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Research Article

Dimercaptosuccinic Acid Scan versus Renal Ultrasound to Investigate Recurrent Urinary Tract Infection

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Abstract

Objectives: To analyze the evolution of kidney damage in small female children diagnosed with recurrent urinary tract infection (UTI), a factor associated with progression of renal damage, and the importance of dimercaptosuccinicacid (DMSA) scan as a valuable indicator of early renal scars. **Methods**: In this retrospective study, 100 female patients aged 5 years or less, diagnosed with recurrent UTI, were recruited at Prince Rashed Military Hospital (PRH). The inclusion criteria are female patients who suffered from recurrent UTI ≥ 2 times and had visited a paediatrics specialist outpatient clinic in Prince Rashid Hospital from 1st March 2021 to 1st June 2022. The researchers received parents' consent to follow the Health Insurance Portability and Accountability Act guidelines. **Results**: The peak age of children with recurrent UTI was 2-3 years, accounted 35% of the total cases. However, the peak age of children who had abnormal DMSA scans was 4-5years. The results of normal ultrasound (US) diagnosis revealed renal scars in 4% of cases. In addition, 60% of patients with 5 times recurrent UTI had a renal scar, compared to 30% with 4 times of recurrent UTI. **Conclusion**: Renal ultrasound is not sensitive enough to detect renal scars. DMSA scintigraphy is complementary to investigate renal scars found in pediatrics patients.

Keywords: Urinary tract infection (UTI); Dimercaptosuccinic acid (DMSA) scan; Vesicoureteral reflux (VUR)

Introduction

Urinary Tract Infection (UTI) is one of the most mutual bacterial infections amongst febrile children 2 years of age [1]. Imaging studies, such as ultrasonography, dimercaptosuccinic acid (DMSA) scintigraphy, and voiding cystourethrography, have been endorsed as the clinical care for young children having a first UTI. The diagnosis is crucial based on the hypothesis that timely detection of urinary tract abnormalities can minimize the risk of renal damage at the time of the infection and in the future [2]. However, a lack of knowledge is noted regarding the appropriate method for testing young children with recurrent UTI.

UTI is an infection that can affect the urinary tract. A bladder infection (cystitis) arises when UTI affects the lower urinary tract. However, when it affects the upper urinary tract, it is known as an upper urinary tract infection (pyelonephritis). Its pathological

causes are either a bacteria or viral infection of the urinary tract, as well as a fungal pathogen causing *E.coli* infection, the most common microorganism that causes UTI, which accounts for 85%of the cases [3]. In addition, the mode of transmission is ascending in 95% of cases and haematogenous in others. The female gender have higher risk of having recurrent UTI than the male gender since females have a short urethra compared to the longer urethra of males [4]. In addition, structural malformations are the risk factors associated with congenital anomalies of the kidney and urinary tract. Commonly, Vesicoureteral Reflux (VUR) is a condition that causes the backward flow of urine from the bladder to one or both ureters, associated with 40% of children with chronic kidney complications [5].

From patients' complaints and findings of previous studies, UTI is an asymptomatic disease that affects children aged 2 years and below. However, the disease can lead to chronic diarrhoea, constipation, irritability and fever. After the age of 2 years, according to the UTI symptoms, the patients mostly complain of abdominal pain, dysuria (i.e., painful micturition), fever of unknown origin [6].

Patients suffering from recurrent UTI at the age of 5 and below suffer from serious complications that could be prevented by choosing the best mode of imaging. The complication is identified in 5%-7% of the cases [7]. Complications include single and multiple renal scars, which might lead to end-stage renal failure [7]. Patients may also suffer from growth failure and systemic hypertension at a young age [3]. This study aims to focus on a sensitive method of early complication detection aiming to decrease renal scars of high-risk patients aged 5 years and below.

Imaging and Definitions

The renal bladder ultrasound studies were conducted using the Philips HDII machine. The HDII System is a general-purpose, mobile, software-controlled, diagnostic ultrasound system, used to develop, manage, and demonstrate ultrasound data. The HDII system is built with the EnVisor architecture and feature set with additional new software and hardware channels. The HDII appearance is similar to the Phillips standard colour scheme. However, the system is effective in measuring the anatomical structures and producing information for doctors and nurses. The system has a fundamental set of imaging models and measurement tools [8]. The appearance of the renal-bladder ultrasound was abnormal if the following conditions are identified: Hydroureter 7 mm in transverse diameter, renal scar characterized by irregular focal renal contour with parenchymal thinning, and/or size of 1 cm difference between kidneys, according to the Society of Fatal Urology guidelines, (which include "pelviectasis without caliectasis") [9]. When the renal size disparity between the kidneys was 1 cm, and/or hydro (uretero) nephrosis was present, children with presumed renal replication abnormalities were categorized as normal.

The DMSA scan was conducted following the institution's routine procedure. For a dosage ranged 1 to 5 mCi, the dose was measured using the weight of kg/70 x normal adult dose=5 mCi. A Philips Prism 1500 single head camera or a Philips Axis head camera is used to image the subjects $1.5e^3$ hours after injection. Two pediatric radiologists independently checked the DMSA scans, blinded to the VUR grade and other studies except when the renal US was used to discern a central scar from hydronephrosis. As previously mentioned, the results were graded using the grading scale adapted from the Randomized Intervention for Children with Vesicoureteral Reflux study [10]. From the latest published recommendations, a retrospective study was conducted on children 'confirmed' with Febrile Urinary Tract Infection (FUTI) following the new American Academy of Pediatrics standards, which included a retrospective examination of urinalysis findings to assess those with the pyuria and the specimen selection procedures.

Materials and Methods

Study Design

This retrospective study protocol obtained ethical approval from the Directorate of Technical Qualification and Manpower Development, which is a division of Royal Medical Services (RMS) by March 2021. At the beginning of this study, the specialist recorded the medical history of each patient, consisting of the age of children when having the first UTI, the frequency, the present complaints such as dysuria and abdominal pain, and any risk factors associated with UTI recurrence. Afterward, the physical examination was conducted that included blood pressure measurement, abdominal examination, and meningo myelocele examination.

The urine culture was performed for the UTI diagnoses. However, we performed a urine culture as stated in Table 1 if any patient is suspected of having UTI. Table 1 presents the mode of samples taken.

Age	Mode of Sample	Number of Colonies
≤1 year	Suprapubic sample	Any number of colonies
1 year-< 2 years	Urinary Catheter sample	10^3
2 years-5 years	Clean Catch sample	10^5

Table 1: Mode of samples taken.

The laboratory tests involve a complete blood count, aiming to detect Leukocytosis and anaemia of chronic illness. Furthermore, a kidney function test is required to demonstrate the values of urea, nitrogen, and creatinine as a baseline. The patients included in the study were to fulfil the ultrasound protocol by referring them to a radiologist where the results were obtained directly. Afterward, they obtain an appointment from nuclear medicine staff within one week and more. After obtaining the results of the required images (i.e., Ultrasound and DMSA scan), the patients were asked to follow up the treatment with the pediatric specialist's clinic. Figure 1 illustrates the patient's flow chart from the 1st visit to the pediatric clinic until the end of the clinical investigation.

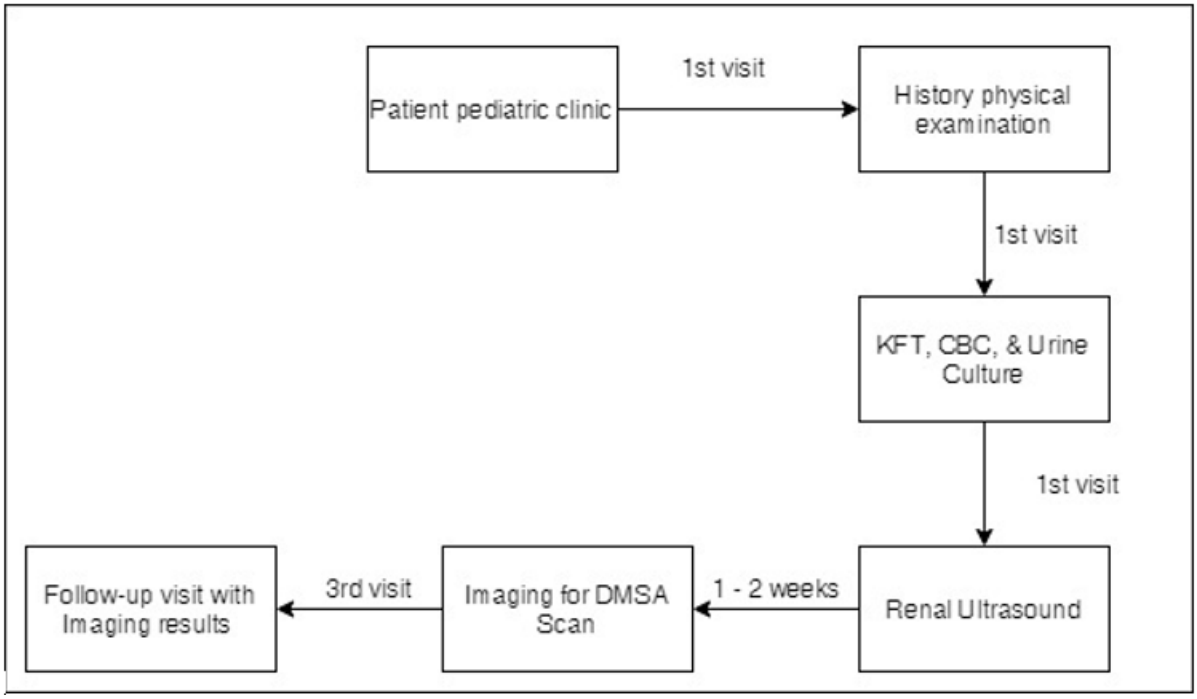

Figure 1: Flow chart of UTI patients.

Patients Selection

This study includes a total of 100 female patients aged 5 years and below. The inclusion criteria are patients who suffered from recurrent UTI 2 times, and those who had visited a pediatric specialist outpatient clinic at Prince Rashid Military Hospital between 1st March 2021 and 1st June 2022. This study obtained the parents' consent to follow the HIPAA guidelines.

Patients were categorized into 5 groups based on the results of the renal ultrasound. These groups are Normal US, Mild hydronephrosis, moderate hydronephrosis, severe hydronephrosis and asymmetry of renal size and echogenicity. Furthermore, patients were grouped into 5 categories based on their ages, while the frequency of recurrent UTI is grouped in another 4 categories.

Results

This study involves 100 eligible patients, aged 5 years and below, who suffer from recurrent UTI. The study categorized patients into five groups based on age. Group 1 was comprised of patients aged from 11 month to 1 year. The ages of the remaining groups were 1 year and above. The results were compared to demonstrate the DMSA results. In this study, the overall percentage of the renal scar was 14% of the selected patients. The peak age of recurrent UTI was in group 3 (ages 2-3 years) accounting for 35% of the patients. The last group (4-5 years old) had the highest percentage of abnormal DMSA scan and the renal scar, as shown in Table 2.

Group	Patients' age at 1st UTI	No. of Patients	No. of Patients with Renal Scars	Percentage of Renal Scars (%)
1	1 month – 1 year	6	2	33%
2	1 year – 2 years	12	1	8%
3	2 years – 3 years	35	2	5%
4	3 years – 4 years	30	3	10%
5	4 year – 5 years	17	6	35%

Table 2: Results of the first comparison using DMSA scan.

Furthermore, the second comparison was conducted based on renal ultrasound and correspond DMSA scan finding (i.e., the patients investigated via both US and DMSA scan) as shown in Table 3. Significantly, the percentage of renal scars is increasing in an aggressive way when the renal ultrasound increases from normal until asymmetric of the kidney (atrophied kidney).

Group	Renal Ultrasound Findings	No. of patients underwent US	No. of patients with Renal Scars using DMSA Scan	Percentages of Renal Scars
1	Normal	43	2	4%
2	Mild hydronephroses	25	2	8%
3	Moderate hydronephroses	20	3	15%
4	Severe hydronephroses	7	3	42%
5	Asymmetry of kidney (atrophied kidney)	5	4	80%

Table 3: Results of the second comparison using both US and DMSA scan.

The third comparison was based on the frequency of UTI. Table IV categorized the patients into four groups. In each group includes, the frequency of UTI, the number of patients, the number of patients with renal scars, and the percentage of renal scars were presented (Figure 2, Table 4).

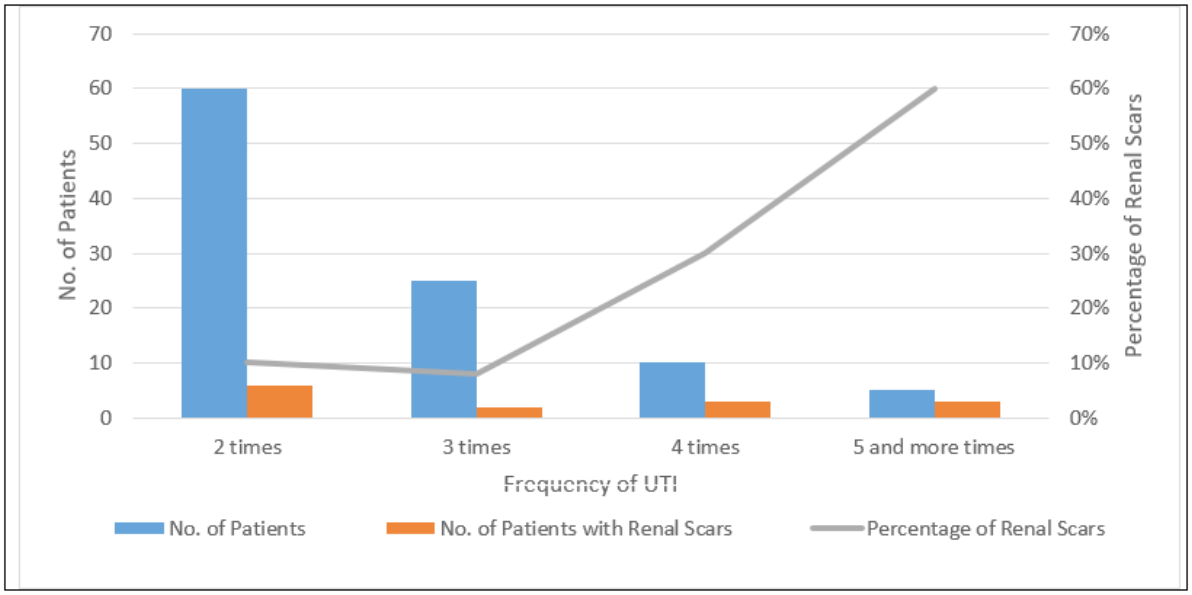

Figure 2: Results of the third comparison.

Group	Frequency of UTI	No. of patients	No. of patients with Renal Scars using DMSA	Percentages of Renal Scars
1	2 times	60	6	10%
2	3 times	25	2	8%
3	4 times	10	3	30%
4	5 and more times	5	3	60%

Table 4: Results of the third comparison.

Discussion

Recurrent UTI is a serious health problem requiring the attention of multiple pediatric specialists, in which 10% of the outpatients use pediatric clinics for treatment. In this study, our patients were females because they face a high risk of UTI recurrence. Imaging techniques facilitate early detection of renal scars, prevent and reduce complications, in addition to the improving of the therapeutic outcomes of prophylactic antibiotics facilitating suitable early surgical interventions.

Ultrasound is one of the most common renal imaging that uses non-invasive radiation available in every hospital. In this method, the patient does not require to have any preparation; nevertheless, it is considered technical and not sensitive for mild and early urine tract pathology (renal scars or mild hydronephrosis) [11]. On the other hand, a DMSA scan is highly sensitive for detecting early and mild pathology (small scars or any change in urinary function fraction). This method (i.e., DMSA scan) is safe because it has no risk of radiation. In this method, the patient must be prepared for at least 3 hours before taking the oral nuclear material [12].

Diagnoses of renal scars and atrophied kidneys are a challenging issue for patients with recurrent UTI. Our study aims to compare renal ultrasound with DMSA scan to identify a sensitive method for early renal damage and provide the number of patients in every category. Even with normal renal ultrasound, the risk of renal scar is 2% [13]. However, our results revealed that the risk of the renal scar was 4% for a normal renal ultrasound. In addition, we show that the sensitivity of renal ultrasound increases in patients with asymmetric kidneys and severe hydronephrosis (i.e., 80% and 42%, respectively) in comparison with low sensitivity when the patient has a normal ultrasound and mild hydronephrosis (i.e., 4% and 8%, respectively).

The results show that the DMSA scan is a sensitive method for finding renal scars and atrophied kidneys. Renal scars formation was significantly correlated with UTI frequency. Our study reported that 60% of patients with renal scars had 5 times recurrent UTI, compared to 30% and 8% of patients who had 4 and 3 times recurrent UTI respectively. Our results were consistent with Najib, et al. [14] as he reported that scar formation increased dramatically (43.7% and 13.5%) with an increase in UTI frequency. Furthermore, the peak age of renal scars associated with recurrent UTI was found in group1 (1 month to 1 year), reflecting a congenital anomaly with a percentage of 35%. However, in group 4 (4 to 5) years, renal scars associated with recurrent UTI accounted for 33% of total patients, reflecting a high frequency of UTI. These findings matched the results of Beiraghdar, et al. who reported that the peak of the renal scar was found among paediatrics aged less than 12 months with an incident rate of 52% [15]. In addition, Vernon et al. reported 27% renal scar cases with paediatrics of age 3 to 4 years [16].

Patients with normal renal ultrasounds are at risk of renal scars. Our findings matched that of Sinha, et al. who concluded that the sensitivity of renal ultrasound to detect renal scar in paediatrics aged 1-5 years was not up to 20% [17]. Christian, *et al.* highlighted that renal ultrasound alone was a poor technique to detect renal scars. In addition, Strak, et al. reported that renal ultrasound sensitivity ranged from 30% to 80% increased significantly with an increase of patient's age [18].

In our study, the overall percentage of renal scars was 14% of cases, lower than the reported incident rate in other studies such as Fong, et al. and Shenoy, et al. who reported the incident rates of renal scars as 22% and 31%, respectively [19,20].

Limitations

In this study, the sample size is small to generalize the results. Moreover, the outbreak of COVID-19 affected the outcome of the study because patients booked appointments at a later date, and it was difficult for the patients to follow up at the pediatric specialist's clinics. Furthermore, the DMSA scan required special preparation, and some patients refused to perform this scan due to radiation issues. This study was limited to the female gender of a specific age (i.e., 5 years and below). We recommend future studies to use samples of both genders aged above 5 years old. We also recommend future studies to use different hospitals to expand the sample size.

Conclusion

Our study recommends both renal ultrasound and DMSA scintigraphy to investigate the assessment of pediatrics with recurrent UTI. Renal ultrasound alone was found to have low sensitivity in detecting renal scars. Early detection and prevention of UTI recurrences play a significant role in preventingpermanent renal complications in pediatrics.

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Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent forms.

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