ROLE OF VARIOUS IMAGING MODALITIES AFTER A FIRST FEBRILE URINARY TRACT INFECTION IN YOUNG CHILDREN

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ABSTRACT

BACKGROUND

UTI in the paediatric population is well-recognised as the cause of acute morbidity and chronic medical conditions such as hypertension and renal insufficiency in adulthood.¹ The goal of imaging studies in children with UTI is to identify anatomic abnormalities that predispose to infection, determine whether there is active renal involvement and to assess whether renal function is normal or at risk.

Aims and Objectives-

- To measure the incidence of renal scarring in patients admitted with first febrile UTI.
- To list renal image findings in patients with first febrile UTI, 1 - 36 months of age.

MATERIALS AND METHODS

A total of 108 patients, 1 - 36 months of age, coming with first febrile UTI, either admitted or on an outpatient department basis during one and a half years, who satisfy the inclusion criteria were studied. Renal scanning with technetium-99m labeled dimercaptosuccinic acid and renal ultrasonography were performed in the acute phase to determine the presence or absence of acute pyelonephritis and anatomical abnormalities, respectively. Contrast voiding cystourethrography was performed approximately one month after diagnosis in those with abnormal ultrasound or abnormal DMSA. Technetium-99m labeled dimercaptosuccinic acid renal scanning was repeated six months later to determine the incidence and severity of renal scarring. Age groups, sex, VCUG, renal ultrasonography and DMSA renal scintigraphy results were analysed.

RESULTS

Out of 108 patients, RBUS was normal in 63 (58%) and abnormal in 45 (42%). Sonogram showed changes consistent with acute pyelonephritis in 27.7% (30/108) of the whole group and in only 57.7% (30/52) of the patients with scintigraphically documented acute pyelonephritis. DMSA was suggestive of acute pyelonephritis in 52 (48%) patients in acute stage and of renal scarring in 22 (20%) at 6 months. All patients who had scarring at 6 months had abnormal initial scan. Out of 69 patients with abnormal ultrasonography or scanning who were subjected to VCUG, 39 had vesicoureteral reflux (56.5%). Renal scarring was more likely to occur in children with documented VUR than those without VUR (17/39 vs. 5/30). Among the patients with VUR, scarring was seen more likely in patients with higher grades of VUR.

CONCLUSION

The renal ultrasound is of limited value in febrile UTI, especially at places where DMSA scanning is available. The use of DMSA during acute illness identifies patients with acute pyelonephritis who are at risk of development of renal scarring later in life. VCUG may demonstrate a relationship between VUR and renal inflammation and identify high-risk group for development of renal scarring.

KEYWORDS

Urinary Tract Infection, VUR, DMSA Scan.

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BACKGROUND

UTI in the paediatric population is well-recognised as a cause of acute morbidity and chronic medical conditions such as hypertension and renal insufficiency in adulthood.¹ The goal of imaging studies in children with UTI is to identify anatomic abnormalities that predispose to infection,

determine whether there is active renal involvement and to assess whether renal function is normal or at risk.¹ The algorithm for the radiographic evaluation of children with febrile urinary tract infection is hotly debated. Three imaging modalities are commonly administered: renal-bladder ultrasound (RUS), voiding cystourethrogram (VCUG) and dimercaptosuccinic acid scan.²

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MATERIALS AND METHODS

This study was conducted in the Postgraduate Department of Paediatrics, SKIMS, Srinagar for a period of two years (from November 2013 to November 2015).

Inclusion Criteria

Patients were enrolled if they met the following criteria: Rectal temperature of at least 38.3° C at presentation or within 24 hours and if a urinary tract infection is suspected. The presence of pyuria (10 or more white cells per cubic millimetre in uncentrifuged urine). Bacteriuria (1 or more gram-negative rods per 10 oil-immersion fields in a Gram-stained smear of uncentrifuged urine). A positive urine culture (at least 50,000 colony-forming units per millilitre, representing a single pathogen) from a specimen obtained by suprapubic aspiration.

Exclusion Criteria

Patients were excluded from the study if they had history of previous episodes of UTI and Pyelonephritis or evidence of renal scarring in DMSA scan in acute phase.

A total of 108 patients 1 - 36 months coming with first febrile UTI, either admitted or on an outpatient department basis during one and a half year who satisfy the inclusion criteria were studied. All patients aged between 1 - 36 months with first febrile UTI who fulfilled the inclusion criteria were evaluated by ultrasound and dimercaptosuccinic acid [DMSA] scintigraphy scan in the acute phase. In those patients with normal ultrasound and normal dimercaptosuccinic acid [DMSA] scintigraphy scan, rescanning was done at 6 months. Those with abnormal ultrasound or abnormal dimercaptosuccinic acid [DMSA] scintigraphy scan underwent voiding cystourethrography and due follow-up and rescanning was done 6 months later.

Imaging Studies

Renal scanning with technetium-99m labeled dimercaptosuccinic acid and renal ultrasonography were performed in the acute phase to determine the presence or absence of acute pyelonephritis and anatomical abnormalities, respectively.³ Renal ultrasound was considered normal if bilateral kidneys were normal and there was no evidence of dilatation of pelvicalyceal system. Hydronephrosis was graded as-

Grade 0

No dilatation, calyceal walls are opposed to each other.

Grade 1

(Mild) Dilatation of the renal pelvis without dilatation of the calyces (can also occur in the extrarenal pelvis). No parenchymal atrophy.

Grade 2

(Mild) Dilatation of the renal pelvis (mild) and calyces (Pelvicalyceal pattern is retained). No parenchymal atrophy.

Grade 3

(Moderate) dilatation of the renal pelvis and calyces. Blunting of fornices and flattening of papillae. Mild cortical thinning may be seen.

Grade 4

(Severe/ Gross) dilatation of the renal pelvis and calyces, which appear ballooned. Loss of borders between the renal pelvis and calyces renal atrophy is seen as cortical thinning.⁴

Contrast voiding cystourethrography was performed approximately one month after diagnosis, in those with abnormal ultrasound or abnormal DMSA. Vesicoureteral reflux was graded according to the classification system of the International Reflux Study Committee; grade I indicates reflux into the proximal ureter without dilatation, grade II reflux into the distal ureter without dilatation and grades III, IV and V reflux into the distal ureter with mild, moderate and severe dilatation, respectively.⁵

Technetium-99m labeled dimercaptosuccinic acid renal scanning was repeated six months later to determine the incidence and severity of renal scarring.³

Definitions

Technetium-99m labeled dimercaptosuccinic acid scans were considered normal if homogeneous uptake of the radioisotope was evident throughout the kidneys and the renal contour was preserved.

Acute pyelonephritis was defined by the presence of focal or diffuse areas of decreased uptake of labeled dimercaptosuccinic acid without evidence of cortical loss or by the presence of diffusely decreased uptake in an enlarged kidney.

Renal scarring was defined by the presence of decreased uptake of labeled dimercaptosuccinic acid associated with loss of the contours of the kidney or by the presence of cortical thinning with decreased volume.³

Statistical Methods

The interpretation of results was done using Fisher and chi-square tests. SPSS (version 20.0) and Microsoft Excel were used for carrying out the statistical analysis of the data.

Long-Term Follow-Up

The children were followed for six months. Urine cultures were obtained at the time of most febrile illnesses. A history of fever or other signs or symptoms compatible with urinary tract infection was elicited during interim visits.

Age groups, sex, VCUG, renal ultrasonography and DMSA renal scintigraphy results were analysed. Before study enrolment, a written consent was required from the parent (s) for all patients. Institutional ethics approval was obtained prior to the study.

RESULTS

A total of 108 children in the age group of 1 - 36 months were included. 47.2% (51 patients) were males and 52.8% (57 patients) were females.

Figure 1. Age Distribution of Patients with First Febrile UTI

All patients following first febrile UTI were evaluated using an initial technetium 99m-labeled dimercaptosuccinic acid scintigram and a renal ultrasonogram within the first week of diagnosis. Of 108 ultrasonograms 63 (58%) were normal, the rest being abnormal as shown in Table 1. Thirty seven patients had findings suggestive of hydronephrosis (34.2%). The initial dimercaptosuccinic acid scan showed that 52 out of 108 children (48.1%) had findings suggestive of acute pyelonephritis. The total number of patients with acute pyelonephritis having ultrasonographic abnormalities associated were 30 (57.7% of total 52 patients).

Findings	No. of Renal Units	No. of Patients
Dilated pelvis	12	7
Absent kidney	1	1
HDN Gr I	9	37
Gr II	16	
Gr III	18	
Gr IV	7	
Normal	153	63

Table 1. USG Findings in Patients with First Febrile UTI

Voiding cystourethrography (VCUG) was performed after a period of 1 month in those children who either had an abnormal ultrasonogram or evidence of acute pyelonephritis on initial DMSA or both. The findings are depicted in Figure 2.

Figure 2. VCUG Findings in Patients in Terms of Renal Units

DMSA scan performed 6 months later showed scarring in 22 patients (20.3%) of overall patients. All children whose initial scans were normal had normal scans at follow-up. 42.3% of the children with acute pyelonephritis (22/52) had evidence of renal scarring 6 months later.

The occurrence of renal scarring in different age groups is tabulated in Table 2. However, no significant relationship could be found (p value > 0.05).

Age in Months	No. of Patients	Renal Scarring	%
Up to 6 Months	43	8	19
7-12 Months	20	6	30
12-24 Months	24	4	17
24-36 Months	21	4	19

Table 2. Age Related Renal Scarring

Out of the total 69 patients who underwent VCUG, renal scarring was more likely to occur in children with documented VUR than those without VUR (17/39 vs. 5/30), p value < 0.017 . Among the patients with VUR, scarring was seen to occur more likely in patients with higher grades of VUR (p value < 0.001) as depicted in Table 2, Figure 3.

Figure 3. Relationship between Cortical Scarring and VUR in Terms of Renal Units

DISCUSSION

Febrile UTI, in particular, is a widely researched topic because of the potential to cause renal scarring resulting in hypertension, preeclampsia, renal insufficiency and end-stage renal disease. Children suffering from UTI are frequently referred for various imaging studies including renal bladder ultrasonogram (RBUS), radionuclide 99-Technetium dimercaptosuccinic acid scan (DMSA), computed tomography (CT Scan) and magnetic resonance imaging (MRI) of urinary tract on an assumption that early detection of urological abnormalities will lead to improved outcomes.⁶ It is the endeavour of paediatric specialists throughout the world to reach an investigation and management protocol that is highly efficacious in preventing the complications of UTI and at the same time does not expose young kids to superfluous and invasive investigations. Our study is an attempt in this direction and it aspires to answer the queries surrounding UTI in children.

Being non-invasive, a renal ultrasonogram (RBUS) is often the first investigation done and was done in all our patients within the first week of diagnosis. Out of 108 patients, RBUS was normal in 63 (58%) and abnormal in 45 (42%). Sonograms showed changes consistent with acute pyelonephritis in 27.7% (30/ 108) of the whole group and in only 57.7% (30/52) of the patients with scintigraphically documented acute pyelonephritis. Poor sensitivity of RBUS in detection of pyelonephritis has been inferred by Bjorgvinsson

et al, Foresman et al and Nguyen et al.^{7,8,9} Bjorgvinsson et al had ultrasonographic changes consistent with acute pyelonephritis in 24% (22/91) of whole group. Foresman et al summarised that ultrasound findings during acute pyelonephritis do not correlate with and are not predictive of presence or grade of VUR on subsequent VCUG. Thus, we conclude that RBUS is not very sensitive for diagnosis of acute pyelonephritis in febrile UTI. Hydronephrosis of varying severity was detected in 37 (34.2%) of our patients. However, as 39 patients did not undergo VCUG as per AAP guidelines, the usefulness of RBUS in detecting VUR could not be evaluated. High false positive rate of ultrasonography could be attributed to high frequency of *E. coli* UTI in our patients, which has been associated with dilatation of urinary tract in acute stage and can lead to erroneous interpretation of hydronephrosis as was reported by Alan S Peterson in 2012.¹⁰ The use of routine ultrasound in children in whom first febrile UTI is diagnosed can be of importance in finding patients with obstructive lesions in developing countries, where use of foetal ultrasonography is still limited. In this study, it was also noted that higher grade VUR (Grade 3 or 4) was more likely to occur among children with abnormal ultrasonographic findings than among those with normal findings (28/63 vs. 3/75; p value < 0.001). Similar findings were seen in a study published in 2003 by Hoberman et al in which vesicoureteral reflux of grade III or IV was more likely to occur among children with abnormal ultrasonographic findings than among those with normal findings (p = 0.02).¹¹ Therefore, the benefit of RBUS in the armamentarium against febrile UTI appears to be its affordability and availability and its ability to detect higher grades of VUR; however, its utility in detecting pyelonephritis looks limited.

Scintigraphy was also done in our patients, both in the acute stage and after 6 months to detect renal scarring. DMSA was suggestive of acute pyelonephritis in 52 (48%) patients in acute stage and of renal scarring in 22 (20%) at 6 months. All patients who had scarring at 6 months had abnormal initial scan. USG findings were suggestive of pyelonephritis in only 30. All children whose initial scans were normal had normal scans at follow-up. Hoberman et al in a study published in 2003 demonstrated similar findings.¹¹ Therefore, we conclude that DMSA appears to be the best available investigation for detection of acute pyelonephritis. It can also predict who is less likely to develop renal scarring in febrile UTI patients. Usefulness of DMSA scan in febrile UTI has been documented by other researchers as well¹¹⁻¹⁹ and has been endorsed by AAP, who now recommend it in all children < 24 months with first febrile UTI. However, routine use of this imaging during acute illness does not alter treatment in the majority of cases and it does not predict who exactly is going to develop scarring. The results of Hoberman et al suggested that in children two years of age or younger who have a first febrile urinary tract infection, the results of approximately 60 to 65 percent of imaging studies will be abnormal. On the assumption of a sensitivity of 85 to 90 percent, nearly 75 percent of young children with fever and clinically significant bacteriuria will have acute pyelonephritis. It may therefore be reasonable for the clinician to assume that nearly all such children have acute pyelonephritis.¹¹

Only those patients whose ultrasonography or scanning revealed abnormalities were subjected to VCUG. In patients

with acute pyelonephritis, patients with VUR were seen more likely to end up in renal scarring than those without VUR (17/30 vs. 5/22; p value < 0.022). Out of the total 69 patients who underwent VCUG, renal scarring was more likely to occur in children with documented VUR than those without VUR (17/39 vs. 5/30; p value < 0.017). Among the patients with VUR, scarring was seen to occur more likely in patients with higher grades of VUR (p value < 0.001). Similar relationship of VCUG with scintigraphic abnormalities was found by Hoberman A et al and Ajdinović et al.^{11,20} Hoberman et al observed degree of vesicoureteral reflux was significantly associated with a higher incidence of renal scarring (p = 0.007).¹¹ Though VUR is also an established important factor in genesis of renal scarring and thereafter hypertension and end stage renal disease, routine use of VCUG in febrile UTI has been questioned by many.^{3,17,18,19,21} However, further research is needed.

The overall incidence of renal scarring in this study was 20.3%, which is lower than the 30 percent previously reported.^{22,23,24} The relatively low incidence observed in this study may have resulted from the active surveillance for and treatment of urinary tract infection in young children with fever. Compared to intravenous pyelography, the renal scintigram is very sensitive for detection of renal scarring in patients following acute pyelonephritis. Earlier studies demonstrated the sequelae of reflux nephropathy i.e. hypertension, renal insufficiency and end stage renal disease in a significant group of patients.^{25,26} But the method of detection used was intravenous pyelography, which was substantially less sensitive than technetium-99m labeled dimercaptosuccinic acid scanning and almost certainly identified children with extensive rather than minimal parenchymal damage. A study of women with scarring using DMSA confirmed that renal function was reasonably well preserved and that the incidence of hypertension was lower than had previously been reported.²⁷

CONCLUSION

To conclude, the results of this study suggest that the renal ultrasound is of limited value in febrile UTI, especially at places where DMSA scanning is available which identifies patients with acute pyelonephritis who are at risk of development of renal scarring later in life. VCUG may also demonstrate a relationship between VUR and renal inflammation and identify high-risk group for development of renal scarring (Patients with high-grade VUR). However, the exact role of these modalities in evaluation and management of patients with first febrile UTI is still being debated and further studies are required in this regard.

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