

RADIONUCLIDE STUDIES IN THE EVALUATION OF URINARY TRACT INFECTIONS

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Objective: To estimate the prevalence of vesicoureteral reflux (VUR) and renal scarring in children presenting with culture proven urinary tract infections (UTI). **Design:** Descriptive study. **Setting:** Tertiary care hospital-based study. **Subjects:** Thirty-two children with proven UTI were evaluated by means of an abdominal ultrasonogram (USG), Technetium-99m Dimercapto Succinic Acid (DMSA) scan and Direct Radionuclide Cystography (DRCG). A micturating cystourethrogram (MCU) was performed to rule out any structural abnormality and to grade VUR. **Results:** A total of 64 renal units in 32 children were evaluated. DMSA scan showed scarring in 27 renal units (42.2%) in 16 patients. Bilateral renal scarring was more common in older (>2 yr) children as compared to younger ones (89% Vs 43%; $p < 0.05$). USG detected abnormalities in 13 renal units (20.3%) in 7 cases. VUR was detected in 37.5% of children of all age group by DRCG. In contrast, MCU showed evidence of VUR in only 13/20 renal units with a sensitivity of 65% as compared to DRCG and did not pick up any additional VUR that could have been missed on the DRCG. Only 3/9 in <2 yr, in contrast to 10/11 in >2 yr were positive for VUR on MCU ($p < 0.05$). However, MCU detected evidence of cystitis in 3 children and a bladder diverticulum in one patient. **Conclusion:** Wherever available, DMSA scan should be considered as a part of the first line investigations in any patient presenting with UTI. DRCG can also be performed in the same sitting to screen for the presence of reflux particularly for girls.

Key words: Urinary tract infection, Dimercaptosuccinic acid scan, Direct radionuclide cystography, Renal scarring, Vesicoureteral reflux.

THE cumulative risk for contracting a symptomatic urinary tract infection (UTI) in childhood is 3% for girls and 1% for boys(1). Vesicoureteral reflux (VUR) when present is the single most significant host risk factor in the etiology of pyelonephritis. Even in the absence of significant VUR, UTI can result in renal parenchymal scars in a subset of patients.

If acute pyelonephritis is promptly diagnosed and treated, permanent renal scarring is unlikely whereas neglected infections cause progressive parenchymal damage. As UTI appears to play a central role in causing and perpetuating this damage, it is recommended that children should undergo imaging evaluation after the first documented UTI(2).

The intravenous urogram is used as conventional modality for the detection of scarring and structural anomalies in children(3). Nuclear imaging techniques have been established to be highly sensitive for the detection of renal scarring and VUR(4,5). In addition, a repeat Dimercapto Succinic Acid (DMSA) scan after 6-12 weeks can differentiate areas of active parenchymal inflammation in the acute phase of UTI from subsequent scar formation(6). Extensive studies are available in the western literature on this subject but there is paucity of data in our pediatric population. The objective of the current study was to estimate the prevalence of VUR and renal scarring in children presenting with culture proven UTI in a tertiary care hospital.

Subjects and Methods

A total of 32 children with proven UTI (bacterial colony forming unit $>10^5$ per ml of urine) presenting to Pediatric Department of Safdarjang Hospital between September 1992 and August 1993 were included in this study. All children with significant colony counts (even first time positive) were evaluated irrespective of number of episodes of fever, crying during micturition, failure to thrive or other signs/ symptoms of UTI. The cohort included 15 girls and 17 boys with ages ranging from 2.5 months to 12 years (13 children below 2 years of age). An informed consent of parents was obtained before including them in the study.

Clinical evaluation of all the children including a detailed history and physical examination was carried out. All children were subjected to kidney function tests including blood urea, serum creatinine, serum electrolytes, X-ray KUB, abdominal ultrasonography (USG) and micturating cystourethrogram (MCU).

Ultrasonographic findings described as diagnostic of acute renal infection include areas of increased cortical echogenicity, dilatation of the renal collecting system, and renal enlargement. Scarring was identified by focal increased echogenicity in the involved area of medulla and cortex which extended beyond the normal area of the renal sinus(7).

The radionuclide studies were done in accordance with the techniques described by our group earlier(8). For the renal cortical scan, 2-3m Ci (74-111 mBq) of Tc-99m DMSA was injected intravenously. The patient was placed before the gamma camera and static images were acquired in anterior and posterior positions at 30 min and at 2-3 hours post-injection phase. Oblique views were acquired as and when needed. During interpretation of the scan, the site, the size, the shape and irregularity in cortical outline were looked for. The degree of radionuclide concentration was observed qualitatively in each kidney. The supra-pubic puncture technique for direct radionuclide cystography (DRCG) was adopted with a 24 gauge needle. A small amount of urine was withdrawn into the syringe to ensure that the needle was in the bladder cavity before injecting the tracer.

Then 1mCi of Tc-99m phytate was injected into the bladder. The patient was placed before the gamma camera and serial images were obtained in a time frame mode using appropriate computer software (frame rate = 1 frame per second; total = 120 frames). No complications were encountered with these procedures.

MCU was done according to the standard protocol. Spot films were obtained to minimize radiation dose. Static cystograms, a voiding film and a post-void film were taken. VUR was graded as less severe or more severe based on the International Reflux Study Committee grading (9,10).

The prevalence of renal scar and reflux, the sensitivity and the specificity of different contemporary modalities were calculated using standard statistical methods. Statistical inferences were made using the chi-square test for comparison. For the sake of the definition, either of the investigation convincingly detecting VUR was considered true positive of reflux or similar criteria were also used for scar.

Results

E. Coli was the commonest organism in 26 cases (81%) in the study population. In the remaining six (19%) patients, *Klebsiella*, *Proteus*, *Pseudomonas* and mixed infections of *E. Coli* plus any of the later organisms were isolated. Fever was present in 28 (87.5%) cases. Signs of systemic upset including pallor, irritability, anorexia, nausea, vomiting, diarrhea, weight loss and convulsions were present in 23 (71.8%) cases. Clinically five patients were diagnosed as having possible parenchymal involvement in the form of flank pain, fever associated with chills and rigors and also palpable kidney. All of them were older than 2 years of age. Acute renal failure was seen in a 10year old female child who was previously asymptomatic. Two patients presented with hypertension; one of them was a 12 year old boy with history of recurrent UTI in the past and the other one was an 8 year old girl, apparently asymptomatic previously.

Blood urea and serum creatinine values were elevated in 3 patients. X-ray KUB was essentially normal in all except showing vertebral anomalies in 2 children. One of these had a spina bifida occulta at level S1 of vertebra and the second had an abnormal bar of bone extending from S1 vertebra to the ilium. Both had VUR on DRCG scanning.

DMSA scan detected cortical scars in 16/32 patients and a total of 27 renal units were scarred. Interestingly in the younger age group (children <2 years), 10 renal units in 7 pateints were scarred while in the older age group, 17 renal units in 9 patients were scarred. Of those patients with scars, bilateral scarring was seen in 89% of older patients and in only 43% of younger patients.

USG demonstrated abnormalities in 13 renal units in 7 patients. However, only 3 renal units in 2 patients were less than 2 years of age. The USG was less sensitive than the DMSA scan in detecting renal scars (*Table 1*).

DRCG detected reflux in 12/32 (37.5%) patients and a total of 20 renal units showed VUR. The prevalence of VUR in the younger age group was 46% and in the older age-group it was 31.6%. All the renal units with higher grade reflux (13/13) had ipsilateral renal scars while 3/7 renal units with lower grades of reflux were associated with scars (p<0.02)

TABLE 1- Correlation Between USG and DMSA Scan Findings

| Age (years) | Renal units abnormal on USG | Renal units with scar on DMSA | Sensitivity of USG in % |
|-------------|-----------------------------|-------------------------------|-------------------------|
| <2 | 3 | 10 | 30.0 |
| >2 | 10 | 17 | 58.8 |
| Total | 13 | 27 | 48.1 |

There was no significant difference in the sensitivity between the two age-groups.

Sixty three per cent of renal units with scars on DMSA scan had an ipsilateral VUR whereas, 85% of renal units with VUR had ipsilateral scars. Ten renal units which showed scars on DMSA scan did not demonstrate concurrent VUR, whereas 3 renal units which were normal on DMSA scan had evidence of low grade VUR on DRCG.

MCU detected VUR in only 13 out of 20 renal units detected by DRCG (Table II) and MCU did not pick up any VUR that was missed on the DRCG. In contrast, MCU missed bilateral high grade reflux in a 2.5 month-old-male child and detected only 33.3% of VUR in children less than 2 years age. However, evidence of cystitis was seen in 3 patients and a bladder diverticulum was seen in one patient by MCU. None of the patients had evidence of bladder outlet obstruction.

Discussion

In this series of 32 patients, the prevalence of VUR was 37.5%. This compares well with the figures of 29-50% as reported by the International Reflux Study Committee(10). The lower prevalence of reflux in the older population is consistent with the fact that VUR is known to undergo spontaneous resolution with age, unless associated with some structural anomalies(11). To establish the true prevalence of VUR at the time of first UTI was not feasible in this

TABLE II-Comparison of DRCG and MCU in the Detection of VUR

| Age (years) | DRCG+ | MCU+ | (%) |
|-------------|-------|------|--------|
| <2 | 9 | 3 | (33.3) |
| >2 | 11 | 10 | (90.9) |
| Total | 20 | 13 | 65.0 |

p < 0.05 for difference between the two age groups.

study due to logistic problems.

The prevalence of scarring in the study population was 50% (renal unit: 42.2%). In similar study designs, prevalences ranging from 13-23% were reported(12,13). Several explanations are possible for the high frequency of scarring and the presence of scars without associated VUR in this study. Patients were selected from a tertiary care hospital and history suggestive of recurrent UTI was available in many (23/ 27) of those with scarring (prior VUR can not be ruled out in remaining children). Undetected, poorly controlled infections at a very young age are a major determinant for the high rate of scarring in our population. In the lower age group (<2 yr), 3/7 children had bilateral scarring, whereas in the age group of >2 years 8/9 had bilateral scarring (p <0.05). The higher frequency of bilateral scarring in the older population as seen in this study is also a pointer in this regard. Spontaneous resolution of VUR could account for the lower frequency of VUR in our study. Previous estimates of scarring associated with VUR were made by intravenous urogram which is known to be less sensitive than DMSA scan in detection of scars(14). However, scarring independent of VUR is also known to occur in susceptible hosts following infections with certain specific bacterial strains like P-fimbriated *E. coli*.

The sensitivity of USG in detecting scarring was 30% in the younger age group and 59% (p >0.05) in older children as compared to DMSA. Though an excellent non-invasive modality, USG is known to be inferior to DMSA in the detection of scars especially in the younger age group(3).

Considering the high frequency of scarring in our population and the poor correlation of clinical findings with evidence of upper tract involvement, all

children presenting with UTI should undergo imaging studies to assess the status of the upper urinary tracts. Further, the International Reflux Study Committee showed that 63% of scars were associated with VUR. In view of the low sensitivity of conventional modalities like USG, especially in the young patient, a DMSA scan which is a more sensitive and specific investigation (*considered as gold standard for scar detection*) should be done, ideally in all patients presenting with UTI. As scarring can occur even with the first UTI, a DMSA scan should be done at the first clinical presentation especially in young patients(14). In our series, DRCG was a simple and sensitive technique for identification of VUR. Also owing to its very low radiation dose, it has an important place in the follow up of patients with VUR(2). MCU, which is associated with considerable irradiation to the gonads may not be a suitable modality for follow up.

The present data suggest that the frequency of scarring and VUR are high in our pediatric population. USG and MCU are not very sensitive techniques specially in children below 2 years to diagnose the renal scars (30% vs 58.8%) and VUR (33% vs 91%), respectively. We recommend, that radionuclide imaging, particularly DMSA scanning, should form an integral part of the initial work-up of UTI where it is available and for subsequent follow up evaluation.

REFERENCES

- 1 Winberg J. Clinical aspects of urinary tract infection. *In: Pediatric Nephrology*. Eds. Holliday MA, Baratt TM, Vernier RL. Baltimore, Williams and Wilkins, 1987, pp 626-646.
- 2 Lerner GR, Fleischmann LE, Perlmutter AD. Reflux nephropathy. *Pediatr Clin North Am* 1987, 34: 747-770.
- 3 Elison BS, Taylor D, Vanderwall H, *et al*. Comparison of DMSA scintigraphy with intravenous urography for the detection of renal scarring and its correlation with vesicoureteral reflux. *Br J Urol* 1992, 69: 294-302.
- 4 McLorie GA, Aliabadi H, Curchill BM, *et al*. 99m Technetium dimercapto succinic acid renal scanning and excretory urography in diagnosis of renal scars in children. *J Urol* 1989, 142: 790-792.
- 5 Majd M. Nuclear medicine in pediatric urology. *In: Clinical Pediatric Urology*, 3rd edn. Eds. Kelalis PP, King LR, Belman AB. Philadelphia, W.B. Saunders Company, 1992, pp 117-165.
- 6 Tappin DM, Murphy AV, Mocan H, *et al*. A prospective study of children with first acute symptomatic *E. coli* urinary tract infection- Early 99m technetium dimercaptosuccinic acid scan appearances. *Acta Pediatr Scand* 1989, 78: 923-929.
- 7 Bjorgvinsson E, Majd M, Egli KD. Diagnosis of acute pyelonephritis in children. Comparison of sonography and Tc-99m DMSA scintigraphy. *AJR* 1991, 157: 539- 545.
- 8 Padhy AK, Gopinath PG, Mitra DK, Bhatnagar V. Direct radionuclide cystogram (DRCG) and urine flow metry (UFMT) in the evaluation of patients with vesicoureteral reflux and/or associated obstructive or neurogenic pathology of lower urinary tract. *Indian J Pediatr* 1989, 56: 483-492.
- 9 Zhang G, Day DL, Loken M, Gonzalez R. Grading of reflux by radionuclide cystography. *Clin Nucl Med* 1987, 2: 106- 109.
- 10 Report of the International Reflux Study Committee. Medical versus surgical treatment of primary vesicoureteral reflux: A prospective international reflux study in children. *J Urol* 1981, 125: 277-283.
- 11 Kunin CM. A 10-year study of bacteriuria in school girls: Final report of bacteriologic, urologic, and epidemiologic findings. *J Infect Dis* 1970,122: 382-394.
- 12 Gleeson FV, Gordon I. Imaging in urinary tract infection. *Arch Dis Child* 1991, 66- 1282-1283.

- 13 Skoog SJ, Belman AB. Vesicoureteral reflux in black children. *Pediatrics* 1991, 87: 538-543.
- 14 Verber IG, Strudley MDR Meller ST 99m Tc dimercapto succinic acid (DMSA) scan as first investigation of urinary tract infection. *Arch Dis Child* 1988, 63: 1320-1325.
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NOTES AND NEWS

ELECTION SCHEDULE OF 5TH INTERNATIONAL CONGRESS OF TROPICAL PEDIATRICS

- September 2, 1996** : Last date for filing nomination papers.
- September 3rd, 1996** : Scrutiny of nomination papers.
- September 16th, 1996** : Last date for withdrawal of nomination papers.
- September 30th, 1996** : Posting of ballot papers.
- November 15th, 1996** : Last date for receiving ballot papers.
- November 23rd & 24th, 1996** : Vote counting and declaration of results.
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IAP ELECTION 1997 SCHEDULE

- September 25th, 1996** : Posting of ballot papers.
- November 15th, 1996** : Last date for receiving ballot papers.
- November 16th & 17th, 1996** : Vote counting and declaration of results.
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XXIV RAJASTHAN STATE PEDIATRIC CONFERENCE

This Conference is to be held at Barmer-Jaisalmer on 26-27 October 96. The conference is being organized by the Department of Pediatrics, General Hospital, Barmer. For further details please contact Dr. R.K. Maheshwari, 105, Old Petrol Pump Area, Station Road, Barmer 344 001, Tel. (02982) 20651 and Dr. S.R. Bhandari, Organizing Secretary, Kalyanpura, Barmer 344 001, Tel. (02982) 20650.

NOTES AND NEWS

PEDICON' 97

It will be a great honor and pleasure for all the members of Ahmedabad Branch of Indian Academy of Pediatrics, to have you all with us at the 34th National Conference of Indian Academy of Pediatrics, "PEDICON'97" at our beloved city of Ahmedabad. This grand academic festival happily coincides with the Golden Jubilee year of the Department of Pediatrics of the B.J. Medical College, Ahmedabad.

High lights of the Conference:

| | | |
|------------------------------|---|--|
| PALS Course | : | 2nd & 3rd January 1997 (8.30 a.m. to 5 p.m.) |
| NALS Course | : | 3rd January 1997 (8:30 a.m. to 5 p.m.) |
| A special practical workshop | : | Common pediatric procedures and equipments 3rd January 1997 (8.30 a.m. to 5 p.m.) |

For only 40 members in each group on first cum first registered basis

| | | |
|--------------------------|---|---|
| General CME | : | 4th January 1997 (8.30 a.m. to 1.30 p.m.) |
| Subspeciality CME | : | 4th January 1997 (2.00 p.m. to 5.00 p.m.) |
| Conference Inauguration | : | 4th January 1997 (6.30 p.m. to 8.00 p.m.) |
| Conference Deliberations | : | 5th January to 7th January 1997 |

Registration Fees Schedule:

| <i>Category</i> | <i>August 1996</i> | <i>October 1996</i> | <i>November 1996</i> | <i>After 1st Dec. 96.</i> |
|--|------------------------|-------------------------|--------------------------|-------------------------------|
| Full Registration | | | | |
| IAP Members/Defence | 800 | 1000 | 1250 | 1500 |
| Non IAP Members | 1100 | 1300 | 1500 | 1700 |
| P.G./Residents | 700 | 800 | 900 | 1200 |
| Partial Registration (***) (Without Lunch & Dinner) | | | | |
| IAP Members/Defence | 500 | 700 | 900 | 1100 |
| P.G./Residents | 400 | 500 | 600 | 700 |
| NALS/Sp. Workshop | 250 | 300 | 350 | 400 |
| CME | 250 | 300 | 350 | 400 |
| PALS | 700 | 700 | 800 | 900 |
| (Includes Rs. 200/- obligatory for the manual). | | | | |
| Accompanying Persons | 700 | 800 | 900 | 1200 |
| (Children less than 10 years are allowed free) | | | | |
| Foreign Delegates (US \$) | 250 | 250 | 300 | 350 |

BANQUET: FREE - Courtesy: Reception Committee.

Partial Registration (***)

With a genuine intention of allowing our honored delegates to have a freedom of choice for food as well as possible reduction in the registration fees this year we are introducing a new category of Partial Registration. In this system the delegates who do not wish to have full heavy lunches and dinners have the option to pay less registration fees and buy food from various stalls that will be put up at the venue. Those delegates who do not opt for this system can pay full registration fees and have regular full meals. We hope the members will appreciate the good intentions of the organizers and co-operate in experimenting this system. In both types delicious, clean food is assured.

All persons attending/participation in the conference must register. Post graduates/residents should send the certificate from the head of the department to avail the registration concession.

Tours

Detailed information about tourist places of interest around Gujarat will be provided on request and individual or group reservations can be arranged for the delegates.

Accommodation

As the conference is during the tourist season you are advised to book your request as early as possible. We are also making efforts to provide hostel and dormitory type of accommodation for limited members. Accommodation is reserved on "First come First serve basis".

Your request for accommodation should include accommodation advance for one day.

Payments and Refund

All payments should be made by Cash/Bank Demand draft drawn in favor of "PEDICON,97" payable at Ahmedabad. Requests for refund will be entertained only after the conference is over, provided the request for cancellation is made before 30th November, 1996. No refund will be paid for the advances given for accommodation. Return journey reservation requests are attended only on receipt of full amount in advance along with the registration fee before 1st November. Registered delegates can avail the railway concession forms from the General Secretary. I.A.P. Kailas Darshan, Kennedy Bridge, Bombay, 400 007.

| NAME: _____ | PAYMENT |
|------------------------------|----------------------------------|
| SEX: _____ VEG/NON: _____ | FULL REG. (IAP MEMB) : _____ |
| ADDRESS _____ | (NON MEMB) : _____ |
| CITY _____ Pincode _____ | (P.G. MEMB) : _____ |
| STATE _____ | PART REG. (IAP MEMB) : _____ |
| PHONE _____ Fax _____ | (P.G MEMB) : _____ |
| ORGANIZATION _____ | NALS/SP. WORKSHOP : _____ |
| DESIGNATION _____ | CME REG. : _____ |
| IAP MEM. NO. _____ | PALS REG. : _____ |
| DD NO. _____ | ACC. MEMBER (ADULT) : _____ |
| BANK NAME _____ BRANCH _____ | ACC. MEMBER (CHILD) : _____ |
| DD AMOUNT _____ | ACCOMMODATION CHRGS : _____ |
| | RETURN JOURNEY CHRGS : _____ |
| | TOTAL AMOUNT : _____ |
| | FOREIGN DELEGATES (US \$): _____ |

ACCOMMODATION : REQUIRED (YES/NO)

HOTEL TYPE : A/B/C/HOSTEL ROOM : SINGLE AC NO. OF PERSONS: _____
DOUBLE NON AC

FROM DATE :/...../1997 DORMITORY

TO DATE :/...../1997 ARR. DATE :/...../1997 ARR. TIME : _____

ARR. MODE : FLIGHT/TRAIN/BUS

| ACCOMPANYING PERSON (S): | | | | TOUR CHARGES FOR: | | |
|--|-------|-----------|-------|-----------------------------------|------------------|------------|
| SR. | NAME | ADLT/CHLD | SEX | VEG/NON | TOUR CODE/NAME : | |
| 1. | _____ | _____ | _____ | _____ | PERSON(S) : | _____ |
| 2. | _____ | _____ | _____ | _____ | | |
| 3. | _____ | _____ | _____ | _____ | TOUR CODE/NAME : | _____ |
| 4. | _____ | _____ | _____ | _____ | PERSON(S) : | _____ |
| 5. | _____ | _____ | _____ | _____ | | |
| Return journey reservation : Required (Yes/No) | | | | *Accommodation type* | | |
| DATE:/...../1997 TIME: _____ | | | | Category | Tariff | Advance |
| MODE: FLIGHT/TRAIN/BUS (In Rs.) (In Rs.) | | | | | Range | Per Member |
| DESTINATION : | | | | | (In Rs.) | (In Rs.) |
| Class: First (AC/Non AC); Second (Ac/Non AC); Sleeper/Seating | | | | Per Day /Person | | |
| SR. | NAME | AGE | SEX | A | 1000-2000 | 2500 |
| 1. | _____ | _____ | _____ | B | 500-1000 | 1000 |
| 2. | _____ | _____ | _____ | C | 200-500 | 500 |
| 3. | _____ | _____ | _____ | Hostel | | |
| 4. | _____ | _____ | _____ | Type Rs. : 350 (Full Conf. Period | | |
| 5. | _____ | _____ | _____ | 5 to 7 Jan. 1997) | | |
| | | | | : 150 (Pre-Conf. CME | | |
| | | | | 4th Jan. 1997) | | |

Mail to reach preferably before 31st August 1996.

To,

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