicated in cases of pyelonephritis with abnormal kidney ultrasonography or DMSA scan results [10]. We also reported a sensitivity of 84.1% and negative predictive value of 80.6% for  $^{99m}\text{Tc}$ -DMSA for prediction of vesicoureteral reflux [11]. Several years ago Almeida reported that three exams (ultrasound, DMSA scan and VCUG) were able to direct the diagnostic approach of UTI and were sufficient in most of the cases but at the same time they emphasized on the importance of the DMSA scan in comparison to ultrasonography in diagnosing unsuspected renal scars [12]. Then Stokland concluded that ultrasonography in isolation can not be recommended for the diagnosis of pyelonephritic renal scarring [13]. After that Lavocat suggested that normal US findings did not rule out renal parenchymal involvement in patients with acute pyelonephritis [7] and Christian reported a sensitivity of 21.7% for detection of renal cortical scarring for ultrasonography in school aged children with recurrent lower urinary tract infection [8]. Later Moorthy showed that ultrasonography cannot be substituted for DMSA scan in the evaluation of focal renal scarring [14] and recently Sinha concluded that if the detection of renal scars is a prime reason for imaging in children with urinary tract infections, ultrasonography alone is inappropriate at any age

and DMSA scan ought to be the primary investigation [15]. Despite the accepted low sensitivity of ultrasound for the detection of renal cortical scarring [6-8], some studies showed an improvement in ultrasound sensitivity [9,16] although there is an ongoing debate over the imaging investigations of children with urinary tract infections with some authorities suggesting that ultrasound alone is an accurate tool to diagnose renal parenchymal scarring post-pyelonephritis. It seems that, precise instruments and the more expert sonologists solve many of the misdiagnoses problems. Despite the previous results Monsor reported the equal sensitivity for DMSA scan and ultrasound over the age of five but not for fewer than five year old children [17]. Barry concluded that the sensitivity in the ultrasound detection of renal scarring can be greatly improved using this method and if no scars were detected at ultrasound an alternative explanation for an abnormal DMSA scintigram should be sought. They showed that using DMSA scintigraphy as the gold standard, ultrasound had a positive predictive value of 93% and a negative predictive value of 95% [9]. Scherz reported that renal ultrasounds that were interpreted as normal always correlated to a normal DMSA scan in asymptomatic patients. In patients presenting with febrile urinary tract infections the correlation between ultrasound and DMSA scan was inconsistent [18]. Roebuck reported an acceptable sensitivity for ultrasonography and showed that the sensitivity of ultrasonography for detection of renal scar, using DMSA as a gold standard, ranged from 37% to 100%, and its specificity from 65% to 99% [19]. A recent publication by Wang of a series of children with pyelonephritis confirmed that ultrasonographic findings are significantly correlated to the severity of inflammation in acute pyelonephritis and along with a high level of C-reactive protein, ultrasonography is helpful in predicting development of renal scarring [20]. It seems newly developed methods for imaging may further enhance sensitivity of ultrasonography for detection of renal damage.

## Conclusions

We concluded that ultrasonography is a sensitive test for detection of renal cortical defects and ultrasonography can also predict the presence of vesicoureteral reflux. In view of the non-invasive nature of ultrasound, general availability, lack of radiation, it's cheaper price and increasing experience in its use we would recommend it as a

first line investigation in urinary tract infection and for detection of renal cortical damage.

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## Conflict of Interest

None declared

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None declared

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