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.

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 VCGU, 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.


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.

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
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. 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. Vescoureteral 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 radiisotope 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.
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).

<table>
<thead>
<tr>
<th>Findings</th>
<th>No. of Renal Units</th>
<th>No. of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dilated pelvis</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Absent kidney</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>HDN Gr I</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Gr II</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Gr III</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Gr IV</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>153</td>
<td>63</td>
</tr>
</tbody>
</table>

Table 1. USG Findings in Patients with First Febrile UTI

Voiding cystourethography (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.

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.

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.

Table 2. Age Related Renal Scarring

<table>
<thead>
<tr>
<th>Age in Months</th>
<th>No. of Patients</th>
<th>Renal Scarring</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Up to 6 Months</td>
<td>43</td>
<td>8</td>
<td>19</td>
</tr>
<tr>
<td>7-12 Months</td>
<td>20</td>
<td>6</td>
<td>30</td>
</tr>
<tr>
<td>12-24 Months</td>
<td>24</td>
<td>4</td>
<td>17</td>
</tr>
<tr>
<td>24-36 Months</td>
<td>21</td>
<td>4</td>
<td>19</td>
</tr>
</tbody>
</table>

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 99m-Tc 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. 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. 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. 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). 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. 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 well and has been endorsed by AAP, who now recommend it in all patients following acute pyelonephritis. Earlier studies have demonstrated the sequelae of reflux nephropathy i.e. hypertension, renal insufficiency and end stage renal disease in a significant group of patients. 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 demonstrated the sequelae of reflux nephropathy in 24% (22/91) of whole group. Foresman et al and Nguyen et al. 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. 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). 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.

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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.

REFERENCES


