Geget (2006) 6 : 55 - 68

Original Article

The Potential Impact of Static Magnetic Resonance Urography on the Diagnosis and Management of Children with Impaired Renal Functions

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ABSTRACT

Background: In children with renal impairment, accurate identification of underlying urinary tract pathology is often faced with difficulties. Ultrasonography (US) has diagnostic limitations in addition to being operator-dependent, while the use of other imaging modalities may be restricted by hazards of iodinated contrast injection and/or decreased accuracy in presence of poorly functioning kidneys. Magnetic resonance urography (MRU) has been proposed as a safe and effective modality which is independent of renal function.

Objective: To assess the role of static MRU in identifying urinary tract abnormalities in children with renal impairment.

Methods: Twenty six children (2-14 years old) were studied, including four cases of acute renal impairment/ failure, 11 cases with stage 3 or 4 chronic kidney disease and 11 with end-stage renal disease. They were subjected to routine clinical, laboratory and imaging workup as well as Static heavily T2 weighted MRU. MRU images were assessed for quality and morphology; with comparison of findings to those of other imaging techniques.

Results: Fifty collecting systems were studied (two patients had single systems). MRU demonstrated additional findings in 13 cases; mostly due to inability of US to identify ureteric lesions and the non-feasibility of excretory urography in cases with renal failure. These lesions were mostly amenable for surgical treatment, thus accurate and timely detection is crucial. Vesicoureteric reflux (VUR) was detected by voiding cystourethrography (VCUG) in seven cases. On MRU, they had dilated ureters with no apparent cause.

Conclusion: MRU is recommended in all cases with renal impairment and pelvicalyceal dilatation on US. When VUR is suspected, VCUG is still the investigation of choice.

INTRODUCTION

Urinary tract disorders are common causes of renal failure in childhood, accounting for 25% of cases of end-stage renal disease (ESRD) in developed and probably much more in developing countries. Urinary tract obstruction is known to initiate a complete sequence of events resulting in renal failure[1].

Suspected urinary tract disorders can be tackled with a wide variety of imaging modalities and diagnostic tests. The conventional used imaging protocols include ultrasound (US), dimercaptosuccinic acid (DMSA) scan, voiding cystourethrography (VCUG) and excretory urography (IVU). These methods are complementary since each of them has its advantages and potential disadvantages and it is not always possible to reach a diagnosis with a single imaging modality[2,3]. Using the appropriate modality is essential as additional examinations can result in increased patient hazards, extra costs and time loss.

When it comes to a child with impaired renal functions, this choice should be more meticulous. The exact morphology of urinary tract abnormalities must be identified to be able to distinguish between urinary system abnormalities that require surgical treatment and those that do not[3]. Many of the commonly used modalities entail ionizing radiation and require iodinated contrast media injection. Although Ultrasonography provides information about the kidney morphology, it cannot fully demonstrate the ureters and is operator dependant[4].

Magnetic Resonance Urography (MRU) has successfully been applied to the pediatric urinary tract[5]. It has recently gained sufficient popularity as a non invasive and safe modality that does not entail ionizing radiation or iodinated contrast injection. It can be performed in poorly functioning and even non functioning kidneys[3]. These characteristics have made it a technique of interest in children with impaired renal functions in whom other modalities are exhausted without a proper diagnosis.

AIM OF THE WORK

The aim of this work is to investigate the value of static MRU in the diagnosis of urinary tract abnormalities in children with impaired renal functions, as well as the potential impact of its use on patient outcome through accurate identification of those requiring surgical interventions.

SUBJECTS AND METHODS

This is a cross-sectional study of 26 children with variable degrees of renal impairment. They were recruited from the Pediatric Nephrology and Hemodialysis Units of Cairo University Pediatric Hospitals and from King Fahd Nephrology Unit, Cairo University over a two year period.

Inclusion criteria:

Inclusion in the study required an age between 2 and 15 years, the diagnosis or suspicion of urinary tract abnormalities and the presence of renal functional compromise in the form of any of the following:

- Acute renal impairment/failure (ARF): defined by an increase in the serum creatinine level of 0.5 mg per dL (44.2 μmol per L) above the upper limit for age quoted by John FN and Michael AP[6] or the need for acute dialysis. This definition is in agreement with the diagnostic criteria of the American Family Physician Academy[7].
- Chronic renal impairment/failure (CRF): with a glomerular filtration rate (G.F.R.) less than 60 mL/min/1.73 m^2, consistent with stage 3 or 4 chronic kidney disease (CKD) as defined by the Kidney Disease Outcomes Quality Initiative of the National Kidney Foundation[8].
- End-stage renal disease (ESRD) patients undergoing regular hemodialysis.

Patients were subjected to:

- History taking and clinical examination, as well as routine laboratory investigations including serum urea, creatinine and estimated G.F.R. according to

Schwarz formula[9], electrolytes (Na, K, Ca), blood pH and bicarbonate, as well as urinalysis and culture.

- Ultrasonographic examination of the kidneys and urinary tract for all cases and VCUG whenever vesico-ureteric reflux was suspected. Available results of imaging studies which had been performed at first presentation were used in patients with ESRD.
- Static heavily T2 weighted respiratory triggered MRU examination using 1.0 Tesla Signa GE and Philips Gyroscan Intera (Netherland) 1.5 Tesla machines, with post processing 3 dimensional maximum intensity projection (MIP) images. In young non-cooperative children, the procedure was conducted under sedation supervised by an anesthesiologist.

Technique of MRU examination:

- Routine axial 2D FSE T2 WI from the upper pole of the kidney to the inferior border of the symphysis pubis to include the whole urinary tract. (TR: 1600, TE: 100, Slice thickness 10 mm, matrix 256 x 256)
- T2 axial and coronal images (from posterior to anterior) by means of the double-echo half-Fourier acquisition single-shot turbo spin-echo (HASTE technique) and multiple thick slab, single shot, turbo spin echo cuts at different angles were performed (TR: 1800, TE: 350, FOV: 40 cm, matrix 512 x 512).
- Fat suppression was applied to suppress signal from fat.
- Post processing was performed by means of the MIP algorithm from the data set of obtained images. This permits 3D reconstruction and rotation of obtained images in order to view different areas without superimposition of structures.

Image interpretation:

- Image quality and morphology were assessed by the radiologist blinded to the results of previous conventional imaging examinations.
- ***Image Quality*** was assessed and scored subjectively into 5 grades from excellent to non depiction of the urinary tract according to Wiltrud et al.[10].
- ***Image morphology*** was assessed as follows:

1. The **kidneys** were assessed for
   - Presence or absence of pelvicalyceal (p/c) system dilatation; if present was graded according to Lee et al. classification into mild, moderate and severe[11].
   - The renal size, outline and parenchymal thickness, number of collecting systems and any associated anomalies.
   - Presence of renal calculi.
2. The **ureters** were assessed for strictures, calculi, dilatation and site of insertion.
3. The **urinary bladder** was assessed for bladder contour, filling and outlet obstruction.
4. Any other associated abnormality.

- MRU results were compared with the findings obtained by ultrasonography as well as other imaging results including those performed at the time of the patient's first presentation on which the clinical management was based.
- Nominal data were expressed as frequency and percentage and were compared using the Chi-Square test. P values less than 0.05 were considered

significant. Sensitivity of both ultrasound and MRU in detecting different lesions were compared.

RESULTS

Fifty collecting systems were studied in 26 children (two children had single kidneys). They included 19 males (73.1%) and 7 females with ages ranging from 2 to 14 years (mean ± SD = 7.5 yr). They included four cases with ARF (15.4%) and 11 cases (42.3%) with each of CRF and ESRD. Table 1 shows the imaging studies done in each group.

VCUG was positive for reflux in seven of nine cases (77.8%). In the tenth case, VCUG was done to identify a post traumatic urethral stricture. Technetium dimercaptosuccinic acid (DMSA) scan was performed for three children. Compared to MRU, DMSA scan was interpreted as normal in a case with ectopic ureteric insertion. Unilateral pelvicalyceal dilatation was detected in one case with primary megaureter (Fig. 1). In the third case the kidneys were non-functioning. Two patients had previously been subjected to intravenous urography (IVU) at earlier stages of their disease. In one of them, an obstructed upper moiety with ectopic ureteric insertion was not identified and in another an ectopic crossed fused non functioning kidney was also not identified.

The different pathologies encountered on US and MRU examinations are shown in table 2. Both ultrasound and MRU were comparable in assessing the kidneys and renal pelves, except for failure of US to identify the two cases with duplicated collecting systems and a case with crossed fused ectopic kidneys (Fig 2). On the other hand, a marked disparity was encountered between the ability of ultrasound and MRU in identifying ureteric pathologies. Although US showed p/c dilatation in all cases of PUJ obstruction, the cause could not be identified in five of them (Fig. 3). US could identify only 13% of dilated ureters shown by MRU. MRU correctly depicted the level of obstruction and the degree of ureteric dilatation; thus identifying the cause of dilatation (Fig. 4) with the exception of the seven cases with VUR demonstrated by VCUG. US also failed to identify ectopic ureteric insertions in three cases (Fig 5). Bladder outlet obstruction by persistent posterior urethral valves was suspected in two cases on both MRU due to over distended bladder and on ultrasound due to large amount of residual urine. Associated vesicovaginal fistula was identified in one case of VUR with dribbling and was confirmed by MR fistulography.

Table 3 shows the 13 cases with discordance between US and MRU and table 4 shows the sensitivity of US compared to MRU in detecting renal and urinary tract pathology.

Table 1: Study groups and different diagnostic imaging modalities performed.

Group	US	VCUG	DMSA	MRU
Acute renal impairment/failure	4	1	2	4
Chronic renal Impairment/ failure	11	3	1	11
End stage renal disease	11	6	0	11
Total	**26 (100%)**	**10 (38.5%)**	**3 (11.5%)**	**26 (100%)**

US: Ultrasound, VCUG: Voiding cystourethrography, DMSA: Dimercaptosuccinic acid scan, MRU: Magnetic resonance urography

Table 2: Different pathologies encountered with ultrasonography and MR urography

Finding	**US**		**MRU**		
	No	%	No	%	
Normal study	3	6	3	6	
P/C dilatation	31	62	31	62	
Dysplastic kidneys(1)	9	18	6	12	
Post obstructive atrophy(2)	8	16	8	16	
Post infectious atrophy(2)	7	14	7	14	
Duplex collecting systems	0	0	2	4	
Crossed fused ectopia	0	0	1	2	
Polycystic kidneys	2	4	2	4	
Renal Calculi	1	2	1	2	
Ureteric dilatation*	3	6	23	46	***p* < 0.001**
Pelviureteric junction obstruction*	1	2	6	12	***p* = 0.049**
Ureteric stricture*(3)	0	0	7	14	***p* = 0.007**
Ureteric calculi	0	0	2	4	
Ectopic ureteric insertion(4)	0	0	3	6	
Ureterocele	1	2	1	2	
Megaureter	1	2	1	2	
Reflux	0	0	0	0	
Bladder outlet obstruction	2	4	2	4	
Vesicovaginal fistula	0	0	1	2	

US: Ultrasound, MRU: Magnetic resonance urography, p/c: pelvicalyceal; * Statistically significant difference

(1) Dysplasia refers to multicystic (n=) and small kidneys (n=) with a moderately dilated, dysmorphic p/c systems without depiction of a stenosis.

(2) **Post obstructive atrophy** refers to small kidneys with dilated p/c systems with smooth outline and regular parenchymal thickness (associated with neglected ureteric strictures), while **post infectious atrophy** refers to small kidneys with dilated p/c systems associated with parenchymal scarring.

(3) Including one mid-ureteric and 6 lower ureteric strictures.

(4) Two in the vagina and one in the contralateral side of the urinary bladder

Table 3: Demographic and Imaging findings in cases with non-concordant MRU and US findings

AGE/GENDER	DIAGNOSIS	US	MRU
7 yr/ M	ARF, Left renal colic	LT p/c dilatation	RT: atrophic LT: p/c dilatation Stone distal left ureter
9 yr/ F	ESRD	RT: atrophic LT: p/c dilatation	RT: atrophic LT: p/c dilatation Stricture distal left ureter
7 yr/ F	CRF, Incontinence	RT: atrophic kidney	RT: atrophic, Ectopic Rt ureter
11 yr/ M	ESRD	Bilateral mild p/c dilatation	Bilateral p/c dilatation Bilateral ureteric strictures
8 yr/ M	CRF	Bilateral p/c dilatation	Bilateral PUJ obstruction
6 yr/ M*	CRF	Bilateral p/c dilatation	Bilateral p/c dilatation RT: PUJ obstruction LT: Duplex kidney
3 yr/ M	ESRD	RT: multicystic dysplastic LT: atrophic	Crossed fused ectopia with p/c dilatation
14 yr/ M	ESRD, Prune Belly	Bilateral p/c dilatation	Bilateral p/c dilatation Stricture distal ureters
6 yr/ M*	CRF	Bilateral p/c dilatation	Bilateral p/c dilatation Distal ureteric strictures
6 yr/ M	ESRD	RT: atrophy LT: p/c dilatation	RT: absent LT: p/c dilatation Ectopic ureter
7 yr/ M	CRF	Bilateral p/c dilatation	Bilateral PUJ obstruction
10 yr/ M	ARF, Lt renal colic	Bilateral post obstructive atrophy	Bilateral post obst. atrophy Left mid ureteric stone
6 yr/ F	ARF, Incontinence	LT: Localized hydrocalicosis	LT: Duplex, obstructed upper moiety, ectopic left ureter

US: Ultrasound, MRU: Magnetic resonance urography, ARF: acute renal failure, CRF: chronic renal failure, ESRD: end-stage renal disease, p/c: pelvicalyceal, PUJ: pelviureteric junction.
* Previous operative intervention

Table 4: Sensitivity of ultrasonography compared to MR urography in diagnosis of renal and ureteric pathology

PATHOLOGY	POSITIVE CASES		SENSITIVITY*	REMARKS
	US	MRU		
Kidney and pelvis:				
P/C dilatation	31	31	100%	
Dysplastic kidneys	9	6	100%	Specificity 93.2%, PPV 66.7%(1)
Other congenital anomalies(2)	2	5	40%	
Acquired lesions(3)	16	16	100%	
Ureter:				
Dilatation	3	23	13%	
Underlying lesions†(4)	3	20	11.1%	MRU: sensitivity 74.1%, $p < 0.001$

US: Ultrasound, MRU: Magnetic resonance urography, p/c: pelvicalyceal

* Sensitivity of US compared to the MRU findings

† Sensitivity was measured in comparison to VCUG in the 7 patients with VUR

(1) Kidneys incorrectly diagnosed as dysplastic by US included crossed fused ectopic kidneys diagnosed as multicystic dysplastic and absent kidney diagnosed as atrophic dysplastic.

(2) Include polycystic kidneys, crossed fused ectopic and duplex collecting systems.

(3) Atrophic kidneys and calculi.

(4) Include reflux, strictures, pelviureteric obstruction, calculi, ureteroceles, megaureters and ectopic insertions.

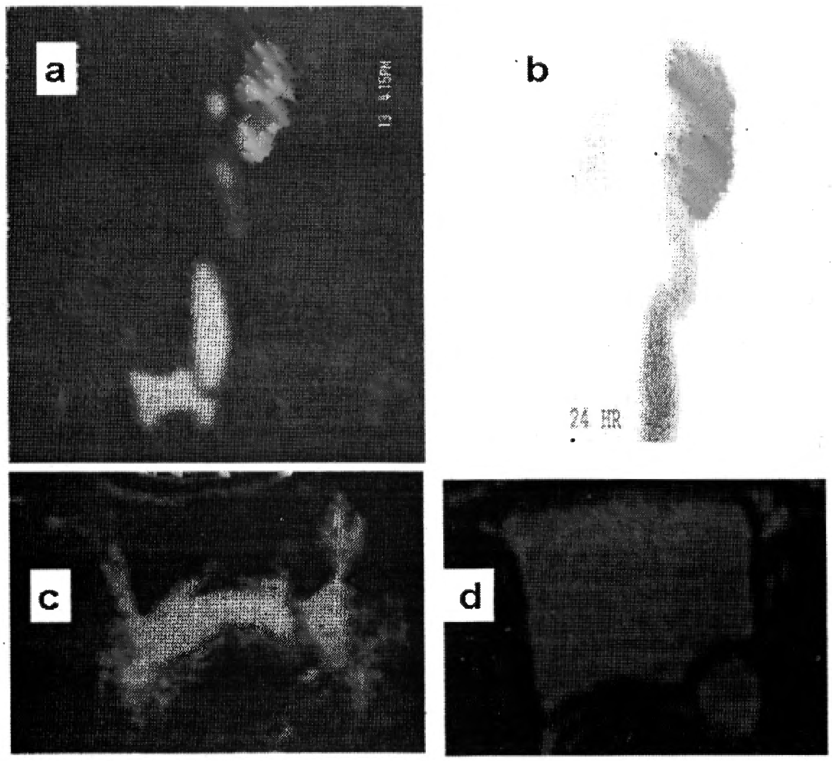


Fig. 1: Six years old female with left primary megaureter showing marked dilatation on MRU (a) and DMSA (b) associated with distal ureterocele seen on ultrasound (c) and axial MRI T2 WI (d).

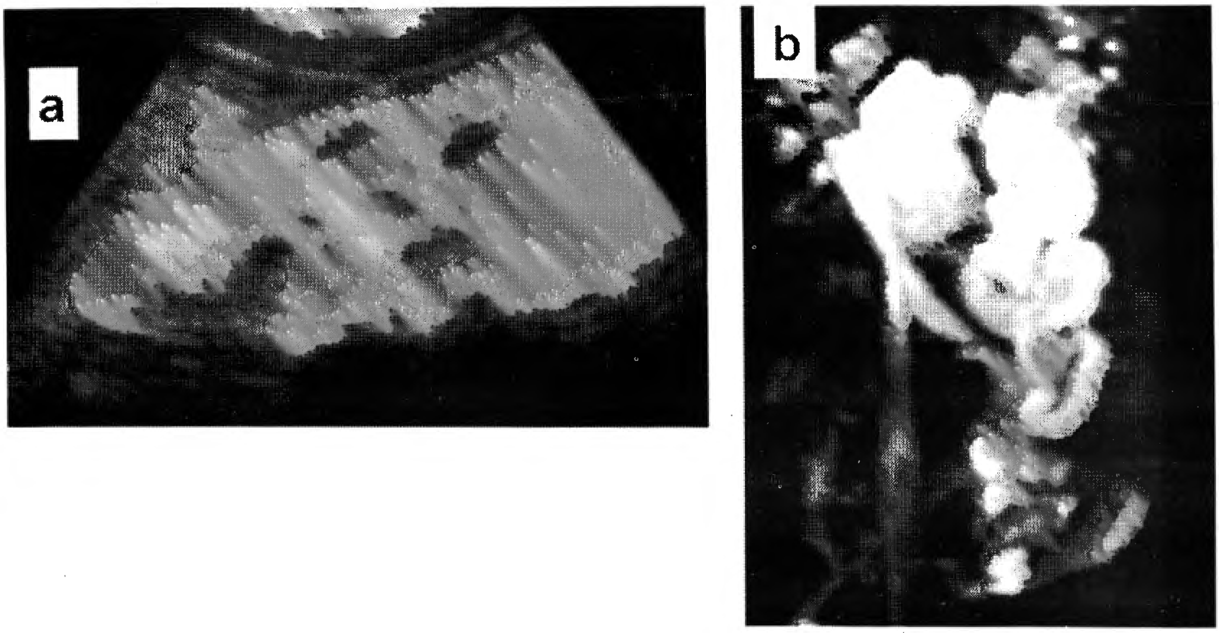


Fig. 2: Three years old male, with ESRD under regular hemodialysis diagnosed as multicystic dysplastic kidney on US (a). On MRU (b), the left ureter is seen crossing the midline to join the right p/c system; crossed fused ectopia. There are also bilateral distal ureteric strictures with back pressure changes.

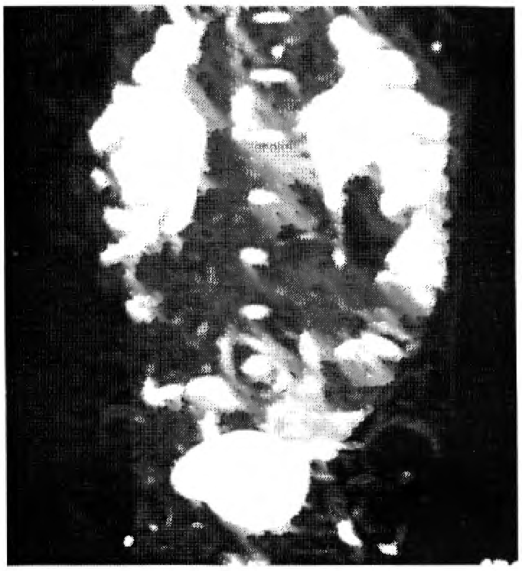


Fig. 3: Bilateral PUJ obstruction showing dilated p/c systems with abrupt arrest at the pelvicalyceal junction and inconspicuous ureters.

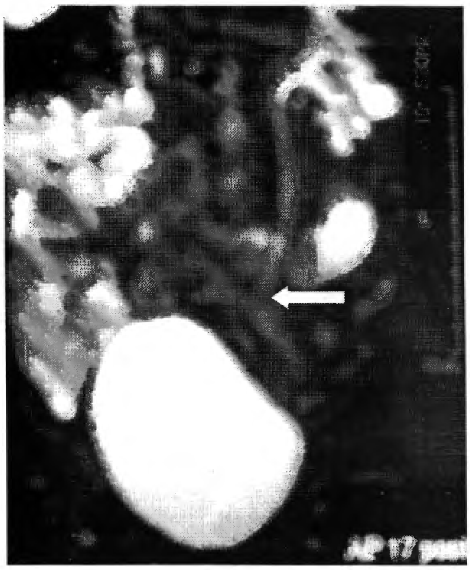
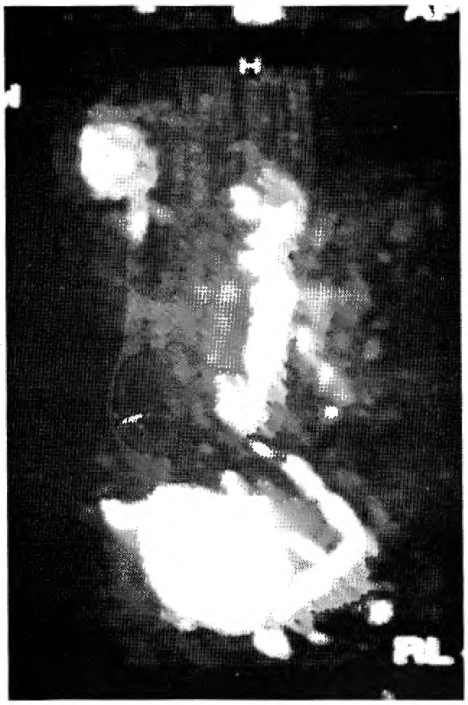


Fig. 4: Seven years old male, presenting with ARF and left renal colic. A stone (arrow) is seen impacted in the distal left ureter in MRU examination.



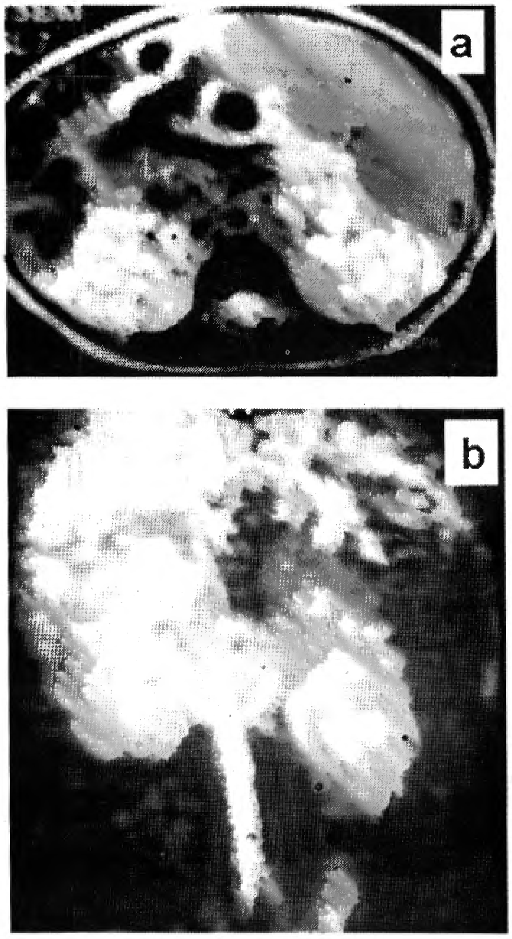


Fig. 5: Showing ectopic ueteric insertions into the vagina in a 7 years old female child with continuous dribbling.

Fig. 6: MRU of a 14 years old male with ARPKD showing bilateral renal cysts and splenomegaly on axial T2 WI (a), associated with intra-hepatic biliary radicle dilatation on MRU (b) images

DISCUSSION

Despite many advances in nephrology, renal replacement therapy and urinary tract imaging, the morbidity and mortality from renal failure is still high. Early attention to underlying urinary tract pathology may prevent the development of intrinsic kidney disease from long standing obstruction[12]. In early cases of renal impairment, urological interventions can help resolution of acute cases and slowing the progression of chronic cases.

When investigating these cases, history and clinical examination combined with blood and urine analysis are usually followed by a dilemma of imaging studies[2]. Ultrasonography is traditionally the primary imaging modality in evaluating the uro-genital tract in neonates, infants and children. US is independent of renal functions and does not entail ionizing radiation or contrast media[4]. However, it shows several intrinsic restrictions and a considerable investigator dependency with varying operator skill and training. Additionally, the quality of sonography images is influenced by varying capabilities of sonography instruments that may lead to missing crucial diagnoses.

Additional imaging studies include VCUG, IVU and scintigraphy[13]. These diagnostic modalities have potential drawbacks limiting their use in the pediatric age group specifically when renal functions are impaired. These include; hazards of ionizing radiation, allergies and nephrotoxicity related to administered contrast media and limited precision in exploring poorly and non functioning kidneys. The appropriate imaging work up should minimize the number of examinations, the radiation exposure, the potential hazards, expenses and discomfort; while maximizing useful clinical information[14]. Therefore, a reliable, preferably noninvasive, imaging technique with the lowest possible radiation burden is necessary to improve the imaging workup in this setting[5,15].

MR urography has successfully been applied to the pediatric urinary tract. It holds a vast potential for both anatomical and functional evaluation in children, infants and neonates with relatively little invasiveness. MR urography is primarily accomplished by two groups of sequences: T2 weighted and excretory T1 weighted gadolinium enhanced sequences after furosemide injection. In the former, heavily T2 weighted sequences are used with patients in whom static fluids can be viewed. This technique is independent of function, does not require the use of contrast media and is especially successful in imaging dilated systems[3]. Excretory MRU can supply additional information in cases with functional kidneys where the cause of obstruction cannot be revealed by static MRU. In June 2006, the FDA advised against the administration of gadolinium-containing contrast agents during MRI examinations of patients with renal impairment. This was related to the potential dangers of developing nephrogenic systemic fibrosis, based on several studies performed as early as 1998[16-18]. Accordingly, the present study investigated the role of morphological assessment of the urinary tract by heavily T2 weighted technique in the diagnosis and management of children with renal impairment and suspected urinary tract pathology.

Fifty collecting systems were examined in 26 children. The examination was successfully conducted in all patients yielding adequate image quality for proper assessment of the urinary tract. Limitations to be considered were the need for sedation in seven cases and the inability of MRU to assess for vesico ureteric reflux as it cannot be performed during micturition. VUR may be suspected by MRU in the presence of dilated systems with no significant obstructive cause. Previous studies with MRU[3,5,19,20], have also reported similar drawbacks. Until new MR imaging techniques come to use, VCUG is still the gold standard for assessment of reflux.

Pelvicalyceal dilatation was equally detected by both US and MRU. However, associated PUJ obstruction and ureteric lesions (strictures, stones and ectopic insertions) identified by MRU were predictably missed by US. There was a statistically significant difference between the ability of ultrasound and MRU in diagnosing ureteric dilatation, PUJ obstruction and ureteric strictures ($p < 0.001$, 0.049 and 0.007 respectively). These findings prove that MRU is specifically superior in assessment of ureteric pathologies starting from the level of the pelviureteric junction down to the distal ureteric insertion. Ureteric pathology may only be suspected (without specification) when the p/c system is dilated on the ultrasound.

Ureteric obstruction results in increased pressure and distension proximal to the point of obstruction, resulting in structural and cellular damage with subsequent loss of renal function. When pressure is relieved in a timely manner the changes in function can be transient; however, when it is not, permanent damage may ensue[(21)].

PUJ obstruction is the most common cause of hydronephrosis in infancy and early childhood. It is bilateral in 30% of cases. PUJ obstruction involved six p/c systems in the present study. In one of these cases affection was bilateral. US and MRU were equally sensitive in detection of p/c dilatation in these cases but US was not specific in identifying the obstructive cause. Diagnosis was made on MRU by the abrupt change in caliber between the proximally dilated p/c system and the inconspicuous ureters[(22)].

Ureteral strictures mostly result from infection, trauma or irradiation therapy[(22)]. In this study, there was a striking number (7 cases) of otherwise undiagnosed ureteric strictures that were only detected on MRU. We failed to identify the etiological cause in most of these patients with the exception of one child with a history of stone passage and another with history of anti reflux surgery.

Ureteral stones are traditionally diagnosed by plain films and spiral CT examinations when a calcified opacity is detected within or along the course of the ureter. This presents a challenge to MRU, at which calcifications are not directly visualized. Nevertheless, two cases were diagnosed by MRU based on the identification of a filling defect inside the ureteral lumen. This sign is not highly specific and may represent a blood clot or tumor[(23)]. Therefore, spiral CT should be used to confirm suspicious calculi.

Ectopic insertion of the ureter stems from abnormal ureteral bud migration. In females, ectopic ureters can terminate at a level distal to the continence mechanisms and thus may be associated with classic continuous dribbling despite a normal voiding pattern[(5,24)]. Two females presenting with dribbling had ectopic ureteric insertions that were only identified on MRU examination. In a third case with a single p/c system, the ureter was seen draining into the contralateral side of the urinary bladder.

Ureteroceles represent cystic dilatation of the intravesical segment of the ureter, usually associated with obstruction of the meatus[(5,25)]. We encountered two urteroceles, involving the ectopic ureter draining the obstructed upper moiety and a second one draining a primary megaureter.

A group of pediatric pathologies that may pose difficulties in terms of conventional imaging methods are duplicated collecting systems, which may be associated with obstruction, ectopic ureters or uretroceles and vesicoureteric reflux in one of the systems[26,27]. Obstructed or atrophic moieties are not identified on IVU and ectopic insertions are difficult to be detected due to contrast dilution. MRU, being independent of renal functions could adequately detect ureteric insertions and collecting system morphology. Two children had duplicated systems one of them presenting with vesicoureteric reflux together with unilateral PUJ obstruction and the other showing ectopic ureteric insertion of a non functioning upper moiety. Both children underwent surgical correction and both were not detected on ultrasound examination. A case of crossed fused ectopia was misinterpreted on ultrasound as multicystic dysplastic kidney and atrophic contralateral one. Diagnosis was made on MRU examination.

Overall, the sensitivity of MRU in depicting renal and ureteric pathologies was high, corresponding to previously reported results[28]. MRU could provide important additional findings compared to the other imaging modalities performed in a considerable number of cases (13 cases). This was mainly based on the inability of ultrasound to identify ureteric pathology, as well as the inability to subject patients with renal failure to intravenous urography. It is therefore reasonable to recommend MRU in patients with dilated p/c systems seen on ultrasound who need accurate identification of the underlying pathology, which is likely to need surgical intervention. This is especially true when renal impairment precludes the use of excretory urography. Given that most of these conditions are amenable to surgical correction and that missed or delayed diagnosis can seriously affect prognosis in terms of renal functions, the cost associated with MRU may be considered well justified. This is in agreement with Michael et al.[5] who suggested that early MR urography may shorten the course of the disease in some patients and may replace some conventional imaging.

To conclude, static MR urography combines a high diagnostic yield (even in children with poorly functioning kidneys) with a favorable safety profile associated with absence of contrast injection and ionizing radiation. Diagnostic limitations include inability to assess reflux and the potential need to confirm suspected calculi with spiral CT. MR urography should be the single investigation to follow in most cases when US is non-conclusive. Young children with recurrent urinary tract infections and those with atrophic scarred kidneys are highly suspected of having VUR and VCUG would be the more appropriate next choice. A diagnostic algorithm is proposed in which MRU plays a critical role (Fig. 7). The authors are aware that formal comparison between the diagnostic accuracy of MRU and either excretory urography or isotopic scanning are still needed to extend this recommendation to children with normal renal functions. Dynamic study with excretory MRU versus scintigraphy could be the subject of further research.

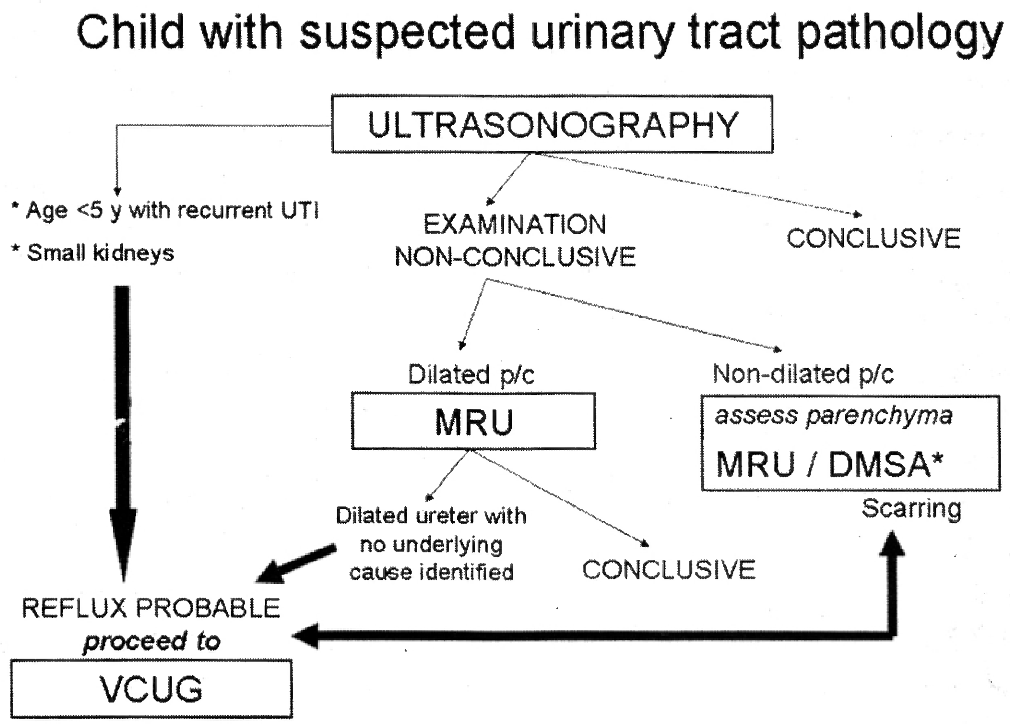


Fig. 7: Suggested algorithm incorporating MR urography for urinary tract imaging in children.

MRU: Magnetic resonance urography, VCUG: Voiding cystourethrography, DMSA: dimercaptosuccinic acid scan, p/c: pelvicalyceal system.
* DMSA may not be applicable in cases of severe renal functional loss due to poor uptake of the radionuclide Options for dynamic scanning include diethylene tetramine pentaacetic acid (DTPA) scan and excretory MRU.

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