

Urinary tract infections and resolution of renal pelvic dilatation in infants

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Abstract

Introduction: Spontaneous resolution is the most common outcome of postnatal renal pelvic dilatation (RPD). Factors which delay spontaneous resolution are poorly studied.

Objectives: To study whether urinary tract infection (UTI) delays spontaneous resolution of RPD and to study the outcomes of postnatally detected RPD at one year of age.

Design: Prospective one year study in a tertiary care hospital in Kerala, India.

Method: All inborn babies detected to have at least grade 1 Society for Fetal Urology (SFU) scale of RPD, between postnatal days 3-5, were followed up until resolution or till one year of age. The subjects were divided into mild group (SFU grades 1 and 2) and moderate to severe group (SFU grades 3 and 4). The outcomes assessed were resolution, UTI and need for surgery.

Results: A total of 50 cases were followed up. The mean age of resolution in the mild group was 13 weeks whereas in the moderate to severe group, it was 30.3 weeks. UTI occurred in 9 (18%) patients. Resolution, in those with UTI, occurred at a mean age of 25.7 weeks compared to 14 weeks in those without UTI ($p=0.01$). Four cases with anteroposterior renal pelvic diameter (APRPD) >10 mm with cortical thinning and recurrent UTI resulted in persistent RPD requiring pyeloplasty within one year of life. All preterms showed resolution ($p=0.006$). Bilateral RPDs showed significantly delayed resolution ($p=0.002$).

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Conclusions: UTIs significantly delay resolution of RPD. Mild RPD resolves within 3 months and moderate RPD resolve around 7.5 months of age. Bilateral RPDs significantly delay spontaneous resolution. Preterm RPDs almost always resolve within one year of life.

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(Key words: postnatal outcome, renal pelvic dilatation, resolution, urinary tract infections)

Introduction

Renal pelvic dilatation (RPD), as determined by prenatal and neonatal ultrasound examination, has a population prevalence of about 2.5%, which decreases to 0.07-0.1% by the age of 2 years¹. It has a wide spectrum ranging from a mild dilatation of the renal pelvis alone (pyelectasis), to massive hydronephrosis with renal parenchymal thinning. Spontaneous resolution of RPD occurs more commonly with lower grades of dilatation whereas there is only a 2.6% chance of spontaneous resolution in those with renal parenchymal thinning². It would be reassuring for the parents and the treating physicians if the time of resolution could be predicted by prospective studies. More importantly, we need to detect RPD which are likely to deteriorate and find out the factors which delay resolution. Children with RPD in fetal anomaly scan and postnatally had 7 times higher risk of hospital admissions related to urinary causes in the first three years of life³.

Most of the studies evaluating the outcomes of RPD are retrospective in nature and fail to bring out the actual natural history⁴⁻⁹. Resolution rates in previous studies vary from 26% to 92%^{10,11}. The rationale for conducting this study is that neither the time of resolution, nor the effect of urinary tract infection (UTI) on RPD could be specified or predicted from these retrospective studies. UTI rates from pooled data ranges from 2.8 to 3.6% in low grade hydronephrosis and varies from 14.6% to 28.9% in those with high grade hydronephrosis¹². Factors which delay spontaneous resolution are also poorly studied. Other outcomes like need for surgery in the first year of life, in those detected with RPD, are also not clear.

Objectives

To study whether UTI delays the resolution of RPD and to study the outcomes of postnatally detected RPD at one year of age.

Method

A prospective one year observational study was conducted from July 2018 to July 2019 in a tertiary care referral hospital in Kerala, India. All inborn babies with a history of antenatal hydronephrosis, during the study period, were screened for RPD on postnatal day 5 and were included in our study if they had at least grade 1 renal sinus status as per Society for Fetal Urology (SFU) grading system^{13,14}. Most of the referred antenatal mothers lacked details of renal sinus in their antenatal scans but their newborns were also included if they were found to have at least grade 1 SFU staging in their first postnatal scan done for any other reason on days 3-5. All babies who had no splitting of renal sinus in their postnatal scans were excluded.

Minimum sample size estimated was 45, in accordance with a similar study previously done by Asl AS, *et al*¹⁵. Data such as sex, gestational age, birth weight, anteroposterior renal pelvic diameter (APRPD) in mm in the last third trimester scan and presence or absence of oligohydramnios in the last scan, were documented. Antenatal factors studied were presence of oligohydramnios, gestational diabetes, and pregnancy induced hypertension. All postnatal follow up ultrasounds were done using the same machine, (GE logiq P5, GE, US Technology, Korea) by the same sonologist throughout the study period.

Data recorded from each postnatal scan included: SFU grade, renal length, APRPD of each renal pelvis, calyceal dilatation, renal parenchymal thickness, ureteral dilatation and bladder wall thickness, if present. Based on the last postnatal scan, patients were divided as "mild group" which comprised SFU grades 1 and 2, and "moderate to severe group" which comprised those with SFU grades 3 and 4. First postnatal scan was scheduled between postnatal day 3 and postnatal day 5. This was because ultrasound performed before 3 days will lead to underestimation of severity of hydronephrosis due to the relative dehydration and decreased glomerular filtration rate that are present immediately after delivery¹⁶. Second postnatal scan was scheduled at 6 weeks. Subsequent follow up scans were scheduled at 12th, 24th and 52nd weeks¹⁷. Patients with two normal ultrasounds were not followed up further¹⁸. Growth assessment and clean catch urinalysis and urine midstream cultures were done at each follow-up visit. Also, suprapubic urine cultures were tested during any febrile episode. Antibiotic prophylaxis with cefadroxil at

5mg/kg/day was given in only those above 10 mm APRPD¹⁹. Micturating cystourethrogram (MCU) was done at 6 weeks in those with APRPD >10mm, worsening hydronephrosis, UTI or if abnormalities of ureter(s), urethra or bladder were present. In case of suspicion of posterior urethral valves (PUV), MCU was done as soon as possible. ^{99m}Tc-diethylenetriaminepentaacetic acid (DTPA) was done at 6-8 weeks only if there was worsening hydronephrosis and/or in those with RPD >10mm²⁰. Blood urea and serum creatinine values were assessed once on postnatal day 5 and repeated if baby developed UTI.

The outcome measures were defined as follows:

1. *Resolution*: This was considered to occur when the APRPD was <5 mm on two consecutive sonograms done at least 4 weeks apart and was the endpoint of follow up. A diagnosis of transient hydronephrosis was made in all cases of resolution.
2. *Urinary tract infection*: This was diagnosed in the presence of significantly positive urine culture of 10⁵ /mL or more colony-forming units of a single organism per ml of midstream clean catch sample. In situations when midstream sample was difficult to obtain, babies less than 6 months of age, or when contaminants were grown in culture, suprapubic aspirate (SPA) was obtained and any growth in urine obtained by SPA was considered significant.
3. *Paediatric surgery referral*: This was done if they had an obstructed renogram with differential renal function <40% or impaired drainage (t1/2 >20 min) or bilateral hydronephrosis or in case of dilated ureter²⁰.

These newborns were followed up till resolution or surgery or until the end of one year if hydronephrosis persisted. The frequency and time required for resolution of RPD (primary outcome) were analysed in both mild and moderate to severe hydronephrosis groups. Other outcomes like frequency of UTI, progression of RPD and the proportion of those who underwent surgery were also analysed in the 2 groups. p <0.05 was regarded as statistically significant.

Ethical issues: Ethical approval was obtained from the Ethics and Research Committee of the Government Medical College Ernakulam, Kerala, India (ERC No. F/19/2017/2). Written informed consent was obtained from the mothers prior to commencement of the study

Statistical analysis was done using SPSS version 20 software. Survival analysis was used to analyse data in which the time until the event of interest occurred. The event studied, here, is resolution of RPD. Survival analysis was done to study the mean times for resolution (Time to Event); as each case has different times of resolution which is the event studied. The starting point of the survival curve corresponds to the 1st postnatal scan. The subjects had frequent follow up times during which ultrasounds were done and the earliest age of resolution was recorded in those cases which showed APRPD less than 5 mm. Those cases who had to undergo surgery were 'censored'. Censoring

means the total survival time for that subject cannot be accurately calculated²¹. Comparison between those with UTI and those without UTI was done by Log rank test, Breslow and Taron ware tests were used to test the equality of survival distribution.

Results

A total of 60 newborns were identified to satisfy the inclusion criteria during the study period. Ten patients were lost to follow up. Of the 50 subjects who completed this study, 40 (80%) were boys and 10 (20%) were girls. The baseline characteristics of the study subjects are described in Table 1.

Table 1: Baseline characteristics (n=50)

Baseline characteristic	Number (%)	Number (APRPD)
Male	40 (80)	
Female	10 (20)	
Term	32 (64)	
Preterm	18 (36)	
Left sided renal pelvic dilatation (RPD)	35 (69)	
Bilateral RPD	09 (18)	
Antenatally detected RPD	28 (53)	23 (<10mm) 05 (>10mm)
Resolution of antenatally detected RPD in immediate postnatal scan	23 (82)	23 (<10mm) 05 (>10mm)
Persistence of antenatally detected RPD in postnatal scan at 6 weeks	05 (18)	0 (<10mm) 05 (>10mm)
Low birth weight	19 (38)	

APRPD: anteroposterior renal pelvic diameter

The earliest antenatally detected RPD was at 18 weeks of gestation. All the 18 (100%) preterms showed resolution compared to 22 (68%) out of 32 term babies. This difference was found to be statistically significant (p = 0.006). There was no statistically significant difference between gender, laterality and resolution. None of the antenatal factors studied, had any significant relation to resolution. The aetiology of RPD were transient or physiological in 37 babies, uretero-pelvic junction obstruction in 12 babies and 1 had posterior urethral valves (PUV). Data from the first postnatal scan showed that 37 (74%) babies had SFU grades

1 and 2. Nine (18%) babies were of SFU grade 3. Grade 4 SFU with cortical thinning was seen in 4 (8%) cases. SFU grade 3 and 4 cases showed resolution in only 5 out of 13 (38.5%) moderate to severe cases as shown in Table 2.

Surgery was done in the 4 cases with SFU grade 4. This included pyeloplasty for 3 patients with pelvi-ureteric junction obstruction and valve ablation for a case of posterior urethral valve.

Febrile UTI was observed in 18% of the total cases. Its frequency and relation to SFU grade is shown in Table 3.

Table 2: Univariate analysis of outcomes with severity of RPD

Outcome	Mild n (%)	Moderate to severe n (%)	OR	95% CI	P value
Resolved	35 (94.6)	05 (38.5)	2.4	1.2-4.9	0.001
Not resolved	02 (05.4)	08 (61.5)			
UTI Present	05 (13.5)	04 (30.8)	0.43	0.13-1.3	0.16
No UTI	32 (86.5)	09 (69.2)			
Surgery done	0 (0)	04 (30.8)	N.A	N.A	0.003
No surgery	37 (100)	09 (69.2)			

Table 3: Urinary tract infection in relation to SFU grade

SFU grade	Cases (n/total)	organism	UTI freq	APRPD	Complications
1	2/32	E.coli	Once	8.9mm	None
2	3/5	E.coli	Once	10mm	None
3	1/9	Enterococcus, E.coli	multiple	9mm	RTA
4	3/4	Klebsiella, Enterococci	multiple	>15mm	FTT, dehydration

Eight out of nine cases of UTI were males. E.coli was the commonest organism isolated. There was no statistically significant relation between UTI and the SFU grade of RPD ($p = 0.16$). Three out of four cases with UTI having SFU grade 4 and 1 case with SFU grade 3, developed multiple episodes of febrile UTI, requiring hospitalisation in each episode within the first 6 months of life despite antibiotic prophylaxis. Frank pyuria was observed twice in a female baby with SFU grade 3 with vesico-ureteric reflux, but with APRPD of only

9mm, who also had renal tubular acidosis. Pyeloplasty resulted in relief of UTI in all these cases.

Resolution occurred only at a mean age of 25.71 weeks, in those with urinary tract infections but in those without UTI, resolution occurred at a mean age of 14.15 weeks. This was found to be a statistically significant difference by both Breslow test ($p=0.01$); and Taron ware tests of significance ($p = 0.026$) as displayed in Table 4.

Table 4: Survival characteristics of study sample

UTI	Cases (n)	Resolved (n)	Censored (n) (%)	Mean survival time (resolution-event) (weeks)	95 % CI
With UTI	09	05	04 (44.1)	25.71	12.59-38.83
No UTI	41	31	10 (24.4)	14.15	8.42-19.886

In the mild group, the mean time of resolution was 12.98 weeks with a confidence interval of 8.96 to 17.00 weeks. In those with RPD above 10mm, the mean time for resolution was 30.3 weeks with a confidence interval of 16.33 to 44.26 weeks. Thirty six (72%) showed resolution at 6 weeks and 42 (84%) resolved by 6 months of age. At 1 year of age, 8 (16%) had persistent renal pelvic dilatation. Resolution in bilateral RPDs were found to be significantly less ($p = 0.002$) at 6 and 12 weeks postnatal scans. Progression of RPD was seen in those with APRPD>10mm ($P = 0.03$) and OR of 4.2.

Discussion

The key findings of this study are that UTI significantly delays resolution of hydronephrosis in the infant. Resolution, in those with UTI, occurred at a mean age of 25.7 weeks compared to resolution at age of 14 weeks in those without UTI. Nine (18%) developed UTI in our study compared to 10% UTI observed by Wollenberg *et al*⁹. We found that only 13.5% of the mild and 30% of the moderate to severe RPDs developed UTI within one year of life. None of Wollenberg’s mild cases developed UTI. However, our finding is similar to the study by Dellagrammaticus where 12.2% of mild RPD developed UTI²². Prospective study by Coelo *et al* revealed that 18% of mild RPD had uropathy and 7.8% had UTI during a medium-term follow-up time²³. Our study also confirms their findings that even mild RPD babies need surveillance for UTI. RPD in preterms was seen to resolve completely but resolution does not depend

on gender, even though RPD is predominant in males.

The majority (72%) of the newborns with SFU grade 1 showed resolution as early as 6 weeks. As expected, majority of our mild renal pelvic dilatations (SFU grade 1 and 2) resolved within one year (80%) compared to 52.7% of mild cases in a study by Lim *et al*². Babu *et al* reported resolution in 71 out of 116 (61.2%) of children²⁴. Our high resolution rate of 80% may be because SFU grade 1 was accorded to all babies who had a barely split sinus irrespective of APRPD as the status of the calices is key in SFU grading. The size of the renal pelvis is less important and does not need to be measured as per the original SFU grading by Fernbach *et al*¹⁴. The mean resolution time in the mild cases was around 3 months. Our study shows that only 38.5% of those with APRPD more than 10 mm, resolved within one year. This delayed and slow resolution could be attributed to the increased rates of UTI (30.8% UTI in APRPD above 10mm). Mami C, *et al* reports that more than 90% of cases of moderate dilatation of the renal pelvis (APRPD 10mm-14.9mm) resolve spontaneously by 12-24 months. However, their UTI rate in the moderate group was only 3.6%¹¹. It is prudent to keep the moderate RPDs under follow up and screen them for UTI at each febrile episode, and advise sonological screening for progression of RPD in those with SFU grade above 2 and APRPD ≥10mm. As expected, there was a highly significant ($p=0.003$) association of surgery for the moderate to severe group. An Indian study by Babu

R, *et al.* reports that none among the unilateral RPD cases with APRPD <15mm required surgery²⁴. However, we report that even if APRPD is 9mm, if the baby has recurrent UTI, despite antibiotic prophylaxis and its unilaterality, if there is a pelvi-ureteric junction obstruction, surgical relief of obstruction provides relief from recurrent UTI.

One major limitation of our study was the limited sample size of moderate to severe group. This could be the reason why Log Rank test for significance showed a p value of 0.06 while the Breslow test and Taron ware showed that UTI significantly delays resolution. Another limitation of the study was that all mothers did not have antenatal ultrasound scan details of renal pelvic dilatation based on SFU grading.

Conclusions

UTIs significantly delay resolution of RPD. Mild RPD resolves within 3 months and moderate RPD resolve around 7.5 months of age. Bilateral RPDs significantly delay spontaneous resolution. Preterm RPDs almost always resolve within one year of life.

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