Retrograde intrarenal surgery for renal stones in children <5 years of age

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ABSTRACT

Introduction: There are very few studies in the literature describing retrograde intrarenal surgery (RIRS) in preschool children. We have evaluated the feasibility, stone-free rate, and complications of RIRS in children <5 years of age. **Methods:** All children <5 years of age and stone size <2 cm (renal/proximal ureteric), who underwent RIRS at our hospital from February 2010 to May 2020 were included in this retrospective study. All children were prestented for the passive dilatation of ureter. A 7.5 Fr flexible ureterorenoscope was introduced over the ureteral access sheath (UAS) or over a guidewire. At 2 weeks, the stent was removed and at 2 months the child was evaluated for residual stones.

Results: A total of 62 children with 67 renal units met the inclusion criteria. The mean age was 42.11 months (4–60 months). Mean weight was 13.31 kg (6–16.3 kg). Mean stone size was 11.9 mm (7.3–18.2 mm). Majority of the stones were in pelvis (37.8%). UAS 9.5/11.5 Fr was placed in 40 (63.5%) children. Mean operative time was 55.2 min; mean hospitalization was 61 h. Four out of the 67 renal units (5.9%) required conversion to minipercutaneous nephrolithotomy in the same sitting, due to access failure. Two cases who developed post-operative fever required a change of antibiotics. Two cases required ureteroscopy for steinstrasse postoperatively. Stone-free rate at 2 months for stones size ≤ 2 mm was 76.3%.

Conclusion: Pediatric RIRS is a promising option in young children as it offers acceptable stone-free rates and a low incidence of high-grade complications. However, it requires expertise and should be offered in tertiary care centres.

INTRODUCTION

The incidence of paediatric urolithiasis is on a rising trend globally,^[1] and the treatment of stones in children poses a major challenge. Percutaneous nephrolithotomy (PCNL) and shock-wave lithotripsy (SWL) are the established forms of treatment for children with renal stones. Following the miniaturization of the instruments and an expanding armamentaria of the available energy sources, retrograde intrarenal surgery (RIRS) can effectively compete with PCNL. Thus, the recent guidelines have also included the flexible ureteroscopy

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as a primary option for the management of ${<}2\ cm$ renal stones in children. $^{[2]}$

SWL has been the preferred method for the treatment of <2 cm stones in children. Noninvasive SWL has major setbacks such as the need for anesthesia, multiple sessions, and steinstrasse requiring additional intervention. The significantly lower stone-free rates (SFR) of SWL as compared to the PCNL and RIRS and the possibility of parenchymal damage to the growing kidney are the major limitations of SWL.^[3,4] A recent meta-analysis by Chen *et al.* found pediatric PCNL to have significantly higher overall

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complications, high number of high-grade complications, and a greater need of blood transfusions as compared to the RIRS.^[5]

The acceptability and utilisation of the mini, ultramini and the micro PCNLs is on the rise and the complication rate of these procedures is comparable with the RIRS and is significantly low. Nevertheless, the complications such as the risk of bleeding requiring transfusion, pleural and visceral injury, although low, have not been completely eliminated, even with the miniaturized PCNLs.^[6-9] Owing to the lower invasiveness and faster clearance of stones as compared to the SWL and PCNL, RIRS is an attractive option for the upper tract calculi, especially in the children. There are very few studies in the literature which have described RIRS in the preschool children.^[10-12] Our objective was to analyze the feasibility of RIRS (as the primary outcome) and the stone-free and complication rates (as the secondary outcomes) in children <5 years old.

METHODS

All children less <5 years of age with a stone size <2 cm (renal/proximal ureteric), who underwent RIRS at our hospital from February 2010 to May 2020 were included in this retrospective study. From our hospital database, demographic data, complete history, clinical examination findings, laboratory reports of complete hemogram, serum biochemistry, urine analysis, and urine culture were retrieved.

Ultrasonography and X-ray findings of the kidney, ureter, and bladder were collected. Either intravenous pyelogram or computed tomography (CT) was performed in all cases. Diuretic renogram was obtained whenever thinned parenchyma with hydronephrosis was noted. Stone size was defined as the maximum diameter of a solitary stone or as the sum of the maximum diameters of all the stones in cases with multiple stones. All the patients submitted a preoperative urine culture. Children with positive results were treated according to the antibiogram and were taken up for RIRS after cultures turned sterile. Preoperative antibiotic cefotaxime 100 mg/kg was administered to all the cases 30 min before the procedure.

All procedures were performed under general anesthesia. A 3.5 Fr, 16 cm double J (DJ) stent was placed in all the children 12 days before the surgery for passive dilatation of the ureter. If required, female urethra was dilated up to 12 Fr and the male external meatus was dilated up to 10 Fr with Hegar dilators. We performed cystoscopy, removed the DJ stent and then performed semirigid ureteroscopy with a 6.5 Fr (Richard Wolf, Germany) scope to assess the distensability of the ureter before the insertion of ureteral access sheath (UAS) and also to deal with the upper ureteric stones (to push it back in to the kidney). Upper ureteric

stones which could be managed with semirigid ureteroscopy were not included in the study. Terumo Guidewire 0.038" (Glidewire[®]; Terumo, Somerset, NJ, US) was placed into the pelvis. UAS (9.5/11.5 Fr, 28 cm, Cook, USA) was placed only if it glided over the guidewire without any resistance. If any resistance was encountered, then the flexible ureterorenoscope (Flex X2, Storz or P6, Olympus) was back loaded over the guidewire, without the access sheath. When sheath less RIRS was performed, the bladder was drained by continuous suprapubic aspiration with an 18 G Intravenous cannula.

Holmium laser lithotripsy (30 W, Quanta) was performed with a 200 μ laser fiber (Quanta system Q1, Italy) using dusting and popcorn modes with appropriate LASER settings (frequency 5-12 HZ and energy 0.5-0.8 J). Lithotripsy was continued until the stone was completely powdered to a size small enough to pass spontaneously. Irrigation was done using a 50 ml syringe by a trained technician, depending on the visibility. Basket (N circle, nitinol stone extractor 2.2 F 115 cm basket; Cook Medical, Bloomington, IN, USA) was used primarily to relocate the stone to the most accessible calyx or to remove one of the last fragments for stone analysis. At the end of the procedure, retrograde pyelography and rigid or flexible ureteroscopy were performed in all the cases to detect any residual stones, intra/extravasation or ureteric injury. A 3.5 Fr, 16 cm DJ stent was placed in all the cases. All bilateral stones were taken up for RIRS in a staged manner, with the contralateral side operated a few weeks later, except in one child who presented with anuria which we have published.

Postoperatively, the children were closely monitored with the help of the pediatrician and the intensive care pediatric anesthetist. If there were no complications, the patients were discharged on the 2nd postoperative day. Any child with fever was evaluated. Children with temperature more than 38°C, elevated total leukocyte counts, and elevated C-reactive protein levels were treated with higher antibiotics as per the hospital antibiogram. Postoperative complications were identified and graded according to the Clavien–Dindo system.^[13]

Stents were removed under general anesthesia 2 weeks after the surgery. Children were followed at 2 months after surgery with an ultrasound KUB to detect residual stones which was repeated every 6 months to detect delayed complications or recurrence. Residual stones ≥2 mm at the end of 2 months were considered to be significant and were classified as a treatment failure when calculating the stone-free rate. Children with complete clearance of stones underwent metabolic evaluation.^[14]

Statistical analysis was performed with the SPSS software version 24 (Statistics for Windows, IBM Corp, Armonk, NY, USA). Descriptive analysis was described as percentages and

mean with standard deviation. Univariate and multivariate analyses were performed to predict the residual stones and complications using the variables. P < 0.05 was considered to be statistically significant.

Retrospective collection of data for this study was approved by the hospital ethics committee (study reg. no. ECR/230/ INST/AP/May 20, 2020 date-May 25, 2020), and written informed consent was obtained from the legal guardian of each patient for undergoing the procedure. Procedure adhered to the ethical guidelines of declaration of Helsinki and its amendments. We confirm the availability of and access to all the original data reported in this study.

RESULTS

A total of 62 pediatric patients were evaluated, out of whom, 5 had bilateral renal stones (67 renal units). Out of these 67 renal units, seven patients had multiple stones in the same renal unit. The demographic data and stone characteristics are presented in Table 1. The youngest child was a 4-month-old boy who presented with anuria due to bilateral upper ureteric stones. The most common location of the stone was the pelvis and the lower pole. Stones were most commonly of the mixed composition (44.4%), followed by calcium oxalate dihydrate (22.2%). Intraoperative and postoperative details are mentioned in Table 2.

One male child had tight urethra and the ureteroscope could not be negotiated and one more child had tight ureter, even after prior DJ stenting, where the semirigid ureteroscope

Table 1: Demographic and stone details				
Variables	Number of cases (%)	Mean±SD		
Age (months)				
0-12	2 (3.2)	42.11±12.8		
13-24	4 (6.4)			
25-36	12 (19.3)			
37-48	21 (33.8)			
49-60	23 (37.0)			
Sex (<i>n</i> =62)				
Male	40 (64.5)			
Female	22 (35.5)			
Side (<i>n</i> =67)				
Right	24 (35.8)			
Left	38 (56.7)			
Bilateral	5 (7.4)			
Weight (kg)	Range (6-16.3 kg)	13.31±1.9		
Number of renal units with				
Single stone	60			
Multiple stone	7			
Stone location (n=74)				
Pelvis	28 (37.8)			
Upper ureter	12 (16.2)			
Upper calyx	7 (9.4)			
Middle calyx	10 (13.5)			
Lower calyx	17 (22.9)			
Stone size (mm)	Range (7.3-18.2)	11.9±2.7		
HU		920.4±420.1		

HU: Hounsfield units, SD: Standard deviation

could not be negotiated. Flexible ureteroscopy failed in two more cases with lower calyceal stones where the stone could not be reached with the scope or with a basket. Hence, a total of 4 cases, out of 67 renal units (5.9%) required conversion to mini PCNL in the same sitting.

UAS 9.5/11.5 Fr could be successfully inserted only in 40 out of 63 renal units (63.5%) even after prior stenting. In the rest 23 renal units (36.5%), flexible ureteroscope was passed directly over the guidewire into the kidney. Age-wise distribution of the access sheath placement is shown in Table 3. UAS placement was not successful in younger children (100% in 0–12 m, 75% in 13–24 m).

Two cases in which UAS was inserted sustained ureteric injury- Grade 1 (mucosal damage) and Grade 2 (submucosal damage)^[15], respectively. These two patients required prolonged DJ stenting for 4 weeks (Clavien IIIb). Urethral injury was not encountered in any patient. Visible hematuria (Clavien grade I) was seen in 10 cases, which subsided spontaneously. None of the cases required irrigation/clot evacuation. Post-operative fever more than 38°C was observed in eight cases (Clavien grade I), all were managed conservatively. Two cases with postoperative fever required change to a higher antibiotic (Clavien grade II). Two cases were re-admitted 1 week post-operatively with pain and fever with stent in situ (Clavien IIIb). On evaluation, they had relatively large stone fragments stuck at the lower end of the ureter, besides the stent, causing a pile up of the fragments above it. They required ureteroscopy for the clearance of steinstrasse. On long-term follow-up, none developed ureteric or urethral stricture. Mean follow-up period was 25.4 ± 4.3 months (6-48 months).

Out of the 63 renal units, 4 were lost to follow-up. These four cases were excluded from the stone free rate analysis. In the remaining 59 patients, ultrasound performed at the end of 2 months revealed stones ≤2 mm in 45 children, providing a stone free rate of 76.3%. Univariate and multivariate analysis of the patients with residual stones [Table 4] was performed. In the univariable analysis, number of stones, stone size, location (middle calyx), and stone density (HU) were significantly associated with residual stones. In the multivariable model, the most significant factors were the location of the stone in the middle and lower calyx and the higher stone density.

Similar analysis was performed for complications [Table 5]. In the univariable analysis, the number of stones, stone size, and the location (lower calyx) were significantly associated with the complications. In the multivariable model, the most significant factors were the stone size, lower calyx, and the higher stone density.

DISCUSSION

In our study, we observed that pre-stenting the ureter facilitated retrograde ureteral access in the majority of the

Table 2: Operative and postoperative details			
Variables	Range	Number of cases (%)	Mean±SD
Operative time (min)	36.4-80.5		55.2±11.4
Lasering time (min)			42.3±15.6
Access sheath used in $(n=63)$		40 (63.5)	
Hospital stay (h)	40.4-83.2		62.1±11.1
Successful retrograde ureteral access failure (<i>n</i> =67)		4 (5.97)	
Lost to follow up $(n=62)$		4 (6.45)	
Residual stone $\geq 2 \text{ mm} (n=59)$		9 (15.3)	
Stone free rate (<i>n</i> =59)		45 (76.3)	
Stone composition		× ,	
Calcium oxalate monohydrate		10 (15.8)	
Calcium oxalate dehydrate		14 (22.2)	
Uric acid		11 (17.4)	
Mixed type		28 (44.4)	
Metabolic abnormalities			
Hypocitratuira		5	
Hypercalciuria		3	
Intraoperative complications where RIRS was done (n=63)			
Ureteric damage			
Grade 1		1 (1.58)	
Grade 2		1 (1.58)	
Postoperative complications (n=63)			
G1		18 (28.5)	
G2		2 (3.17)	
G3a		0	
G3b		4 (6.43)	

RIRS: Retrograde intrarenal surgery, SD: Standard deviation

Table 3: Access sheath placement according to age distribution				
Age months	Number of cases	Access sheath used in (%)		
0-12	2	0 (0)		
13-24	4	1 (25)		
25-36	12	8 (66.6)		
37-48	21	9 (42.8)		
49-50	24	22 (91.6)		
Renal units	63	40		

cases. Stone-free rate was 76.3% with the majority of the complications being Grade 1 or 2. Cases where the flexible scope could not be negotiated till the stone were converted to mini-PCNL (4 out of 67 renal units [5.9%]).

There are many recent studies in the literature describing the feasibility and safety of RIRS in children.^[16-21] However, only a few studies describe the outcomes of RIRS in a cohort like ours. Smaldone *et al.*^[17] and Kim *et al.*^[18] have published their results in 100 cases. Both these groups combined semirigid ureteroscopy and flexible ureteroscopy, so they included a smaller cohort of RIRS as compared to our study. Also, they included children above 10 years of age, in whom the technical aspects of RIRS are similar to that of the adults. We have restricted our study to children <5 years (anatomically smallrt ureters and urethrae) to assess the feasibility and outcomes of RIRS in this population.

We have opted for elective preoperative DJ stent placement in all the cases, as earlier studies by Samldone and Kim had shown very low success rate of primary RIRS or primary ureteroscopy in children <5 years. We had a successful retrograde access in 94.02% (63 out of 67) of the patients. We used the Flex X2 (Karl Storz Ltd) and Olympus P6 which are the smallest available flexible ureteroscopes but could not negotiate the ureter in one patient, despite pre-stenting. Further miniaturization of flexible scopes both in the diameter and the length may avoid pre-stenting and ureteric injuries in the future.

The use of access sheath in children is still debated. Erkurt *et al.*^[11] *et al.* have described RIRS in 65 children who were not routinely pre-stented. They placed an access sheath in 61.5% of the cases and noted two ureteric wall injuries due to the sheath placement. Berrettini *et al.*^[10] had placed an access sheath in 15 out of 16 children weighing <20 kg and have reported ureteral perforation in 1 case. We were able to pass the access sheath in 63.5% (40 out of 63 cases) and noted two ureteric injuries Grade 1 and Grade 2 according to classification described by Traxer and Thomas.^[15] Both these cases were managed with prolonged DJ stenting for 4 weeks. At follow-up for a mean period of 32 months, these two cases did not reveal any ureteric stricture, which we attribute to the prior stenting.

Our retrograde access failure rate was 5.9% (4 out of 67 cases). Similar findings were reported by Erkurt *et al.*^[11] who had a failure rate of 7.7% (5 out of 65 cases). A systemic review by Ishii *et al.*^[22] showed that the children <6 years of age had a higher failure rate of establishing the retrograde access when compared to those more than 6 years (4.4 vs. 1.7%). The four cases in our study, in whom the retrograde access failed,

Table 4: Univariate and multivariate analysis of residual stones				
Dependent: Residual stone	Absent	Present	OR (univariable)	OR (multivariable)
Number of stones				
Single	49 (89.1)	6 (10.9)	-	-
Multiple	4 (57.1)	3 (42.9)	6.12 (1.01-35.28, <i>P</i> =0.039)	0.00 (0.00-1.97, <i>P</i> =0.235)
Stone sizemm_				
Mean±SD	11.7 (2.6)	13.9 (2.9)	1.34 (1.03-1.80, <i>P</i> =0.034)	2.73 (1.05-18.54, P=0.124)
LocationPelvis				
Absent	29 (85.3)	5 (14.7)	-	-
Present	24 (85.7)	4 (14.3)	0.97 (0.22-4.05, <i>P</i> =0.963)	187.54 (0.47-120,660,972.55, <i>P</i> =0.167)
LocationUpper.Calyx				
Absent	47 (85.5)	8 (14.5)	-	-
Present	6 (85.7)	1 (14.3)	0.98 (0.05-6.89, <i>P</i> =0.985)	-
LocationLower.Calyx				
Absent	41 (91.1)	4 (8.9)	-	-
Present	12 (70.6)	5 (29.4)	4.27 (0.99-19.80, <i>P</i> =0.052)	15,999.54 (28.74-131324688332.82, <i>P</i> =0.032)
LocationMiddle.Calyx				
Absent	47 (90.4)	5 (9.6)	-	-
Present	6 (60.0)	4 (40.0)	6.27 (1.27-31.12, <i>P</i> =0.022)	20,821.60 (29.30-105,893,798,577.87, <i>P</i> =0.029)
LocationUpper.Ureter				
Absent	43 (86.0)	7 (14.0)	-	-
Present	10 (83.3)	2 (16.7)	1.23 (0.17-6.07, <i>P</i> =0.814)	457.42 (0.45-177,615,767.23, <i>P</i> =0.109)
Stone densityHU_				
Mean±SD	853.5 (402.1)	1314.4 (301.3)	1.00 (1.00-1.01, <i>P</i> =0.010)	1.01 (1.01-1.03, <i>P</i> =0.008)

AIC=26.7, C-statistic=0.992, H and L= χ^2 (8) 0.60 (P=1.000). OR: Odds ratio, SD: Standard deviation, AIC: Akaike information criterion

Table 5: Univariate and multivariate analysis for complication				
Dependent: Complications	Absent	Present	OR (univariable)	OR (multivariable)
Number of stones				
Single	36 (65.5)	19 (34.5)	-	-
Multiple	1 (14.3)	6 (85.7)	11.37 (1.77-223.13, <i>P</i> =0.029)	-
Stone sizemm_				
Mean±SD	11.1 (2.2)	13.4 (2.9)	1.41 (1.14-1.80, <i>P</i> =0.002)	1.55 (1.20-2.12, <i>P</i> =0.002)
LocationPelvis				
Absent	22 (64.7)	12 (35.3)	-	-
Present	15 (53.6)	13 (46.4)	1.59 (0.57-4.48, <i>P</i> =0.375)	-
LocationUpper Calyx				
Absent	34 (61.8)	21 (38.2)	-	-
Present	3 (42.9)	4 (57.1)	2.16 (0.44-11.88, P=0.344)	-
LocationLower.Calyx				
Absent	31 (68.9)	14 (31.1)	-	-
Present	6 (35.3)	11 (64.7)	4.06 (1.29-13.96, <i>P</i> =0.020)	4.42 (1.16-19.07, <i>P</i> =0.035)
Location_ Middle Calyx				
Absent	31 (59.6)	21 (40.4)	-	-
Present	6 (60.0)	4 (40.0)	0.98 (0.23-3.87, P=0.982)	-
LocationUpper.Ureter				
Absent	29 (58.0)	21 (42.0)	-	-
Present	8 (66.7)	4 (33.3)	0.69 (0.17-2.50, <i>P</i> =0.584)	-
Stone DensityHU				
Mean±SD	867.9 (427.7)	998.2 (404.8)	1.00 (1.00-1.00, <i>P</i> =0.230)	1.00 (1.00-1.00, <i>P</i> =0.032)

AIC=71.2, C-statistic=0.811, H and L= χ^2 (8) 7.54 (P=0.479). OR: Odds ratio, SD: Standard deviation, AIC: Akaike information criterion

underwent miniPCNL in the same sitting without any difficulty.

We had a stone-free rate of 76.3% (45 out of 59 cases). Lower stone-free rates were reported in the systematic review by Ishii *et al.*^[22] where the mean (range) stone burden was 9.8 (1–30) mm and the mean (range) SFR was 87.5 (58%–100%) after the initial therapeutic URS. A similar systemic review by the same authors Ishii *et al.*^[23] which had a mean age of 7.3 years reported the mean stone-free rate across the three studies of 85.5% (range 58.0%–93.0%) after the initial ureteroscopy. We aimed for complete powdering of the stone, small enough to pass spontaneously. Repeated basketing of the stone fragments is cumbersome more so if the access sheath is not used. We used basket only for stone relocation or stone removal for the analysis at the end of the procedure. Children with residual stones, more than 6 mm (n = 4) underwent relook RIRS, but we did not include them in the analysis of the present study to assess the outcomes of primary RIRS.

Postoperative complications seen in our study were comparable to most of the pediatric case series. Erkurt *et al.*^[11] had reported an overall complication rate of 27.7% but they did not use the Clavien system, and long-term follow-up was not available. Berrettini *et al.*^[10] had studied the use of access sheath in RIRS for children <20 kg. The complication rate was 37.7%, out of which, only 18.8% were of Clavien grade I. We too had an overall complication rate of 38% and a higher proportion (28.5%) of Grade I complications. In the systematic review by Ishii *et al.*^[22], a higher complication rate (24.0 vs. 7.1%) was observed in children whose mean age was <6 years. We had only four cases in Clavien group 3b (6.43%), out of which 2 cases required readmission as per the hospital protocol.

Limitations of our study are its retrospective nature and non-analysis of cost-effectiveness. The utilization of ultrasound for follow-up may not be as objective as the non-contrast CT to assess the exact SFR. Further, long-term prospective studies are required to establish a clear consensus regarding routine pre-stenting and access sheath requirements. The access sheath helps in the movements in RIRS. In its absence, stabilizing the penis between little and ring finger and rotating the scope with index and thumb gently will transmit the movements inside the kidney. If such a thing cannot be done, then we relocate the stone into a capacious calyx and proceed with popcorning.

CONCLUSION

Pediatric RIRS is a promising option in young children as it offers an acceptable stone free rates and a low incidence of high grade complications. However, it requires expertise and should be offered at tertiary care centres.

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