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Imaging studies in urinary tract infection in Libyan children

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Abstract: Acute pylonephritis is a common occurrence and results in irreversible renal damage which may lead later in life to arterial hypertension and renal insufficiency. This article is to review of the current role and controversies in imaging revealed VUR in 27.4% (14 of 51) patient with normal RUS. RUS has 22% sensitivity and 68% specificity in detecting VUR and 67% sensitivity and 47.7% specificity in detecting renal the kidneys to evaluate patients with acute pylonephritis. Patients and methods: retrospective study including 180 patients with acute pylonephritis (132 girls and 48 boys) mean age four years were uroradiologicalimages had been performed for them. Renal ultrasound and RUS were obtained at the time of diagnosis, voiding cysto urethrography (VCUG) was performed for 178 patients 4 - 6 weeks later, 99m technetiumdimer-captosuccuinic acid scan (DMSA) was performed for 155 patients 4 - 6 months after the infection. Results: RUS was abnormal in 190 renal units (51%) renal scaring was detected only in 9 (2.5%) kidneys by RUS, 37% (66 of 178) patients who underwent voidingcystourethrogram had abnormal VCUG. VCUG showed vesicoureteral reflux in 63 patients (35%), VCUG abnormalities whatever it is with positive predictive value of 79.8% and negative predictive value of 32%. VUR was bilateral in 53%, right side in 22%, left side in 25% of patients. Regarding the grade of VUR, it was grade I - II in 11%, grade III in 22%, and grade V - IV in (67%), 30% of patient with VUR were older than 5 years. DMSA revealed renal scarring in 74% (115 of 155) of patients. Renal scarring was seen in 86% of refluxing kidneys (risk factor 1.3, p = 0.005) and seen in 95% of kidneys with grade (IV - V) vesicoureteral reflux. Conclusion: renal ultrasound remains necessary in order to detect urinary tract abnormalities although it is not reliable to confirm the presence or absence of VUR. Significant incidence of VUR in children with UTI, VCUG is the golden standard in detecting VUR. Renal scarring is commonly seen and it was significantly correlated with the presence of VUR and the risk of scarring greatly increased with severe reflux.

Keywords: urinary tract infection, renal ultrasound, voiding cystourethrography, vesicouretral reflux, 99m technetiumdimercaptosuccunic acid scan, renal scarring.

Introduction

Acute pyelonephritis is a bacterial infection of the kidney that causes a tubulointerstitial inflammation of the renal parenchyma (1, 2). Acute renal infection is of varying severity, from uncomplicated acute infection to progressively worsening stages of interstitial inflammation, because histological specimens are difficult to obtained, exact clinical correlation with these various stages of inflammation is impossible. (1, 3-5). Therefore, the primary goal of renal images are to provide information about the nature, the extent of the disease and to identify significant complication. The diagnosis and treatment of children with documented UTI involves multiple imaging modalities and the strategy for uroradiological evaluation remains debatable. It has been proposed that some children with UTI do not need to undergo voiding cystourethrography (VCUG), dimercaptosuccunic acid (DMSA) scanning, especially if their renal ultrasound examination (RUS) is normal and having no history

of fever. In this article, it is tried to presents a review of the current role of and controversies in imaging the kidneys to evaluate patients with acute renal infection and to investigate whether imaging studies altered management or improved outcome in children with urinary tract infection.

Materials and methods

One hundred and eighty patients (132 girls and 48 boys) having a mean age of 4 years and ranging between 15 days and 14 years were included in a retrospective study from January 2000 to December 2003 and were presented to and evaluated in pediatric nephrology unit in Tripoli children's hospital with the diagnosis of acute pyelonephritis which defined as positive urine culture (growth of more than 105 colonies forming unit of a single organism per milliliter or any growth form supra pubic puncture specimen. Urine samples were collected as suprapubic puncture for the infants and clean mid stream urine for older children, in addition to symptoms and signs of acute pyelonephritis. All patients were regularly seen in the pediatric nephrology clinic where routine urinalysis and renal function test were done on regular basis and they were kept on prophylaxis antibiotic until their full evaluation completed their assessment. These patients were classified according to their age and sex into 3 groups, group 1: younger than 1 year, group 2: between 1 and 5 years and group 3: older than 5 years.

All the patients underwent renal ultrasound (RUS) examination at the time of presentation by an experienced pediatric nephrologist with Aloka apparatus equipped with five MHz frequency transducer; anterior, posterior, longitudinal and transverse views of each patient were obtained. Voiding cystourethrography (VCUG) performed for 178 patients. VCUG had been done after 4 - 6 weeks of the attack while patients had sterile urine urethral catheterization and retrograde filling of the bladder with radio graphic contrast and saline via gravity through a small catheter were done. The bladder and ureters were monitored throughout the filling and voiding phases under fluoroscopic were observed and post micturation film was taken. During this study, good drainage of the urine from the bladder and the ureters with adequate filling of the bladder was tried false negative results. Vesicuuretheric reflux (VUR) was graded according to the international reflux classification from I-V, taking in consideration the other anomalies such to avoid as posterior urethral valve, duplicated system; etc.

The 99m Technetium dimercaptosuccunic acid (DMSA) scanning was performed for 155 patients usually after 4 - 6 months of the infection in nuclear medicine center, read by a consultant of nuclear medicine, using a gamma camera computer system, the DMSA scan was performed with the patient supine and immobilized in a vacuum pillow, 2 - 3 hrs after intravenous injection of 99m technetium DMSA , anteroposterior and posterior anterior view was taken. DMSA scan was used for identification of residual parenchymal damage and not as a diagnostic tool during acute phase; it was considered abnormal if focal or diffuse areas of diminished or absence of cortical uptake with or without preservation of cortical outline, care was taken not to consider central defects located over the pelvicalyceal system as abnormal, areas of diminished uptake in association with volume loss represent old scars, complete absence of the radiotracer uptake interpreted as aplasia, images are also evaluated for the size of the kidneys, their shape and location.

The study group was comprised 180 patients. For data analysis, right and left kidney was considered separately in some occassions such as (RUS, scintigraphy)

Statistical methods used in data analysis are descriptive: mean, p-value, sensitivity and specificity.

Results

UTIs in children are subtle, can have long term consequences and are much more common than many clinicians suspected. One hundred eighty children aged from 15 days to 14 years (mean age of 4 years) were studied. They were 132 girls (73%) and 48 boys (27%) as shown in Table 1.

Table 1: Distribution of patients according to their age and sex

Age (Years)	Female (%)	Male (%)	Total
< 1	*11 (6%)*	*23 (12.7%)*	*34 (19%)*
1 – 5	*75 (42%)*	*19 (10.5%)*	*94 (52%)*
> 5	*46 (25.5%)*	*6 (3%)*	*52 (29%)*
Total	*132 (73%)*	*48 (27%)*	*180*

Table 2: Ultrasound findings according to renal (RU)

Ultrasound findings	Total (RU)	%
Normal	170	49
Abnormal	190	51
Hydronephrosis	147	40
Hyperechogenicity	18	5
Stone shadow	14	4
Small kidneys	14	4
Loss of corticomedullary differentiation	12	3.5
Irregular outline? Scarring	9	2.5
Ectopic kidneys	6	2
Unvisualized kidneys? Aplasia	5	1.4
Enlarged kidneys	4	1

In Table 2, VCUG was performed in 178 patients; it was normal in 112 (63%) patients and abnormal in 66 (37%) patients. The abnormal VCUG showed 94 VUR in 63 (35%) Patients, four patients has posterior urethral valve and severe bilateral VUR in two patients have duplex system with bilateral VUR, two patients have bladder diverticulosis, one of them has unilateral VUR, one patient has bilateral stones with bilateral VUR, one patient had neurogenic bladder with bilateral VUR, one patient has trabeculated bladder, and one patient has dilated urethra. Vesicoureteric reflux was bilateral in 31

patients (53%), right sided in 15 (22%) patients and left sided in 17 (25%) patients. Mild grade (I - II) were seen in 10 VUR (11%), 21 VUR (22%) had moderate grade (III) and 63 VUR (67%) had grade (IV, V), 38 (41%) - VURs were seen in 25 (39%) boys and 38 (61%) girls. Among 20 patients (32%) younger than one year who had VUR, 17 (75%) were boys and 5 (25%) were girls. While 24 (38%) patients aged between 1 - 5 years who had VUR, 20 (84%) were girls and 4 (16%) were boys and among the third group of patients whom older than 5 years VUR had been seen in 19 patients (30%), 6 (32%) patients were boys and 13 (68%) patients were girls as shown in Table 3.

Table 3: Distribution of VUR according to patient's age and sex

Age	Males		Females		Total
	Bilateral	Unilateral	Bilateral	Unilateral	
< 1 year	7 (11%)	8 (13%)	3 (5%)	2 (3%)	20 (32%)
1 – 5	4 (6%)	-	11 (17%)	9 (14%)	24 (38%)
> 5 years	3 (5%)	3 (5%)	3 (5%)	10 (16%)	19 (30%)
Total	14 (22%)	11 (17%)	17 (27%)	21 (33%)	63 (100%)

Among 51 patients with normal renal ultrasonography, VCUG revealed VUR in 14 (27.4%). Patients, their age from 7 month to 9 years, 13 girls and one male were found. 11 patients had ≥ grade III VUR, grade II in 4 patients. It was bilateral in 4 patients one of them has duplex system, right sided in 7 patients, and left sided in 3 patients. Re-implantation had been done for six of them. The renal ultrasound has 22% sensitivity and 68% specificity in detecting VUR. VCUG revealed 73 (51%) VUR out 143 kidneys with hydronephrosis, in three patients with bilateral VUR, hydronephrosis was seen in one side only while their VCUG. Revealed bilateral VUR. DMSA scintigraphy had been performed for 155 patients, it showed scarring in 115 (74%) patients, 4 patients have aplasia; 2 patients had hypoplastic kidneys, one patient has ectopic hypoplastic kidney; one patient has ectopic non-scarred kidney.

Ninety-four kidneys with VUR, out of them 82 (87%) were scarred. Ten kidneys with grad I-II VUR, 5 (50%) kidneys out of them were scarred, 21 kidneys with grade III, 17 (81%) of them were scarred .on the other side among 63 kidneys with grade IV-V VUR 60 (95%) of them were scarred.

Table 4*:* The relation between renal scarring and reflux grading

Grade of the reflux	No. of .VUR	Scarring
I, II	*10*	*5 (50%)*
III	*21*	*17 (81%)*
IV, V	*63*	*60 (95%)*

Discussion

Clinical and uroradiological evaluation of children with UTI is needed to identify those at risk of long term renal damage which may result in hypertension and impaired kidney function. The search has been aimed at such as obstruction, abnormal kidney size, location, and VUR. UTI is a common clinical problem in infants and children and suggest that the introduction of proper and active medical treatment policy is mandatory to minimize or even prevent parenchymal scarring (7, 8). The clinical criteria for pyelonephritis are not universally accepted by all nephrologists if the implication in published work is assessed carefully. The clinical inability to differentiate upper from lower UTI is highlighted by the finding that almost third of children diagnosed with pyelonephritis by standard clinical criteria had no parenchymal defects when studied with both renal scintigraphy and MRI (9). Imaging studies are used to determine both whether a renal infection is present and to show the extent of the infection. It is common practice, especially in male neonates, to perform routine imaging by RUS, VCUG and renal scan (7, 10).

In 1991, the Royal College of Physician recommended the performance of US, VCUG, and DMSA studies in infants younger than one year, and US and DMSA for those between 1 and 7 years (11), those recommendations are not based on firm evidence (12). The American Academy of Pediatrics (AAP) recently recommended performing an RUS and VCUG in infants 2 - 24 months old with UTI the clinical contribution of the DMSA scan has been questioned (13, 58). The AAP Task forces that renal ultrasonography of the kidneys and bladder should be used during the acute phase of UTI to detect parenchymal infection or structural anomalies which may compromise usual treatment (12). Renal ultrasonography is known to be safe, simple, painless, non invasive and non traumatic to the child and the family.

In the present study, it is good at detecting anatomical abnormalities, assessing bladder emptying, presence of stone shadow, and sign of acute pyelonephritis such as increased kidney size, hyperechogenicity, loss of corticomedullary differentiation due to interstitial edema (8, 14, 15). Unfortunately, it is less reliable at detecting focal renal parenchymal scarring which has been detected only in (5%) of patients by RUS, in contrast, DMSA scintigraphy showed diminished radiotracer uptake in (74%) of patients. Similar finding was found in other studies (8, 15, 19, 30) which have found that RCS is more sensitive than RUS in detecting sign of permanent renal parenchymal damage due to acute pyelonephritis. However, RUS is less precise than other methods for detecting vesicoureteric reflux and its grade (8, 15, 25-28).

In this study, it had low sensitivity and relatively low specificity at which it was found that 27% of the patients with normal RUS their VCUG revealed VUR which was of significant grade in most of them they were almost girls aged between 7 months to 9 years. Previous studies (7, 13, 15, 26, 27) showed that VUR has been consistently found in approximately one third of children who have at least one urinary tract infection. In this study, 35% of patients with UTI have VUR by VCUG which was bilateral in more than half (53%) of them, VUR was more common among girls (61%), the highest number of patients (38%) having VUR was diagnosed between 1 - 5 years of age. Reflux nephropathy accounts for 7 - 17% of end stage renal disease worldwide (29, 30), therefore, this high incidence seems to be enough to recommend performing VCUG for all patients with proven UTI even in those older than 5 years as our results revealed that (30%) of patients with VUR were older than 5 years. Most of recent studies (26, 27, 38, 40 - 42, 56, 58), as well as ours shows high incidence of renal parenchymal involvement (74%) detected by renal cortical scintigraphy in children assessed for pyelonephritis, which in our study could be due to recurrent UTI or it may be due

to acute changes which still not resolve so, RCS allowed the diagnosis of renal parenchymal changes that were not detected by RUS. The problem is that not all defects seen on DMSA study represent true scaring (41). It is known from animal studies (31, 34) that acute pyelonephritis produces a defect in the DMSA scan which may persist for some time after acute infection. Jakobsson and Svensson (39) showed prospectively that significant resolution may occur up to 5 months after UTI. Therefore, to confirm scaring, it is probably necessary to wait for at least 6 months after the treatment of an acute UTI. (41, 56, 58) as in other studies (36, 40, 44-46), our results shows that renal scarring was significantly ($p = 0.005$) correlated with the presence of reflux (87%) and the risk of scarring greatly increased (95%) with sever reflux. Interest in detecting reflux with ultrasound developed because of concern with the gonadal radiation of the existing techniques, the use of radionuclide voiding cysto urethrography had been recommended for VUR follow up studies, US has been used to detect reflux in many ways (50-52); contrast enhanced US VCUG has been developed as an alternative to conventional X ray VCUG. (Recently described refinement of the original technique was compared with a conventional VCUG as a golden standard; the sensitivity of US method was 100% with a specificity of 97% (53). Also, color Doppler of the bladder has been used to detect the presence of the reflux (54).

In conclusion, renal ultrasonography remains necessary in order to detect urinary tract abnormalities although it is not reliable to confirm the presence or absence of VUR and renal parenchymal changes. VCUG is the golden standard in detecting VUR. High incidence of VUR was found in children even more than 5 years. Renal scarring was commonly seen in patients with acute pylonephritis and it was significantly correlated with presence of gross VUR. Renal cortical scintigraphy is the preferred imaging study for the evaluation of children with acute pyelonephritis and in detecting renal scarring. It can be recommend that a proper evaluation and active medical treatment policy is mandatory to minimize or even prevent renal scarring. Performing VCUG in all children with UTI regardless their age, sex and their renal ultrasound result, in order to initiate, continue or stop prophylactic antibiotic on a hard basis and a proper timing of surgical intervention if needed in attempt to prevent renal damage. Creation and introduction of safe, comfortable and sensitive method such as contrast enhanced US. VCUG for detection and follow up of VUR are recommended.

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