Original Article

Feasibility, efficacy, and safety of retrograde intrarenal surgery in <1-year age group: A single-center experience

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Abstract

Purpose: Urolithiasis in infants is uncommon. Percutaneous nephrolithotomy, extracorporeal shockwave lithotripsy, and retrograde intrarenal surgery (RIRS) are the management options. RIRS is the least studied of these options in infants. In our series of 23 cases, we aim to assess the feasibility, efficacy, and safety of RIRS in <1-year age group.

Materials and Methods: This was a retrospective analysis of a series of 23 infants who underwent RIRS in our hospital from January 2018 to March 2021. Children who were <12 months of age and had the largest stone size of <20 mm were included in the study.

Results: Twenty-three patients (male – 15; female – 8) were included in the study. The mean age was 10 ± 2.31 months (range, 4–12 months). The mean stone size was 11.6 ± 2.96 mm (range, 7.5–19 mm). The mean operative time was 29.44 ± 7.45 min (range, 17–42 min). Six patients (22.2%) had mild hematuria (Clavien I), and seven patients (25.9%) had postoperative fever. Stone size had a significant positive correlation with laser time, operative time, and intraoperative intravasation, but no significant association with stone-free rate. At 2-month follow-up, 4 (three patients) out of 27 renal units had residual stones (stone-free rate [SFR] – 85.1%). No patient had long-term complications like urethral or ureteric stricture or stone recurrence during the given follow-up period.

Conclusion: RIRS is a feasible and minimally invasive treatment for renal stones in infants with acceptable SFRs.

Keywords: <1 year age, infants, renal stones, retrograde intrarenal surgery, urolithiasis

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INTRODUCTION

Pediatric urolithiasis is on the rising trend globally, yet it is quite uncommon in the <1-year age group.[1-4] Guidelines for the management of renal stones in this specific population are lacking. Percutaneous nephrolithotomy (PCNL) and shockwave lithotripsy (SWL) are the preferred treatment modalities even today.[5] Retrograde intrarenal surgery (RIRS) is a less explored option in infants because of fear of injury to the small urethra and ureter. Literature on RIRS in this specific age group is scarce. Our objective is to present the feasibility, efficacy, and safety of RIRS in infants.

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MATERIALS AND METHODS

This was a retrospective analysis of a series of infants who underwent RIRS in our hospital from January 2018 to March 2021. Children <12 months of age and had the largest stone size of <20 mm were included in the study. Patients with anatomical anomalies, active infection, bleeding diathesis, previously operated genitourinary tract, stones inaccessible for flexible ureteroscope, or failed insertion of flexible ureteroscope due to tight ureter even after stenting (encountered in two patients, where PCNL is done), were excluded from the study. Institutional Ethical Committee approval was obtained.

Demographic data, clinical presentation, imaging, laboratory reports, operative details, and postoperative follow-up were retrieved from the hospital database. Preoperatively, all patients underwent a complete hemogram, renal function test, serum biochemistry (electrolytes, uric acid, and calcium), urine analysis, urine culture, ultrasonogram, and plain radiograph of the kidney, ureter, and bladder (KUB). Intravenous urogram (IVU) or noncontrast computed tomography (CT) scan was done in all patients. Patients with positive urine culture were treated preoperatively with appropriate antibiotics and then taken up for surgery. All patients received cefotaxime 100 mg/kg intravenously 1 h before surgery and continued for 48 h in the postoperative period. Under short general anesthesia (mask ventilation + intravenous sedation without endotracheal intubation), a 3.5 Fr/16 cm double"-*J*" stent was placed after doing a retrograde pyelogram (RGP), in all patients 12–14 days before RIRS.

Surgical technique

All cases were done by a single surgeon with more than 5 years of experience in doing RIRS. RIRS was done under general anesthesia. If required, the external urethral meatus was gently calibrated up to 10 Fr with Hegar dilators. Forceful meatal dilatation was not done in any of the patients. Indwelling DJ stent was removed, and then, semirigid ureteroscopy was performed with a 6/7.5 Fr ureteroscope (Richard Wolf, Germany) to assess the distensibility of the ureter and also to push any upper ureteric stones into the kidney. We avoid doing laser lithotripsy in the upper ureter. Ureteral access sheath (UAS) insertion was not attempted in any patient. Two guidewires (Terumo Guidewire 0.018" and 0.038" (Glidewire®; Terumo, Somerset, NJ, US) were placed in the pelvis. Then, the flexible ureterorenoscope (Flex-XC 8.5 Fr, or Flex-X2S 7.5 Fr; Karl Storz, Germany or URF-P7 7.95Fr, Olympus, Germany) was back-loaded over the 0.038" guidewire. Initial RGP was done in patients with any upper ureteric kink or multiple calyceal calculi. The bladder was drained by continuous suprapubic aspiration with an 18 G intravenous cannula in all male patients or a 5 Fr feeding tube in a few female patients whenever feasible. Irrigation was done manually using a 50 mL syringe. Lithotripsy was done using a Holmium laser (30 W, Quanta) with a 200 μ laser fiber (Quanta system Q1, Italy). Dusting and popcorn modes with appropriate laser settings (frequency 5–12 Hz and energy 0.5–1.0 J, maximum energy setting was 1 J/12 Hz = 12 W) were used until the stone was completely powdered, to a size small enough to pass spontaneously. One small fragment was extracted at the end, with basket (NGage or NCircle, Nitinol Stone Extractor 2.2 Fr, 115 cm; Cook Medical, Bloomington, IN, USA) in all cases for stone analysis, done by Fourier transform infrared spectroscopy. At the end of the procedure, RGP was done to look for any residual stones, intravasation, or extravasation. The ureter was inspected for any ureteric injury while withdrawing the flexible ureteroscope and graded according to Olivier Traxer's "Endoscopic classification of ureteral wall injury after RIRS" (Grade 0–4).[6] A 3.5 Fr, 16 cm DJ stent was placed in all the cases. Patients with bilateral renal stones were operated in a staged manner. The side with obstructing stone and larger stone burden was operated first.

Postoperatively, the children were closely monitored with the help of a pediatrician and an intensivist. Postoperative complications were recorded and graded according to the modified Clavien–Dindo system. Any child with fever was evaluated with total leukocyte count (TLC) and C-reactive protein (CRP) levels. Children with temperatures more than 39°C (high-grade fever) and elevated TLC and CRP levels were treated with higher antibiotics as per the hospital antibiogram.

Stents were removed under short general anesthesia (intravenous sedation), 2 weeks after the surgery. Children were followed at 2 months after surgery with an ultrasound KUB to detect residual stones. Residual stones ≥2 mm at the end of 2 months were considered to be significant. All patients underwent spot urine analysis (calcium, phosphorus, magnesium, oxalate, uric acid, citrate, protein, and creatinine) for complete metabolic evaluation at 2 months. Children were given specific stone preventive pharmacotherapy according to the stone composition and metabolic abnormality.

All patients were followed up at 2 months, 6 months, 9 months, and 6 monthly thereafter. Patients were evaluated for any long-term complications like urethral and ureteric strictures or recurrence of stones. For the follow-up of urethral strictures, we rely on the history of crying or straining while micturition, any reduction of urinary stream, and postvoid residual assessment during ultrasonography. Any symptoms of voiding difficulty or high proliferative vitreoretinopathy will be further evaluated with uroflowmetry and retrograde urethrogram. For the follow-up of ureteric stricture, we look for any hydroureteronephrosis in the follow-up scan. Further evaluation like CT or IVU will be done if any hydroureteronephrosis is noted in ultrasonography.

Outcomes measured

Operative time was defined as the time between the insertion of a flexible ureterorenoscope into the urethral meatus and removal from the meatus. The laser time was defined as the total time the laser is in usage, obtained from the machine.

Statistical analysis

Data were coded and recorded in MS Excel spreadsheet program. SPSS v23 (IBM Corp. New York, United States) was used for data analysis. Descriptive statistics were elaborated in the form of means/standard deviations and medians/interquartile ranges for continuous variables, and frequencies and percentages for categorical variables. If data were found to be nonnormally distributed, appropriate nonparametric tests in the form of the Wilcoxon test were used. The Chi-squared test was used for group comparisons for categorical data. In case the expected frequency in the contingency tables was found to be <5 for >25% of the cells, Fisher's exact test was used instead. Linear correlation between two continuous variables was explored using Pearson's correlation (if the data were normally distributed) and Spearman's correlation (for nonnormally distributed data). Statistical significance was kept at $P < 0.05$.

RESULTS

Twenty-three patients (male – 15; female – 8) were included in the study. The demographic details are given in Table 1. The mean stone size was 11.6 ± 2.96 mm (range, 7.5–19 mm). The most common stone location was the renal pelvis.

The mean operative time was 29.44 ± 7.45 min (range, 17–42 min). The mean laser time was 18.66 ± 5.2 min (range, 8–29 min) [Table 2]. The mean amount of irrigation fluid used was 331.4 mL (range 220–420 mL). Intraoperative bladder drainage was done by suprapubic aspiration in 19 patients and a feeding tube in four patients. Intravasation and extravasation of contrast at the end of the procedure were observed in 6 (22.2%) cases and 2 (7.4%) cases, respectively. Ureteric injury was seen in 5 (18.5%) patients. All patients had low-grade ureteric injury (Grade 0–3 cases; Grade 1–2 cases) [Table 3].

Table 1: Characteristics of the study population

Basic details	Mean±SD	Median (IQR)	Minimum–maximum
Age (months)	10.00±2.32	11.00 (9.00–12.00)	4.00–12.00
Weight (kg)	7.80±1.26	8.00 (7.50–8.60)	4.50–9.50
Gender, *n* (%)			
Male		15 (65.2)	
Female		8 (34.8)	
Stone laterality, *n* (%)			
Unilateral		19 (82.6)	
Bilateral		4 (17.4)	
Number of stones, *n* (%)			
Single		22 (81.5)	
Multiple		5 (18.5)	
Side, *n* (%)			
Right		14 (51.9)	
Left		13 (48.1)	
Location, *n* (%)			
Upper ureter		8 (29.6)	
Pelvi-ureteric junction		6 (22.2)	
Pelvis		12 (44.4)	
Upper calyx		1 (3.7)	
Middle calyx		4 (14.8)	
Lower calyx		2 (7.4)	

SD: Standard deviation, IQR: Interquartile range

Table 2: Intraoperative data

Procedure	Mean±SD	Median (IQR)	Minimum–maximum
Total stone size (mm)	11.49±2.72	11.00 (9.25–14.00)	7.50–16.00
FURS size, *n* (%)			
Flex-X2S 7.5 Fr		10 (37.0)	
P7 Olympus 7.95 Fr		10 (37.0)	
Flex-XC 8.5 Fr		7 (25.9)	
RIRS time (min)	29.44±7.46	30.00 (23.00–35.00)	17.00–42.00
Laser time (min)	18.67±5.20	18.00 (16.00–20.50)	8.00–29.00

SD: Standard deviation, IQR: Interquartile range, RIRS: Retrograde intrarenal surgery, FURS: Flexible ureterorenoscope

Statistical analysis revealed that the stone size had a significant positive correlation with laser time, operative time, and intraoperative intravasation, but no significant association with stone-free rate [Table 4]. Lower pole stones had a significant association with intraoperative intravasation ($P = 0.043$), but no significant association with postoperative complication or the stone-free rate [Table 4]. Stone size, intraoperative intravasation, and extravasation had a significant association with postoperative complications (hematuria), but no association with postoperative fever. The lasing time and operative time did not have a significant association with postoperative fever or hematuria [Table 5].

When the different FURS used in the series are considered, a significant association was noted between scope size and intravasation (P – 0.014) and postoperative

Table 3: Summary of complications and outcome

Complications and outcome	Mean±SD	Median (IQR)	Minimum–maximum
Ureteric injury grade, *n* (%)			
None		22 (81.5)	
0		3 (11.1)	
1		2 (7.4)	
Postoperative complications: Fever (yes)		7 (25.9)	
Postoperative complications: Hematuria (yes)		6 (22.2)	
CD grade of postoperative complications: Fever, *n* (%)			
None		20 (74.1)	
I		4 (14.8)	
II		3 (11.1)	
CD grade of postoperative complications: Hematuria, *n* (%)			
None		21 (77.8)	
I		6 (22.2)	
Catheterization (days)	1.26±0.66	1.00 (1.00–1.00)	1.00–4.00
Hospital stay (days)	2.33±0.62	2.00 (2.00–2.50)	2.00–4.00
Residual stones at 2 months (yes), *n* (%)		5 (18.5)	
Size of residual stones at 2 months	2.40±0.55	2.00 (2.00–3.00)	2.00–3.00

CD: Clavien–Dindo, SD: Standard deviation, IQR: Interquartile range

Table 4: Association of stone size and location with various parameters

Parameter	Total stone size (mm)	*P****	Lower pole stone		*P****
			Yes (*n*=2)	No (*n*=25)	
Laser time (min)	Correlation coefficient (*r*)=0.65	<0.001[a]	22.50±7.78	18.36±5.05	0.546[b]
Operative time (min)	Correlation coefficient (*r*)=0.5	0.009[a]	31.00±12.73	29.32±7.30	0.781[b]
Intraoperative intravasation					
Yes	15.17±0.98	0.001[b]	2 (100.0)	4 (16.0)	0.043[e]
No	10.44±2.04				
Intraoperative extravasation					
Yes	15.50±0.71	0.056[b]	0	2 (8.0)	1.000[e]
No	11.17±2.56				
Ureteric injury grade					
None	11.24±2.86	0.317[c]	2 (100.0)	20 (80.0)	1.000[e]
0	11.33±0.58		0	3 (12.0)	
1	14.50±0.71		0	2 (8.0)	
Postoperative fever					
None	11.25±2.46	0.601[c]	0	20 (80.0)	0.060[e]
CD Grade 1	11.32±3.51		1 (50.0)	3 (12.0)	
CD Grade 2	13.33±3.79		1 (50.0)	2 (8.0)	
Postoperative hematuria					
None	10.82±2.44	0.043[b]	2 (100.0)	19 (76.0)	1.000[e]
CD grade 1	13.83±2.48		0	6 (24.0)	
Hospital stay (days)	Correlation coefficient (rho)=0.36	0.062[d]	3.50±0.71	2.24±0.52	0.011[b]
Residual stones at 2 months					
Yes	11.20±2.28	0.875[b]	0	5 (20.0)	1.000[e]
No	11.56±2.85				

***Significant at $P<0.05$, [a]Pearson's correlation, [b]Wilcoxon–Mann–Whitney *U*-test,[18] [c]Kruskal–Wallis test, [d]Spearman correlation, [e]Fisher's exact test. CD: Clavien–Dindo

Table 5: Association of postoperative complications with various parameters

	Postoperative fever		*P****	Postoperative hematuria		*P****
	Yes (*n*=7)	No (*n*=20)		Yes (*n*=6)	No (*n*=21)	
Total stone size (mm)	12.19±3.47	11.25±2.46	0.559[a]	13.83±2.48	10.82±2.44	0.043[a]
Lower pole stone, *n* (%)	2 (28.6)	0	0.060[b]	0	2 (9.5)	1.000[b]
Laser time (min)	19.43±4.35	18.40±5.55	0.846[a]	22.17±6.24	17.67±4.55	0.107[a]
Operative time (min)	28.86±6.34	29.65±7.96	0.846[a]	32.83±8.54	28.48±7.05	0.242[a]
Intraoperative intravasation, *n* (%)	3 (42.9)	3 (15.0)	0.290[b]	4 (66.7)	2 (9.5)	0.011[b]
Intraoperative extravasation, *n* (%)	1 (14.3)	1 (5.0)	0.459[b]	2 (33.3)	0	0.043[b]
Ureteric injury grade, *n* (%)						
None	6 (85.7)	16 (80.0)	1.000[b]	5 (83.3)	17 (81.0)	0.481[b]
0	1 (14.3)	2 (10.0)		0	3 (14.3)	
1	0	2 (10.0)		1 (16.7)	1 (4.8)	

***Significant at $P<0.05$, [a]Wilcoxon–Mann–Whitney *U*-test,[18] [b]Fisher's exact test hematuria (P – 0.014). Flex-XC 8.5 Fr had the largest proportion of patients with these complications (57.1%). No significant association was noted between scope size and other parameters such as fever, ureteric injury, and stone-free rates (SFRs).

Six out of 23 (26%) patients had mild hematuria (Clavien I), which resolved spontaneously within 24 h in all the patients. Postoperative fever was observed in 7 (25.9%) patients. Five patients had a low-grade fever (<39°C, normal TLC and CRP levels) (Clavien I) <48 h, which did not require any change of our antibiotic protocol. Two patients had high-grade fever >39°C, raised CRP and TLC (Clavien II), and required change of antibiotics and expert management by the pediatrician. The median duration of catheterization was 1 day (range, 1–4 days). The median hospital stay was 2 days (range, 2–4 days). At 2-month follow-up, 4 (three patients) out of 27 renal units had residual stones (SFR – 85.1%). The size of the residual stones was 2–3 mm. All these patients were asymptomatic, and no further intervention was needed. Stone analysis showed mixed stone composition in 7 out of 23 patients (30%). Hypocitraturia (17.3%) and hypercalciuria (13%) were the common metabolic abnormalities detected. The mean follow-up period in our series was 24.3 (range, 15–38) months. No patient had long-term complications like urethral or ureteric stricture. No recurrence of stones was noted during the given follow-up period.

DISCUSSION

Urolithiasis in infants is uncommon, and the true incidence is unknown.[7] Symptomatology is quite different from the adults, with excessive crying and hematuria being the predominant symptoms.[8] Sometimes, this may lead to a delay in diagnosis, and the patient may present with oliguria or anuria, urosepsis, and renal failure. In our series, one patient with bilateral upper ureteric and renal calculi presented with anuria, fever, and elevated creatinine.

The infantile age group is generally defined as children <1 year. Management of renal stones in infants poses a great challenge. There is a paucity of literature regarding the treatment of renal stone disease in this specific group of patients. Metabolic abnormalities and recurrence of stones are commonly encountered in children than adults.[9] The goals of treatment are complete stone clearance with less morbidity, avoidance of repeated procedures, and recurrence of stones thereby reducing damage to the developing kidney.

Extracorporeal SWL (ESWL) and PCNL are the commonly used procedures in infants. Only a few studies with limited sample sizes are available evaluating the safety and efficacy of these procedures in infants. Turna *et al*. reported the safety and efficacy of ESWL in their study of 36 infants and reported an SFR of 84.6% and only transient hematuria in 15 patients.[10] There are higher possibilities of steinstrasse and re-treatment rates with ESWL, requiring multiple anesthesia sessions. There is also a theoretical risk of damage to the developing kidneys caused by shockwaves.

Zeng *et al*. evaluated the safety and efficacy of PCNL in <3-year children and reported an SFR of 85% in a single setting, no need for blood transfusion in any patients, and no deterioration of renal function.[11] Pelit *et al*. reported the outcomes of mini-PCNL in 74 infants (10–36 months) in their retrospective study. They reported 84.7% SFR at 1 month, but five patients required blood transfusion, one case of pleural injury, one case of bowel injury, and one case of urinoma.[12] Jackman *et al*. described the mini-perc technique in children and underlined that creating a smaller PCNL tract will cause less tissue and nephron injury, especially in pediatric patients with small and fragile kidneys.[13] Despite the miniaturization of the PCNL tract, fear of major complications such as adjacent organ injury and severe bleeding still lingers, especially in infants who do not tolerate bleeding well.

RIRS is well established as an alternate procedure to ESWL and PCNL in adults for stones <2 cm.[5] Even in children, its safety and efficacy are being established by recent studies. Kim *et al*. reported on the largest series of pediatric RIRS (age group 3–218 months) for stone size averaging 6.1 mm and reported 100% success.[14] We have recently published our experience of RIRS in children <5 years and reported an SFR of 76.3% with the majority of the complications being Grade 1.[15]

RIRS is a less often sorted modality in infants, due to the lingering skepticism in handling such small ureters and urethras, and this is reflected in the paucity of literature to date. Li *et al*. reported the largest series of RIRS in infants. They studied RIRS in 55 children and reported an SFR of 94.6% and grade I complication in 40% of patients. However, they have included children up to 36 months. Hence, this study is also not an exact representation of our study population (<12 months).[8]

We have not used UAS in any of our patients. The safety of UAS usage in children has been reported in a few studies recently. Berrettini *et al*. assessed the safety of UAS in 16 children and reported no long-term complications.[16] However, RIRS with UAS in infants has not been evaluated till now, to warrant its safe usage. Bladder drainage in the absence of UAS is important, and we have achieved this by suprapubic aspiration or drainage through a feeding tube.

Two frequent problems we encountered in infants are kink in the upper ureter, hindering the negotiation of FURS, and exaggerated movement of the kidney with respiration. Mertz maneuver and two guidewires helped us to overcome the upper ureteric kink. With the help of an experienced pediatric anesthesiologist, respiratory movements could be controlled.

The mean operative time and laser time in our series are 29.44 min and 18.66 min, respectively, for a mean stone size of 11.6 mm. This is comparable to the one reported by Li *et al.* in which they reported a mean operation time of 30 min for a mean stone size of 10 mm.[8]

Hematuria and fever are the most common complications observed in our series. Hematuria is mild and resolved spontaneously in all cases within 24 h. A low-grade fever is observed in 21.7% of our patients, which resolved within 48 h without change in our antibiotic protocol. Out of four cases of bilateral RIRS, two cases had a high-grade fever postoperatively, which required a change to higher antibiotic, extended hospital stay, and catheterization. The incidence of postoperative fever reported in adults is 1.7%–18.8%.[17] Our previous study of RIRS in children <5 years reported fever in 12% of patients.[15] The increased incidence of fever in infants can be due to nonusage of UAS and the low capacity of the pelvicalyceal system not tolerating the irrigation fluid pressure, leading to intravasation or bacteremia. Long-term complications like urethral and ureteric stricture were not observed in our study. We have not seen stone recurrence in any of our patients in the given follow-up period (mean 24.3, range 15–38 months).

SFR in our series is 85.1% at 2 months, which is comparable to SWL and PCNL in infants. In their study of RIRS in 55 infants, Li *et al*. reported an SFR of 95%.[8]

RIRS is a feasible and less invasive option in infants, with acceptable SFRs. However, even in experienced hands, it is a technically demanding procedure. Three sessions of general anesthesia are required (preprocedure stenting, RIRS procedure, and stent removal), which is a disadvantage. There is a high chance of postoperative fever with RIRS in infants when compared to adults and children, which should be dealt with extreme care to avoid septic complications. This demands a team of pediatric anesthesiologist, pediatrician, and intensivist for intraoperative and postoperative care.

Strengths and limitations

To the best of our knowledge, ours is the only study available to date on the feasibility of RIRS in this age group (infants – <1 year age), with a reasonably good follow-up period (mean 24.3 months). All the surgeries were done by a single surgeon, which eliminates the bias factor.

Limitations of our study are

1. Small sample size
2. Retrospective nature of the study
3. We have not included fluoroscopic exposure, laser energy usage per case, and temperature changes in our analysis
4. Possible limitation of the reproducibility of the technique by beginners, which cannot be commented on.

CONCLUSION

RIRS is a feasible and minimally invasive treatment for renal stones in infants with acceptable SFRs. A team of experienced endourologist, pediatric anesthesiologist, pediatrician, and intensivist is required for a successful and safe outcome.

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Conflicts of interest

There are no conflicts of interest.

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