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FOLLOW-UP OF KIDNEY SCARRING AFTER URINARY TRACT INFECTIONS USING TECHNETIUM-99M DIMERCAPTOSUCCINIC ACID SCAN IN PAEDIATRIC JORDANIAN SUBJECTS WITH ACUTE PYELONEPHRITIS

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ABSTRACT

Background: A urinary tract infection is the main frequent bacterial infection in young paediatric subjects. If a urinary tract infection is not managed, acute pyelonephritis might lead to kidney insult, kidney scarring and chronic renal failure. Early confirmation and management of a urinary tract infection is crucial to avoid kidney scarring. The most frequent risk factor of kidney scarring in paediatric subjects following urinary tract infection is vesicoureteral reflux. Technetium-99m dimercaptosuccinic acid (Tc 99m DMSA) scan is the cornerstone to confirm kidney scarring after a urinary tract infection. **Objective:** The objective was to evaluate the frequency and risk factors of kidney scarring after urinary tract infection in paediatric Jordanian subjects and following management of acute pyelonephritis by Tc 99m DMSA scan. **Methods:** Our prospective, double-blind investigation included 110 paediatric subjects (< 10 years old, both sexes) with confirmed urinary tract infection and acute pyelonephritis of which kidney cortical lesions were ascertained by primary Tc 99m DMSA scans, at King Hussein Hospital, King Hussein Medical City, Amman, Jordan, during the period of 2010–2020. Subjects were classified into two groups based on kidney scars and risk factors of kidney scars, such as sex, age at confirmation, hydronephrosis, vesicoureteral reflux score and voiding cystourethrogram. The kidney-scarred group (GI, n = 43) and the non-kidney scarred group (GII, n = 67) were formed based on Tc 99m DMSA scans. For age at confirmation, subjects were placed into two groups: < 1 year and > 1 year. The Tc 99m DMSA scan was performed to evaluate the presence of kidney scars. The Tc 99m DMSA scan was pathological if there was one or more sites of reduced cortical uptake with or without cortical outline. Voiding cystourethrogram and Tc 99m DMSA scans were done within a 2–4-month follow-up. Vesicoureteral reflux was scored following voiding cystourethrogram (I–V). Kidney scars were scored as type I, no more than two scars; type II, more than two scars with some normal parenchyma between them; type III, generalised damage to the whole kidney; and type IV, end stage. The chi-square test was used to determine the significance of correlation between categorised parameters. Logistic regression was done to assess the risk factors for kidney scarring. **Results:** Overall, 43 of 110 subjects (39.1%) had kidney scars based on Tc 99m DMSA scan. There were no remarkable discrepancies in terms of sex and hydronephrosis between the kidney-scarred and non-scarred groups. Age at confirmation > 1 year had a 4.7 times greater frequency of kidney scarring. Vesicoureteral reflux influenced kidney scar production. A vesicoureteral reflux score of III or IV had a 13.6 times greater effect on kidney scar production than a vesicoureteral reflux score of I or II. Paediatric subjects with previous recurrent urinary tract infection experienced kidney scarring. First and recurrent episodes of urinary tract infections were remarkable when compared with increasing vesicoureteral reflux ($P < 0.005$) and kidney scar ($P < 0.05$). There was a genitourinary abnormal ultrasound in 31 of 110 (28.2%) subjects, of whom 9 (29.0%) experienced kidney scarring following the first episode of a urinary tract infection. Kidney scars were found in 43 of 110 (39.1%) subjects, of whom 9 (20.9%) were experiencing the first episode of a urinary tract infection. The Tc 99m DMSA scan was pathological in 11 of 43 subjects (25.6%) with normal ultrasound, of whom 8 subjects were experiencing a recurrent urinary tract infection and 3 subjects had pyelonephritis. **Conclusion:** Vesicoureteral reflux scores and age at confirmation are risk factors of kidney scarring when using Tc 99m DMSA scan following acute pyelonephritis. Increased hydroureteronephrosis and younger age were more correlated with recurrent episodes of urinary tract infection and kidney scarring. Non-invasive Tc 99m DMSA scan is preferred over invasive procedures for follow-up of paediatric subjects with recurrent urinary tract infection.

KEYWORDS: Acute pyelonephritis; Kidney scar; Vesicoureteral reflux; technetium-99m dimercaptosuccinic acid; paediatric subjects; urinary tract infection.

INTRODUCTION

Five per cent of infants with fever have a urinary tract infection.[1] Most subjects with a urinary tract infection have acute pyelonephritis and kidney scarring. Early confirmation and management of a urinary tract infection in paediatric subjects < 2 years of age is crucial due to the increased frequency of kidney scarring.[2] The final objective of management is to avoid definitive kidney insult. Acute pyelonephritis is one risk factor of kidney scarring and its intensity is high if associated with vesicoureteral reflux (the risk factors are sex, age and hydronephrosis), late management and recurrent urinary tract infections.[3] A urinary tract infection is the main frequent bacterial infection in young paediatric subjects. In a male infant, recurrent urinary tract infection requires assessment for malformations, which includes ultrasound, voiding cystourethrogram (VCUG), cystoscopy and technetium-99m dimercaptosuccinic acid (Tc 99m DMSA) kidney scan.

A Tc 99m DMSA scan is the main sensitive confirmation method to recognise acute pyelonephritis during an acute urinary tract infection and to ascertain the site of future kidney scar 3–6 months following the infection.[4] Overall, 42%–60% of subjects with acute pyelonephritis have kidney scars.[5] Tc 99m DMSA scan is the cornerstone of confirmation of kidney scarring after a urinary tract infection. During the first episode of a urinary tract infection, kidney scarring is absent to minor if there are no coexisting abnormalities. Kidney scarring is seen following a first urinary tract infection with fever. Voiding cystourethrogram (VCUG) is an invasive method for the confirmation of vesicoureteral reflux. Kidney scarring is associated with intense vesicoureteral reflux. Ultrasound could spot urogenital abnormalities, which could then be followed up to examine vesicoureteral reflux. If there are no abnormalities, vesicoureteral reflux might be missed, until there is a urinary tract infection. Tc 99m DMSA scan is a non-invasive technique, can evaluate kidney parenchymal affection and might be employed to spot kidney scars following the first episode of urinary tract infection.

Our objective was to evaluate the frequency and risk factors of kidney scarring after urinary tract infection following management of acute pyelonephritis in paediatric Jordanian subjects by Tc 99m DMSA scan.

METHODS

This prospective, double-blind investigation included 110 young paediatric subjects, aged < 10 years, of both sexes. They had a confirmed urinary tract infection and acute pyelonephritis, of which kidney cortical lesions were ascertained by primary Tc 99m DMSA scans during the first episode of a urinary tract infection, at King Hussein Hospital, King Hussein Medical City, Amman, Jordan, during the period of 2010–2010. Approval was obtained from the ethical and research board review committee of the Royal Jordanian Medical Services, and the parents of the subjects provided written informed consent. Subjects with chronic renal disease, acute renal insult or urinary tract infection after urethral catheterisation and operation were excluded.

Subjects were classified into two groups based on kidney scars and risk factors of kidney scars, such as sex, age at confirmation, hydronephrosis, vesicoureteral reflux score and VCUG. The kidney-scarred group (GI, n = 43) and the non-kidney scarred group (GII, n = 67) were formed based on Tc 99m DMSA scans. A second Tc 99m DMSA scan was done 4 months following the last urinary tract infection with kidney cortical lesions. The Tc 99m DMSA scan was pathological if there were one or more sites of reduced cortical uptake with or without cortical outline. All subjects had a Tc 99m DMSA scan within the 4–6-month follow-up period. The Tc 99m DMSA scan was performed to evaluate the presence of kidney scars.

Hydronephrosis was diagnosed if there was > 0.5 cm of kidney pelvic anteroposterior diameter on ultrasound. VCUG was used to score vesicoureteral reflux as: I, reflux limited to the ureter; II, reflux up to the kidney pelvis; III, reflux into a slightly dilated ureter and pelvicalyceal system; IV, moderately dilated ureter and blunting of the fornix; and V, a tortuous ureter with intense dilatation of the ureter and pelvicalyceal system.[6] For age at confirmation, subjects were divided into two groups: < 1 year and > 1 year. Urinary tract infection was scored as a first or recurrent episode. VCUG and Tc 99m DMSA scans were done within a 2–4-month follow-up period. Vesicoureteral reflux scoring was performed following VCUG. Kidney scars were recognised and scored as type I, no more than two scars; type II, more than two scars with some normal parenchyma between them; type III, generalised damage to the whole kidney; and type IV, end stage ‘shrunken’ (kidney with little or no uptake of DMSA, < 10% of the total function).

Statistics

Categorical parameters were compared using Student’s t-test or the chi-square test. Logistic regression was done to assess the risk factors for kidney scarring. $P < 0.05$ was considered statistically significant.

RESULTS

Of 110 subjects with cortical lesions after a primary urinary tract infection, kidney scarring was recorded using Tc 99m DMSA scan in 43 (39.1%) subjects (Table I). Of these subjects, 17 (39.5%) were boys and 26 (60.5%) were girls. There was no remarkable discrepancy between males and females according to kidney scars ($P > 0.05$). The average age at confirmation was 13 months. Paediatric subjects with scars based on Tc 99m DMSA scans were remarkably older (average age: 21 months) than those with no scars (average age: 8 months). Paediatric subjects aged > 1 year had a 4.7 times greater frequency of kidney scars than those aged < 1 year (Table II; $P < 0.05$).

Thirty-nine of 110 (35.5%) paediatric subjects had hydronephrosis seen on ultrasound. There was no remarkable discrepancy between subjects with hydronephrosis and kidney scars (Table III; P > 0.05). Vesicoureteral reflux was recorded in 45 (40.9%) subjects following a first urinary tract infection. There was an association between vesicoureteral reflux and kidney scarring using Tc 99m DMSA scan 4–6 months following a first urinary tract infection (P < 0.005). Kidney scarring was remarkably more frequent in subjects with a reflux of ≥ III than in subjects with no reflux. Subjects with a vesicoureteral reflux score of III or IV had a 13.6 times greater frequency of scarring than those with a I–II reflux (Table IV).

The first episode of a urinary tract infection was recorded in 64 (58.2%) subjects. The ultrasound showed genitourinary abnormality in 31 of 110 (28.2%) subjects, of whom 9 (29.0%) experienced kidney scarring following the first episode of a urinary tract infection. Moderate-severe hydroureteronephrosis was the frequent recorded pathology. During a urinary tract infection, 75 of 110 (68.2%) subjects experienced ultrasound pathologies such as hydronephrosis (20/75, 26.7%), cystitis (10/75, 13.3%), posterior urethral valve (8/75, 10.7%), pyelonephritis (9/75, 12%), ureteropelvic junction abnormalities (5/75, 6.67%), left duplex kidney (2/75, 2.67%) and right solitary kidney (3/75, 4%), which was more frequent in subjects with recurrent urinary tract infection (90/110, 81.8%). Positive reflux was found in 65 of 90 (72.2%) subjects, mostly in recurrent urinary tract infection.

Based on ultrasound, kidney scars were found in 43 of 110 (39.1%) subjects; for 9 (20.9%) of these subjects, it was a first episode of a urinary tract infection. All subjects with pathological ultrasound of moderate-severe hydroureteronephrosis experienced kidney scarring within the follow-up period. Tc 99m DMSA scan was pathological in 11 of 43 (25.6%) subjects with a normal ultrasound, of whom 8 subjects experienced recurrent urinary tract infection and 3 subjects had pyelonephritis (Table V). Within the first episode of a urinary tract infection, 9 subjects experienced positive reflux, of whom 3 experienced kidney scarring and had a posterior urethral valve. Without reflux, 3 subjects had a type I kidney scar within the follow-up due to recurrent urinary tract infection. Increased hydroureteronephrosis (108/110, 98.2%), urinary tract infection (37/110, 33.6%) and younger age (76/110, 69.1%) were more correlated with recurrent episodes of urinary tract infection and kidney scarring (Table VI).

DISCUSSION

Some lesions found on scans 3 months following a urinary tract infection could be temporary.[7] The scarring period for the first urinary tract infection is debatable. Regarding age at confirmation, paediatric subjects aged < 1 year have more kidney scarring.[8] and paediatric subjects aged > 1 year have more kidney scars following primary infection.[9] The increasing kidney is more liable to inflammation and inability with more vesicoureteral reflux.[10] In this investigation, paediatric subjects with scars were older during acute pyelonephritis than those with no scars. Some older paediatric subjects with pyelonephritis had an undiscovered urinary tract infection. Late confirmation and management of urinary tract infections might lead to kidney scarring. Younger paediatric subjects are more liable to scarring. Recurrent urinary tract infection should be followed up with ultrasound after an acute infection, a Tc 99m DMSA scan 4–6 months later and VCUG after the acute episode.

Regarding the association between hydronephrosis and urinary tract infection, the most frequent factor leading to collecting system dilatation is vesicoureteral reflux.[11] Ultrasound cannot exactly spot vesicoureteral reflux, but hydronephrosis might be accompanied by acute pyelonephritis. In this investigation, hydronephrosis after the primary urinary tract infection did not influence the formation of kidney scars. Late management led to a high incidence of kidney scarring. There was no discrepancy between inflammation and the production of kidney scars.[12,13] Recurrent urinary tract infection contributes to constipation and vesicoureteral reflux. Kidneys that show positive scans are more susceptible to urinary tract infection. All paediatric subjects with moderate-severe hydroureteronephrosis had kidney scarring. High-score hydroureteronephrosis is correlated with a high risk of urological abnormalities. There is a remarkable association between the pathological scan and scar production. Cortical scarring was seen in paediatric subjects with posterior urethral valves with vesicoureteral reflux following the first episode of urinary tract infection. When there is no vesicoureteral reflux, kidney scarring might be found sporadically.

Vesicoureteral reflux is the retrograde passing of urine from the bladder into the ureter. Subjects with vesicoureteral reflux might have definitive kidney scarring following a first urinary tract infection.[11] Vesicoureteral reflux was scored from I to V[10] for prognosis. The frequency of intrarenal reflux begins to reduce after the age of 6 years. When the kidney increases, it rarely causes kidney scars.[9] Vesicoureteral reflux might be considered a risk factor for kidney scars because it is a risk factor for acute pyelonephritis. This investigation demonstrated that vesicoureteral reflux increases the risk of kidney scars. There was an increased frequency of kidney scarring with higher vesicoureteral reflux scores. Subjects with a vesicoureteral reflux score of III or IV had a 13.6 times greater frequency of kidney scaring that subjects with a vesicoureteral reflux score of I or II. Of note, the vesicoureteral reflux scores were higher and there was greater kidney scarring when there was recurrent urinary tract infection. There was an increased frequency of urinary tract infection in paediatric subjects with vesicoureteral reflux as the main risk factor for recurrent urinary tract infection. Vesicoureteral reflux induces

recurrent urinary tract infection by increasing bladder pressure and transmitting this pressure to the kidney, leading to reflux nephropathy and scar production. Vesicoureteral reflux scores and age were risk factors of kidney scarring based on Tc 99m DMSA scans following acute pyelonephritis. Late confirmation and management of a urinary tract infection might cause kidney scarring. Older paediatric subjects had more kidney scars. Recurrent urinary tract infection is frequent in young paediatric subjects.

Hydroureteronephrosis (high scores), congenital malformations (posterior urethral valve and duplex kidney) and higher scores of vesicoureteral reflux were the frequent risk factors correlated with recurrent urinary tract infection and kidney scarring. Control of paediatric subjects with recurrent urinary tract infection depends on the age of symptoms and the intensity of other clinical features. Long-term follow-up should be encouraged to recognise hazards such as worsening kidney function. The frequency of kidney scarring was increased in recurrent urinary tract infection because the absence of vesicoureteral reflux is not protective, and kidney scarring might happen without it. Non-invasive DMSA is preferred over invasive methods to follow up paediatric subjects with recurrent urinary tract infection.

In conclusion, vesicoureteral reflux scores and age at confirmation are risk factors of kidney scars based on Tc 99m DMSA scans following acute pyelonephritis. Increased hydroureteronephrosis and younger age were correlated with recurrent urinary tract infection and kidney scarring. Non-invasive DMSA scan is preferred over invasive procedures to follow up paediatric subjects with recurrent urinary tract infection. A Tc 99m DMSA scan is indicated to assess younger paediatric subjects with a first episode of a urinary tract infection with an increased score of hydroureteronephrosis confirmed by ultrasound and in recurrent urinary tract infection.

Table I: Characteristics of the paediatric subjects.

	GI (kidney scarring)	GII (no kidney scarring)	P
No.	43	67	
Sex (no, %) Female Male	 26 17	 34 33	>0.05
Mean age at confirmation (months)	21	8	<0.05
Pathological ultrasound	74 (67.3%)		
Kidney scar present (based on technetium-99m dimercaptosuccinic acid scan) I II III IV V	 43 (39.1%) 24 (55.8%) 16 (37.2%) 2 (4.7%) 1(2.3)		

Table II: Kidney scars based on age at confirmation.

	GI (kidney scarring)	GII (no kidney scarring)	Overall
< 1 year, no. (%)	23 (28.8)	57 (71.2)	80
> 1 year, no. (%)	20 (66.7)	10 (33.3)	30

Table III: Kidney scars based on hydronephrosis (diameter > 0.5 cm).

	GI (kidney scarring)	GII (no kidney scarring)	Overall
Present, no. (%)	16 (40)	24 (60)	40
Not present, no. (%)	27 (38.6)	43 (61.4)	70

Table IV. Kidney scars based on the vesicoureteral reflux score.

	GI (kidney scarring)	GII (no kidney scarring)	Overall
Not present, no. (%)	18 (26.5)	50 (73.5)	68
I–II, no. (%)	4 (30.8)	9 (69.2)	13
III–IV, no. (%)	23 (79.3)	6 (20.7)	29

Table V: Comparison of parameters for the First and Recurrent episode of a urinary tract infection.

Parameter	First episode (63)	Recurrent episode (47)	P
Pathological ultrasound	36 (57.1)	38 (80.9)	>0.05
Positive voiding cystourethrogram	25 (39.7)	39 (82.9)	<0.005
Kidney scar (technetium-99m	13 (20.6)	30 (63.8)	<0.05

dimercaptosuccinic acid scan)			

Table VI: The association between kidney Scarring and Urinary tract infection.

	Renal scarring	
	Positive	**Negative**
Kidney–ureter–bladder ultrasound	18/43 (41.9%)	16 /67 (23.9%)
Voiding cysto-urethrogram	21/43 (48.8%)	12/67 (17.9%)

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