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# Comparison of Renal Ultrasonography and Technetium 99-M Dimercaptosuccinic acid Renal Cortical Scintigraphy in Identifying Renal Parenchymal Defects in Febrile Urinary Tract Infection In Children Less than Five Years Age

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**Abstract**

**Background**: *UTIs are common infections that happen when bacteria, often from the skin or rectum, enter the urethra and infect the urinary tract. The infections can affect several parts of the urinary tract, but the most common type is a bladder infection (cystitis). Dimercaptosuccinic acid (DMSA) scintigraphy is the gold standard in the evaluation of renal parenchymal defects and is widely used in the pediatric population. As more recent ultrasound equipment was purchased at our tertiary pediatric center, our objective was to evaluate if renal ultrasound (US) results are equivalent or sufficient when compared to DMSA scintigraphy in the assessment of renal anomalies.*

**Aim and Objective**: *To find out whether renal ultrasonography or dimercaptosuccinic acid renal scintigraphy can be used as the first imaging modality after a case of febrile Urinary tract infection in children less than 5 years of age.*

**Methods**: *This prospective observational study was conducted in the Pediatric department of KMCH, Coimbatore from MAY 2019 – DECEMBER 2019. . 90 children with culture-proven febrile Urinary tract infection from the department of pediatrics KMCH will be included in the study to compare technetium-99m DimercaptoSuccinic Acid renal cortical scintigraphy and Ultrasound KUB in detecting renal parenchymal defects in Febrile Urinary tract infection in children.*

**Results**: *In our study out of 90 children 53.3% were males and 46.7% were female. All children included in this study were significant Urine Culture Positive. The most common organism isolated in urine culture was E. coli followed by Klebsiella. In our study, the sensitivity and specificity of USG KUB in detecting Renal parenchymal abnormalities in comparison with DMSA is 12 % and 95.4 % respectively. And the positive predictive value of USGKUB is 50% and the negative predictive value is 73.8 % in detecting parenchymal defects in children when compared to DMSA.*

**Conclusion**: *It is observed from our study that although ultrasonography has a good specificity in the detection of renal parenchymal defects when compared with DMSA, it has low sensitivity, positive predictive value, and negative predictive value. Thus we conclude that at present Ultrasonography cannot be substituted for DMSA in identifying renal parenchymal defects in children with Febrile UTI. Dimercaptosuccinic acid scan done at presentation identifies children with acute pyelonephritis and at six months later identify those children with scarring*

**Keywords:** *Urinary Tract Infection, Ultrasound Kidney Ureter Bladder, Di Mercapto Succinic Acid renal scintigraphy, Micturating Cysto Urethrogram, Escherichia Coli.*

## Introduction

Urinary tract infection is a common infection in children with variable Symptomatology.UTI is defined by symptoms (which include fever, vomiting, lethargy, jaundice in neonate and fever, diarrhea, vomiting, abdominal pain and poor weight gain in young children and fever, dysuria, urgency, frequency, abdominal or flank pain in older children) and positive culture in the urine. Recurrent UTI is defined as the second episode of culture-proven UTI.[1] In girls, the first Urinary tract infection usually occurs during infancy and toilet training. Most of all UTIs are ascending infections. The bacteria arise from the fecal flora, colonize the perineum, and enter the bladder via the urethra. In uncircumcised males, the bacterial pathogens arise from the flora beneath the prepuce. In some cases, the bacteria causing cystitis ascend to the kidney to cause pyelonephritis[2]. Rarely, renal infection occurs by hematogenous spread, as in endocarditis or some bacteremic neonates. If bacteria ascend from the bladder to the kidney, acute pyelonephritis can occur. Normally, the simple and compound papillae in the kidney have an antireflux mechanism that prevents urine in the renal pelvis from entering the collecting tubules.[3] However, some compound papillae, typically in the upper and lower poles of the kidney, allow intrarenal reflux. Infected urine stimulates an immunologic and inflammatory response, causing renal injury and scarring. Children of any age with a febrile UTI can have acute pyelonephritis and subsequent renal scarring, but the risk is highest in those younger than 2 years of age. Certain bacteria have characteristics that favor the establishment of infection.[4] The pathogenesis of E.coli is based in part on the presence of bacterial pili or fimbriae on the bacterial surface. There are two types of fimbriae, type I and type II. Type I fimbriae are found in most strains of E. coli. Attachment to target cells can be blocked by D –mannose in the host, these fimbriae are referred to as mannose sensitive. They have no role in pyelonephritis.[5] The attachment of type II fimbriae is not inhibited by mannose, and these are known as mannose resistant. These fimbriae are expressed by only certain strains of E. coli. The first step in an E. coli UTI is the attachment of the bacteria to the mannose receptor on the umbrella cells, the cells lining the bladder. These bladder-lining cells may take E. coli into the cell, where the bacteria replicate in the nutrient-rich environment, forming intracellular bacterial communities.[6] When the lining of the bladder is shed, E. coli may betake up in the cells of the bladder wall, where they form quiescent intracellular reservoirs.[7] The dormant QIRs are completely protected from antibiotics and maybe a source of recurrent infections. Much current research is attempting to prevent the initial attachment of bacteria to the bladder wall that can lead tothe IBCs and QIRs The lipopolysaccharide of the bacteria binds to CD14 on the cell surface, activating toll-like receptor 4.[8] Through subsequent steps, this activates transcription factor nuclear factor κB (NF-κB), which migrates into the cell nucleus, stimulating the production of inflammatory factors, including cytokines, chemokines, nitric oxide, and transforming growth factor β.[9] These mediators induce an inflammatory response, which increases vascular permeability and recruitment of neutrophils to resolve the infection, but the mediators are also responsible in part for the ensuing kidney scarring[10]

## Methods

This prospective observational study was conducted in the Pediatric department of KMCH, Coimbatore from MAY 2019 – DECEMBER 2019. 90 children with culture-proven febrile Urinary tract infection from the department of pediatrics KMCH will be included in the study to compare technetium-99m Dimercaptosuccinic Acid renal cortical scintigraphy and Ultrasound KUB in detecting renal parenchymal defects in Febrile Urinary tract infection in children. The Positive Predictive Value, specificity, sensitivity of the study done by Maryse Marceau- Grimard et al (2014) is 64%, 93%, 32% respectively in the division of urology, QC, Canada. Based on the above observation, the Sample size calculated

using n-master software (designed by CMC Vellore) using the diagnostic test, on calculating sample size using PPV at 95% Confidence Interval and precision of 10% was89.Culture proved febrile Urinary tract infection in children less than 5 years of age.

**Inclusion Criteria:** Symptomatic child with growth of ≥ 5*10 POWER 4 colony forming units (CFU)/mL organisms from a catheterized specimen, ≥ 10 POWER 5 CFU/mL organisms from a clean catch, midstream, or bag specimen, Any number of pathogens from a suprapubic specimen. first episode or recurrent Urinary tract infection 3.age less than 5 years.

**Exclusion Criteria:** Ectopic kidneys. horseshoe or malrotated kidneys, renal agenesis post-renal transplant. After getting informed consent from the parents/attenders of the children who fulfill the inclusion and exclusion criteria, the prospective study will be conducted in KMCH. Totally 90 children with culture-proven febrile Urinary tract infection from the department of pediatrics KMCH will be included in the study to compare technetium-99m Dimercaptosuccinic Acid renal cortical scintigraphy and Ultrasound KUB in detecting renal parenchymal defects in Febrile Urinary tract infection in children. Ultrasound Kidney Ureter Bladder is done at the presentation of a child with febrile urinary tract infection. Ultrasound KUB is routinely assessed for size, shape, Location, renal anomalies, echogenicity, corticomedullary differentiation, the regularity of cortical outline. Imaging is performed using SUPERSONIC EXPLORER. RENAL PARENCHYMAL DEFECTS are defined as in barry et al. Clin Radiol.1998;53:747-51 as an approximation of sinus echoes to the cortical surface with or without underlying calyceal dilatation, irregularity of cortical outline, or a difference in prone renal length. Doppler studies are not routinely performed. Technetium -99m Dimercaptosuccinic acid renal cortical scintigraphy is performed in a standardized protocol at presentation. Each scintigraphy is interpreted by one of our two nuclear medicine specialists, who are unaware of the Ultrasound results. Imaging is performed at least two hours following isotope administration using a dual detector gamma camera (SIMENS) with a high-resolution, low-energy collimator for the delayed planar images and single-photon-emission computed tomography (SPECT). Tc99m DMSA static images are acquired in anterior and posterior projection using 128 ×128 as well as the 256 ×256 image matrix 3 hours after intravenous injection of mean 55.5 MBq/1.5 mCi(minimum dose of 18.5MBq/500 μCi). RENAL PARENCHYMAL DEFECTS are considered when at least one of the criteria was met, as in Patel et al. Pediatr Radiol. 1993;23:506-9 diffuse or sharp indentation in renal contour with thinning of the cortex, any shaped defects with loss of renal volume, degree of photopenia or absent activity and heterogeneous uptake of renal radionuclide[37]. The wedge shape defect in the cortex with distortion of the cortical contour is considered as the scar. The regions of interest around the kidney contours are drawn manually and each divided into three sub-regions (upper, median, and lower segments) for easier and accurate analysis. Acute pyelonephritis changes are defined as areas of photogenic with preservation of normal renal contour.

**Statistical Analysis**

The data will be entered intoan MS Excel sheet and analyzed using the SSPS package. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV), and other parameters will be analyzed with appropriate methods after data collection. Comparisons between Ultrasound and Dimercaptosuccinic acid scan findings were made using a 95% confidence interval (CI) of the area under the curve (AUC) analysis; p ≤0.05 was considered significant.

**Results**

**Table 1** Age - Wise Patient Distribution of Children with UTI

| Age Group | Frequency | Percent |
|---|---|---|
| < 1 year | 48 | 53.30% |
| 1 - 2 years | 19 | 21.10% |
| 2 - 3 years | 8 | 8.90% |
| 3 - 4 years | 11 | 12.20% |
| 4 - 5 years | 4 | 4.40% |
| Total | 90 | 100.00% |

Table: 1 Total number of children who fulfilled the criteria for this study were 90. Out of this,48 were males and 42 were females. Ultrasound Kidney Ureter Bladder kidneys are done at presentation. Technetium -99m Dimercaptosuccinic acid renal cortical scintigraphy is performed in a standardized protocol at the presentation of a child with febrile urinary tract infection. In our study out of 90 children, 53.3% were males and 46.7% were females

**Table: 2** Urine Culture Positivity in Children with UTI

| Urine Culture Positive | Frequency | Percent |
|---|---|---|
| Yes | 90 | 100.00% |

Table: 2 A urine culture result indicating the presence of bacterial growth often triggers a prescription for an antimicrobial agent. However, the diagnosis of UTI in hospitalized patients is not always straightforward, and antimicrobial therapy may not be appropriate just because there is bacteriuria. All children included in this study were significant Urine Culture Positive.

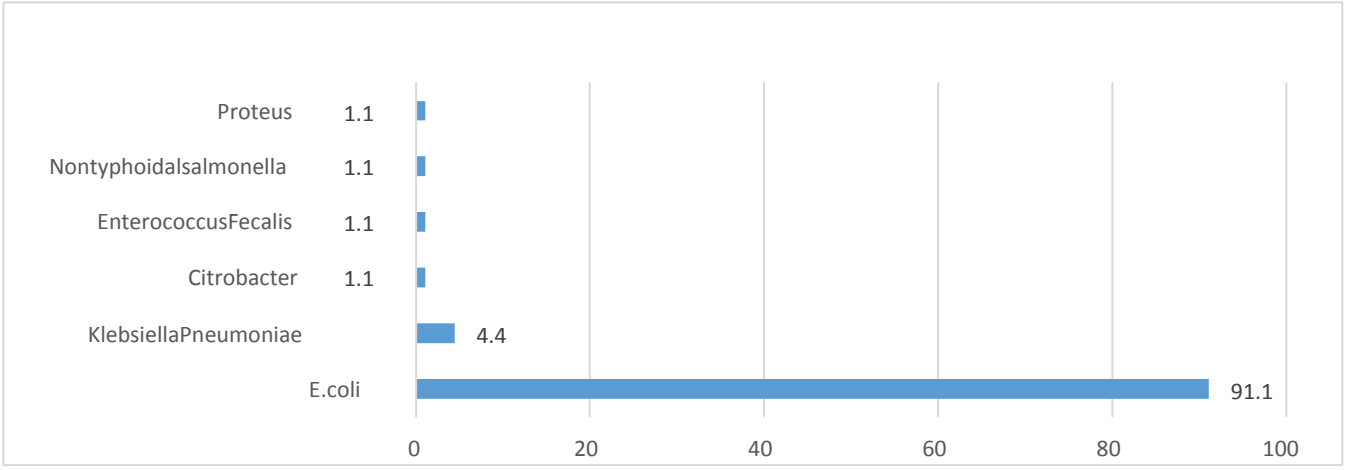
**Table 3** Distribution of the First Episode and Recurrent UTI in children

| | Frequency | Percent |
|---|---|---|
| First episode UTI | 84 | 93.3% |
| Recurrent UTI | 6 | 6.7% |
| Total | 90 | 100.0 |

**Table: 4** First Episode UTI in Percentage of and Recurrent Children

| Organism | Frequency | Percent |
|---|---|---|
| E.coli | 82 | 91.1% |
| Klebsiella pneumoniae | 4 | 4.4% |
| Citrobacter | 1 | 1.1% |
| Enterococcus fecalis | 1 | 1.1% |
| Nontyphoidal salmonella | 1 | 1.1% |
| Proteus | 1 | 1.1% |
| TOTAL | 90 | 100 |

**Graph: 1** Organism Isolated in Urine Culture in Children with UTI




Graph :1 The most common organism isolated in urine culture was E. coli followed by Klebsiella. Symptoms of infection with *E. coli* 0157 typically appear 3 to 4 days after being exposed to the bacteria. However, symptoms may appear as early as 24 hours or as late as 1 week later. In terms of the pathophysiology of *Klebsiella pneumonia*, we see neutrophil myeloperoxidase defense against *K. pneumoniae*. Oxidative inactivation of elastase is involved, while LBP helps transfer bacteria cell wall elements to the cells.

**Table: 5** Comparisons between Ultrasound and Dimercaptosuccinic Acid Scan Findings

| USG KUB | DMSA POSITIVE | DMSA NEGATIVE | TOTAL |
|---|---|---|---|
| **USG POSITIVE** | 3 | 3 | 6 |
| **USG NEGATIVE** | 22 | 62 | 84 |

Table: 5 using 95% confidence interval (CI) area under the curve (AUC) analysis which showed the following results.

**Table 6** Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of USG KUB When Compared to DMSA

| | |
|---|---|
| Sensitivity of USG | 12% |
| Specificity of USG | 95.4% |
| Positive predictive value of USG | 50% |
| Negative predictive value of USG | 73.8% |

Table: 6 In our study, the sensitivity and specificity of USG KUB in detecting Renal parenchymal abnormalities in comparison with DMSA is 12 % and 95.4 % respectively. And the positive predictive value of USGKUB is 50% and the negative predictive value is 73.8 % in detecting parenchymal defects in children when compared to DMSA

**Discussion**

Urinary tract infection (UTI) is one of the most common bacterial diseases of childhood, with a reported prevalence in one study of 8.4% in girls and 1.7% in boys by the age of 7 years.1 Diagnostic imaging of the urinary tract in children with a history of UTI has been accepted practice since the 1960s, and seminal studies from this decade2 showed a high incidence of abnormalities, particularly chronic pyelonephritis, and vesicoureteric reflux, showing that the condition was far from benign[11].The incidence of febrile UTI in healthy children is 1–3%.Subsequent renal parenchymal changes occur in 40% of those with VUR and 6% of those without VUR. Surgical management gains priority about the degree of parenchymal involvement. This is why renal screening should be performed with a high-sensitivity apparatus, especially since we now know that neither US nor DMSA is precise enough to detect VUR. imaging protocols in children with UTI continue to be a subject of debate.[12] A recent paper detailing a systematic approach to ultrasound specifically for the detection of renal scarring shows promise as a means to improve ultrasound sensitivity. In the context of UTI, ultrasound is generally the first-line investigation that allows the identification of structural abnormalities, both congenital and acquired.[13] The sensitivity of ultrasound in detecting renal cortical scarring, however, is not high and renal scintigraphy by technetium-99m dimercaptosuccinic acids (DMSA) scanning is now generally accepted as the most sensitive form of renal parenchymal imaging. In our study in the incidence of UTI was 48 (53.3%) in males and 42 (46.7%) in females, which is comparable to the study done by Montini G, et al Male, and Female percent is 68.7: 31.3.[14] Thus males are more affected than females. Similar male preponderance was also noted in the above study. The common age of presentation of children in our study about 53.3% is less than 1 year of age. This is comparable to a study done by Moorthy I, et al where E.coli is isolated in 59 children followed by klebsiella which is grown in 23 children.[15] Nammalwar BR et al also concluded that E.coli is the most common organism isolated in UTI. In our study, the sensitivity of USG KUB is 12% and specificity of USG KUB is 95.4% and positive predictive value is 50% and negative predictive value is 73.8 % in detecting parenchymal defects in children when compared to DMSA.[16] This is comparable to a study done by Patel K et al, where sensitivity and specificity of USGKUB in detecting focal renal scars when compared to DMSA is 5.2% and 98.3% and positive predictive value and negative predictive value is 50% and 75.8 % respectively.[17] In a meta-analysis, Peters CA et al. found that Tc-DMSA scintigraphy was superior to USG, and concluded that it is the gold standard technique for renal parenchymal imaging.[18] In a study done by Rajiv Sinha et al., USG was claimed to be

inappropriate for imaging UTI in patients with documented UTI.[19] we concluded that USG and concluded that Tc-DMSA is the most sensitive method in the detection of renal. scars. But ultrasonography is very useful in characterizing the defects seen on DMSA cortical scan and in detecting obstructive uropathies that may be associated with UTI.[20]

**Conclusion**

Urinary tract infection is one of the most frequently encountered clinical problems. UTI serves as a marker of underlying anatomic and functional abnormalities. Infants and young children are at higher risk than older children for incurring acute renal injury which progresses to renal scarring. As USGKUB is easily available at all centers, we proceeded to compare it with Technetium 99m DMSA which is available at particular centers. It is observed from our study that although ultrasonography has a good specificity in the detection of renal parenchymal defects when compared with DMSA, it has low sensitivity, positive predictive value, and negative predictive value. Thus we conclude that at present Ultrasonography cannot be substituted for DMSA in identifying renal parenchymal defects in children with Febrile UTI. A dimercaptosuccinic acid scan done at presentation identifies children with acute pyelonephritis and at six months later identify those children with scarring.

**References**


1. Ayazi P, Mahyar A, Noroozian E, Esmailzadehha N, Barikani A. Comparison of renal ultrasonography and dimercaptosuccinic acid renal scintigraphyin febrile urinary tract infection. Le infezioniin Medicina.2017: n.4,323-329.
2. Barry BP, Hall N, Cornford E, et al. Improved ultrasound detection of renal scarring in children following urinary tract infection. ClinRadiol.1998;53:747–51
3. Bhatnagar V, Mitra D, Agarwala S.,et al. The role of DMSA scans in the evaluation of the correlation between urinary tract infection, vesicoureteric reflux, and renal scarring. PediatrSurgInt18, 128–134 (2002)
4. Bjorgvinsson E, Majd M, Eggli KD. Diagnosis of Acute Pyelonephritis in children: Comparision of sonography and 99m-Tc DMSA scintigraphy. AJR Am J Roentgenol.1991:157(3),539-543.
5. Das R N, Chandrashekhar TS, Joshi H S, Gurung M, Shrestha N, Shivananda PG. Frequency and susceptibility profile ofpathogens causing urinary tract infections at a tertiary care hospital in western Nepal. Singapore M J2006;47(4):281-285.
6. Dharmalingam A, Pawar SU, Parelkar SV, Shetye SS, Ghorpade MK, Clive GH, et al. Tc-99m ethylenediamine and Tc-99m dimercaptosuccinic acid scintigraphy-comparison of the two for detection of scarring and differential cortical function. Indian J Nucl Med 2017;32:93-7.
7. HitzelA, Liard A, Vera P, Manrique A, Menard J, Dacher J. Color and Power Doppler Sonography Versus DMSA Scintigraphyin Acute Pyelonephritis and prediction of renal scarring. J Nucl Med 2002;43(1):27-32.
8. HobermanA, Charron M, Hickey RW, et al. Imaging studies after a first febrile urinary tract infection in young children. N Engl J Med. 2003;348(3):195–202.
9. Jakobsson B, Nolstedt L, Svensson L, Soderlundh S, Berg U. 99m Technetium dimercaptosuccinic acid scan in the diagnosis of acute pyelonephritis in children: relation to clinical and radiological findings. PediatrNephrol1992;6:328-34.
10. Jepson RG, Williams G, Craig JC. Cranberries for preventing urinary tract infections. Sao Paulo Med J . 2013;131:363.
11. Kliegman RM, St Geme III JW, Blum NJ, Tasker RC, Shah SS, Wilson KM. Nelson textbook of pediatrics. 21 ed. Philadelphia: Elsevier; 2020, pp2789-95.
12. Marceau-Grimard M, Marion A, Côté C, Bolduc S, Katherine Moore MD, Dimercaptosuccinic acid scintigraphyvs.

ultrasound for renal parenchymal defects in children. Canadian urological association journal.2017:11,260-264.

13. Montini G, TullusK, Hewitt I. Febrile urinary tract infections in children. N Engl J Med. 2011;365:239–50.
14. Montini G, Zucchetta P, Tomasi L, et al. Value of Imaging Studies After a First Febrile Urinary Tract Infection in Young Children: Data From Italian Renal InfectionStudy
15. Moorthy I, Wheat D, Gordon I. Ultrasonography in the evaluation of renal scarring using DMSA scan as the gold standard. PediatrNephrol2004;19(2):153e6.
16. Nammalwar BR, Vijayakumar M, Sankar J, Ramnath B, Prahlad N. Evaluation of theuse of DMSA in culture-positive UTI and culture-negative acute pyelonephritis. Indian Pediatr. 2005;42:691-6.
17. Patel K, Charron M, Hoberman A, Brown ML, Rogers KD. Intra observer and inter-observer variability in the interpretation of DMSA scans using a set of standardized criteria. PediatrRadiol 1993;23:506-9.
18. Peters CA, Skoog SJ, Arant BS Jr, et al. Summary of the AUA guideline on management of primary vesicoureteral reflux in children. J Urol . 2010;184:1134–1144.
19. Rajiv Sinha, Devdeep Mukherjee, Jayati Sengupta, Subasasis Saha, and Susmitha Banerjee. The yield of Imaging Performed as per Indian Society of Pediatric Nephrology Guidelines in Children with Urinary Tract Infection. Indian Pediatr.2017;54:749–751.
20. Roebuck D J, Howard R G, Metreweli. How sensitive is ultrasound in the detection of renal scars? BJR 1999;856(72):345-348.