

# Does the presence of non-refluxing hydroureter impact the management and outcome of high-grade hydronephrosis?

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## Abstract

**Introduction:** We aimed to evaluate the impact of non-refluxing hydroureter on the initial management of high-grade hydronephrosis (HGH) management. Moreover, we evaluated the occurrence of febrile urinary tract infection (fUTI) and surgical intervention for conservatively managed units.

**Methods:** Patients' charts with postnatal hydronephrosis from 2008–2014 were retrospectively reviewed. We included patients who presented in the first year of life. All included patients had HGH (Society of Fetal Ultrasound [SFU] grades 3 and 4) and all were non-refluxing using voiding cystourethrogram (VCUG). We categorized renal units into two groups: with hydroureteronephrosis (HUN) and without hydroureter (isolated hydronephrosis [IH]). We recorded the initial management. We evaluated the impact of non-refluxing hydroureter on hydronephrosis fate, fUTI, and change to surgery for those managed conservatively.

**Results:** We included 169 patients (180 units). IH was diagnosed in 146 units (137 patients), whereas 34 units (32 patients) had HUN. Median followup was 42.9 months. A total of 25.3% (37/146) of IH units had initial surgical management in comparison to 5.1% (2/34) of HUN units ( $p=0.01$ ). During conservative management, nine HUN patients (30%) and 11 IH patients (10.7%) experienced fUTI ( $p=0.009$ ). Surgical intervention after failed conservative management was indicated for 12 IH units (11%) and six HUN units (18.8%) ( $p=0.25$ ). Anteroposterior diameter (APD) worsening was significantly associated with the change to surgery in IH group ( $p=0.003$ ). More than half (52.3%) of IH units resolved during conservative management in comparison to 18.7% of HUN ( $p<0.001$ ). HUN had longer time to resolution (log rank=0.004).

**Conclusions:** IH units had more initial surgical interventions. The fUTI rate was much higher in association with dilated ureter even under antibiotic coverage. HUN was associated with less and slower resolution rate.

## Introduction

Traditionally, the management of non-refluxing high-grade hydronephrosis (HGH), either isolated hydronephrosis (IH) or due to primary hydroureteronephrosis (HUN), was surgical. Yet more recent studies have shown that there is a potential for spontaneous resolution for non-refluxing HGH. As such, there is a move toward non-surgical management whenever possible, with surgical management being reserved for the failure of initial conservative management.<sup>1–4</sup>

Society of Fetal Ultrasound (SFU) grade 3–4 hydronephrosis has traditionally been considered to be the risk group more inclined to early surgical and medical management.<sup>5</sup> In the current study, we present our approach to the postnatal management of non-refluxing HGH. In this study, our aim was to evaluate the impact of dilated ureter on the management of HGH. Moreover, we aimed to evaluate the impact of dilated ureter on the fate of hydronephrosis and the occurrence of febrile urinary tract infection (fUTI) during conservative management. Our hypothesis was that the presence of hydroureter could increase the fUTI rate and could affect the resolution rate while managed conservatively, but would have less initial surgical interventions in comparison to IH.

## Methods

The study was conducted retrospectively in a single tertiary center. Following a search through medical records, we reviewed patients' charts who presented to our urology clinic with postnatal hydronephrosis during their first year of life, in the period between January 2008 and August 2014. We included patients who had HGH (SFU grades 3–4). Patients with non-functioning kidneys, vesicoureteric reflux (VUR) and those with <2 years of followup were excluded. Patient demographics, laterality, and hydronephrosis grade were recorded. All data pertaining to serial ultrasounds, voiding cystourethrogram (VCUG), and mercaptoacetyl-triglycine (MAG-3) renal scan were reviewed. Further, all data related to the fUTI occurrence, continuous antibiotic

prophylaxis (CAP), circumcision status, and hydronephrosis outcome were recorded and analyzed.

SFU grade 3 was defined as renal pelvic dilation associated with dilation of all calyces. SFU grade 4 was defined as SFU grade 3 with the addition of notable parenchymal thinning. Depending on dilated ureter diameter, we defined hydroureter as distal ureteral diameter  $\geq 7$  mm.<sup>4</sup> To measure the ureteral diameter, ultrasound studies that were done in the first year of life were all reviewed to be sure of the status of hydroureter. The ureteral diameter was measured in the transverse plane, posterior to the bladder; then, the greatest diameter in all first-year ultrasounds was recorded. Ureteral diameter was measured while the bladder was full.

VUR was initially assessed in all patients using cyclic VCUG. The presence of VUR was examined during both filling and voiding phases and patients with reflux were excluded.

Febrile UTI was defined as body temperature  $>39$  °C associated with pyuria and positive urine culture with a single pathogen at  $>50000$  CFU/ml. The fUTI occurrence was extracted from patients' charts and microbiology reports.

Initial renogram was indicated for all patients with grade 4 hydronephrosis or at the surgeon's discretion. Renogram findings were reviewed by one urologist (A.H). Regarding the HUN group, the region of interest was drawn around the kidney, dilated pelvicalyceal system, and dilated ureter. Renogram curve types were obstructive or non-obstructive. Obstructive curve was considered when continuously rising or slow down-sloping without adequate washout ( $<50\%$ ) in response to furosemide. Non-obstructive renogram was defined as  $T_{1/2} < 10$  minutes with complete tracer washout. Otherwise, the renogram was considered equivocal.

In our approach, the initial management line, either conservative or surgical, depended on the presence of indications for surgical management. Initial surgical management was indicated if differential renal function (DRF) was  $<40\%$  and, at the same time,  $T_{1/2}$  was  $>20$  minutes. Moreover, other indications included patients with grade 4 single functioning kidney or bilateral grade 4 hydronephrosis.

Conservative management depended primarily on serial ultrasound scans and counselling regarding fUTI and constipation prevention. Febrile UTI counselling included recognition teaching and proper genital hygiene. Moreover, older children were counselled on regular bowel and bladder habits to prevent constipation. The timeline of conservative management protocol is illustrated in Fig. 1. CAP was indicated for SFU grade 4 cases and for patients who experienced a second fUTI episode. We discontinued CAP if HGH was downgraded to low-grade hydronephrosis or the patient was toilet trained. Followup renograms beyond the initial one were indicated in cases of upgrading of SFU grade 3 or stable SFU grade 4.

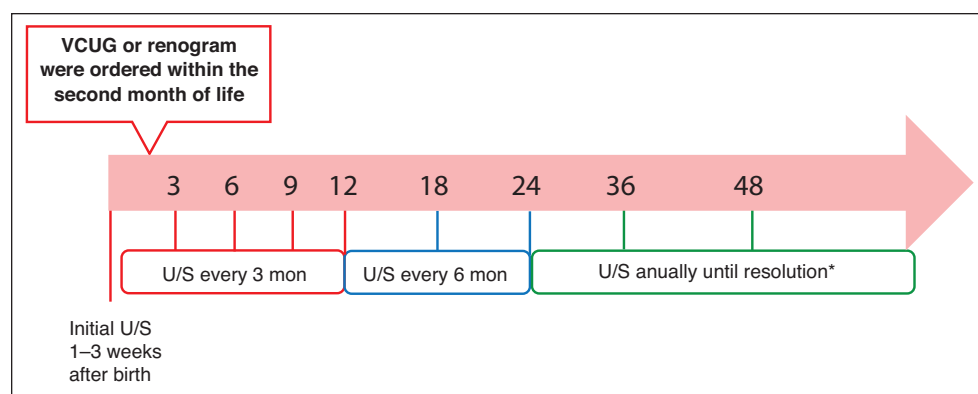
We considered a failed conservative management with required surgical intervention if one of the following findings were observed: 1) upgrading hydronephrosis on two subsequent ultrasounds; 2) renal scintigraphy findings of decreased DRF  $>10\%$  and worsening drainage in association with worsening of hydronephrosis (by ultrasound). Moreover, recurrent fUTI ( $>2$  times) was considered an indication for surgery. If a patient experienced his first fUTI under CAP (breakthrough fUTI), we would discuss with the family a change of antibiotic and performing male circumcision or offer surgical intervention. Whereas in the case of a second breakthrough fUTI, surgical intervention would be warranted.

The hydronephrosis outcome was reviewed concerning the hydronephrosis fate and surgical intervention. The outcome was categorized as resolved, persistent, downgraded, or worsened. Resolved hydronephrosis was defined as a spontaneous disappearance of pelvicalyceal dilation and a ureter diameter  $\leq 4$  mm if hydroureter was initially present. We considered a  $\leq 4$  mm ureteral diameter as reported by others as a normal finding in children.<sup>6,7</sup> Worsening hydronephrosis was defined as upgrading of hydronephrosis, DRF worsening  $>10\%$ , and presence of obstructive pattern on followup renogram.

Our primary outcome was to evaluate the effect of the non-refluxing hydroureter on the management of HGH. Our secondary outcomes were to evaluate the conserva-

tive management in terms of the fate of hydronephrosis, fUTI, and the need for surgery in relation to the presence of non-refluxing hydroureter.

The Statistical Package for the Social Sciences (SPSS®, version 20; SPSS Inc., IBM Corp., Armonk, NY, U.S.) was used to record patient data and for statistical analysis. Chi-squared test was used for analysis of categorical data while the Mann-Whitney U-test was used for continuous data. We used Kaplan-Meier survival plot to eval-



**Fig. 1.** The timeline of conservative management of high-grade hydronephrosis. \*Followup was ended if resolution was documented in two consecutive ultrasounds (U/S). VCUG: voiding cystourethrogram.

uate the hydronephrosis resolution, regarding the presence of hydroureter. A  $p < 0.05$  was considered significant.

## Results

Of the total 543 reviewed patients, 223 (236 units) were diagnosed with HGH. Forty-two VUR units (40 patients) and six non-functioning renal units (six patients) were excluded. Of the remaining patients, we excluded non-resolved eight units (eight patients) with followup  $< 2$  years.

Total eligible cases included 169 patients (180 units). IH was diagnosed in 146 units (137 patients), whereas 34 units had HUN (32 patients). Patients' demographics are demonstrated in Table 1. Patients presented at a median age of 0.5 months (0.03–11.7). The median followup period was 43.7 months (11–108.7).

## Initial line of management

Twenty-five percent (37/146) of IH units underwent initial surgical intervention in comparison with 5.9% (2/34) of HUN units. Notably, most HUN units were managed conservatively (94.1%) while 75% of IH units were managed conservatively ( $p = 0.01$ ).

Both HUN units had initial surgical intervention at ages one and seven months. Both underwent cutaneous ureterosomy, then later on, both had ureteral reimplantation at ages

12 and 19.1 months respectively. All IH units that had initial surgical intervention underwent dismembered pyeloplasty at a median age of 3.5 months (1–18.1).

## Renal function

IH units that underwent initial surgical interventions had median DRF of 43% (12–100) with median  $T_{1/2}$  of 26 minutes (4.8–172). Three IH units underwent surgeries because of single functioning kidneys. Moreover, three patients with bilateral grade 4 hydronephrosis underwent surgical interventions. However, none of the three patients had obstructive renograms with a median  $T_{1/2}$  of 12.6 minutes (4.8–22). Two HUN units were operated initially due to DRF  $< 40\%$  (15% and 34%). These HUN units had  $T_{1/2}$  of four minutes and 20.5 minutes.

For renal units that had initial conservative management, 25/30 (83.3%) patients with HUN (28 units) and 63/103 (61.2%) IH patients (67 units) underwent MAG-3 studies. Non-obstructive renogram was diagnosed in 24/28 HUN units (85.7%) and 54/67 IH units (80.6.1%) ( $p = 0.55$ ). Remaining IH units (10/68) had equivocal renogram studies or obstructive renogram (2/68) while remaining HUN were three equivocal renograms and one obstructive. Regarding renal units with obstructive renograms, the two IH units showed improvement on followup ultrasound scan while the HUN unit had surgical intervention at age 12.3 months. The

**Table 1. Demographics and characteristics of all included patients**

		HUN (32 patients, 34 units)	IH (137 patients, 146 units)	p
Age at presentation median(range)		0.5 (0.06–6.9)	0.5 (0.03–11.7)	0.75*
Gender	Male, n (%)	21 (65.6)	111 (81)	0.06 <sup>^</sup>
	Female, n (%)	11 (34.4)	26 (19)	
Laterality	Unilateral, n (%)	22 (68.8)	102 (74.5)	0.51 <sup>^</sup>
	Bilateral n (%)	10 (31.2)	35 (25.5)	
	Bilateral HG/bilateral (HG + LG)	2/8	9/26	
Side	Right, n (%)	12 (35.3)	35 (24)	0.18 <sup>^</sup>
	Left, n (%)	22 (64.7)	111 (76)	
SFU	Grade 3, n (%)	23 (67.6)	96 (65.8)	0.83 <sup>^</sup>
	Grade 4, n (%)	11 (32.4)	50 (34.2)	
Ureteral diameter median (range)		9.1 (7–17.5)	0 (0–6.6)	$< 0.001^*$
Antibiotic prophylaxis, n (%)		19/34 (55.9)	48/137 (33.6)	$< 0.03^*$
Circumcision status, n (%)		6/21 (28.6)	33/111 (33.7)	0.9 <sup>^</sup>
Renograms	Patients, n (%)	28/32 (87.5)	95/137 (69.3)	0.043 <sup>^</sup>
	DRF, median (range)	50% (12–73)	49% (12–100)	0.96*
	$T_{1/2}$ , median (range)	4.7 min (1.1–115)	9.3 min (0–650)	0.03*
	Curve			
	Obstructive, n (%)	2 (6.9)	39 (37.9)	0.03 <sup>^</sup>
First-line management	Non-obstructive, n (%)	23 (79.3)	54 (52.4)	
	Equivocal, n (%)	4 (13.8)	10 (10.7)	
	Conservative, n (%)	32 (94.1)	109 (74.7)	0.01 <sup>^</sup>
	Surgical, n (%)	2 (5.9)	37 (25.3)	

<sup>^</sup>Chi-squared test was used for statistical analysis. \*Independent Samples Mann-Whitney U-test was used for statistical analysis. DRF: differential renal function; HG: high-grade; HUN: hydroureteronephrosis; IH: isolated hydronephrosis; LG: low-grade; SFU: Society of Fetal Ultrasound.

median Post-Lasix  $T_{1/2}$  of the HUN group was 4.7 minutes (1–32) and 4.1 minutes (1–53) for the IH group ( $p=0.89$ ).

### Febrile UTI during conservative management (Table 2)

Febrile UTI was diagnosed in 30% (9/30) of HUN patients in comparison to 10.7% (11/103) of IH patients ( $p=0.009$ ). The median initial ureteral diameter of HUN units that developed fUTI was 10 mm (7–11.7). Thirty-two percent of IH patients received CAP in comparison to 63.3% of HUN patients. The median duration of CAP was higher in the HUN group in comparison to the IH group (13 months vs. 6 months) ( $p<0.001$ ). Despite CAP, 33.3% of HUN patients (3/9) and one IH patient had breakthrough fUTI ( $p=0.17$ ). HUN and IH patients who did not receive CAP were followed for a median duration of 41.1 months (13–83.5) and 35.4 months (11–91), respectively.

Notably, none of the circumcised patients has developed fUTI. Three circumcised HUN patients (60%) and 6/26 IH patients (23.1%) had CAP ( $p=0.1$ ). On the other hand, 4/15 uncircumcised patients with HUN (26.7%) and 7/62 uncircumcised patients with IH (11.3%) experienced fUTI ( $p=0.13$ ).

### Fate of hydronephrosis during conservative management (Table 2)

Sixty-three percent of HUN units and 78.9% of IH units were downgraded or resolved ( $p=0.06$ ). The median age at

resolution was 38.7 months (6.3–81.3) (Table 3). The median initial ureteral diameter for resolved HUN units was 7.2 mm (7–9.7). Most of patients with resolved hydronephrosis had  $<5$  ultrasounds until documented resolution (66.7% for HUN and 79.2% for IH). Before resolution, a followup renogram was needed for only 21% of IH patients while it was only needed for one HUN patient ( $p=0.82$ ). In terms of survival analysis, the presence of hydroureter had decreased the resolution rates ( $p=0.004$ ).

Worsening hydronephrosis was observed in 6/32 (18.7%) HUN units and 12/109 IH units (11%) ( $p=0.5$ ). Regarding the HUN group, two units (SFU 3) showed upgrading on followup ultrasound while four units (SFU 4) showed worsening hydronephrosis on renogram followup. Two of these SFU 4 units had DRF decline  $>10\%$  and the remaining two units had obstructive renogram. For the IH group, no units had declined renal function during followup. Worsened grade 4 IH units had obstructive followup renogram while SFU 3 showed upgrading to grade 4 with the presence of obstructive renogram.

### Subsequent surgical interventions (Failed conservative management)

Nineteen percent of conservatively managed HUN units (6/32) and 11% of IH units (12/109) underwent surgical interventions ( $p=0.25$ ). There was no difference in the medi-

**Table 2. Clinical course of patients who had initial conservative management during followup**

		HUN (30 patients, 32 units)	IH (103 patients, 109 units)	p
Followup period, median (range)		57.2 months (17.6–106.1)	42.4 months (11–108.7)	0.17*
Gender	Male, n (%)	20 (66.7)	88 (85.4)	0.02
	Female, n (%)	10 (33.3)	15 (14.6)	
Laterality	Unilateral, n (%)	19 (63.3)	76 (73.8)	0.26
	Bilateral, n (%)	11 (36.7)	27 (26.2)	
	Bilateral HG/bilateral (HG + LG)	2/9	6/21	
SFU	Grade 3, n (%)	23 (71.9)	90 (82.6)	0.18
	Grade 4, n (%)	9 (28.1)	19 (17.4)	
Antibiotic prophylaxis	Patients, n (%)	19/30 (63.3)	33/103 (32)	$<0.001^{\wedge}$
	Duration median (range)	13 months (3–48)	6 months (3–24)	
Circumcision, n (%)		5/20** (25)	26/88** (29.5)	0.67
fUTI, n (%)		9/30 (30)	11/103 (10.7)	0.009 <sup>^</sup>
Breakthrough fUTI, n (%)		3/9 (33.3)	1/11 (9.1)	0.17
Recurrent fUTI, n (%)		4/9 (66.7)	2/11 (18.2)	0.2
Fate of hydronephrosis				
Resolved, n (%)		6 (18.7)	57 (52.3)	$<0.001^{\wedge}$
Downgraded, n (%)		14 (43.9)	29 (26.6)	0.06 <sup>^</sup>
Worsening, n (%)		6 (18.7)	12 (11)	0.25 <sup>^</sup>
Stable, n (%)		6 (18.7)	11 (10.1)	0.19 <sup>^</sup>
Failed conservative management	Changed to surgery, n (%)	6/32 (18.7)	12/109 (11)	0.25 <sup>^</sup>
	Grade 3/4	2/4	6/6	0.5
	Age at surgery, median (range)	12.6 months (5.1–56)	15.2 months (7–36)	0.9*

<sup>^</sup>Chi-squared test was used for statistical analysis. \*Independent Samples Mann-Whitney U-test was used for statistical analysis. \*\*The total number represents males. fUTI: febrile urinary tract infection; HG: high-grade; HUN: hydroureteronephrosis; IH: isolated hydronephrosis; LG: low-grade; SFU: Society of Fetal Ultrasound.



**Table 3. Resolved hydronephrosis after conservative management**

		HUN (6 patients, 6 units)	IH (55 patients, 57 units)	p
Time till resolution, median (range)		41.1 months (20.9–62.1)	31.8 months (11–81.3)	0.53
Gender	Male, n (%)	3 (50)	47 (85.5)	0.03
	Female, n (%)	3 (50)	8 (14.5)	
Antibiotic prophylaxis, n (%)		2 (33.3)	17 (30.1)	0.9
fUTI, n (%)		0 (0)	2 (3.6)	0.63
Followup ultrasound, n (%)	≤5	4 (66.7)	45 (79.2)	0.38
	>5	2 (33.3)	10 (20.8)	
Followup renograms, n (%)		1/6* (16.7)	5/24* (20.8)	0.82

\*Numbers are presented in relation to those had initial renograms. fUTI: febrile urinary tract infection; HUN: hydroureteronephrosis; IH: isolated hydronephrosis.

an age at surgery between both groups ( $p=0.9$ ). In the HUN group, the causes of surgical interventions were worsening hydronephrosis (four units) and recurrent fUTI (two units). All of the IH were operated after conservative management due to worsening hydronephrosis.

The median last anteroposterior diameter (APD) before surgery of IH units was 26.3 mm (15–40) in comparison to a median initial APD of 11 mm (5.6–25) ( $p=0.003$ ). Similarly, the median preoperative APD (16 mm) of HUN units was not significantly changed from the initial ones (11 mm) ( $p=0.17$ ). On the other hand, the median ureteral diameter of HUN units before surgery was 13 mm (9.6–19) while the median initial diameter was 11 mm (8–16) ( $p=0.34$ ).

Preoperatively, we ordered a repeated renogram for all patients. For those with IH, six units (50%) had obstructive renograms, equivocal in two units (16.7%), while the remaining had non-obstructive curves. None of these IH units had an initial obstructive renogram. On the other side, four HUN units, that had worsening hydronephrosis and underwent surgical interventions, had obstructive curves when repeating renograms.

Two of six HUN units that underwent surgical intervention after conservative management had >1 procedure. Cutaneous ureterostomy was performed at ages five and 4.8 months. Later on, ureteral reimplantation was done at ages 9.8 and 19.2 months, respectively.

## Discussion

With respect to the long-term management of antenatal hydronephrosis and the advent of conservative management of HGH, the objectives have been to design an approach that avoids surgery but preserves renal function and prevents fUTIs. With milder hydronephrosis grades, a purely conservative approach is broadly accepted.<sup>8,9</sup> With higher hydronephrosis grades, the trend in the available literature indicates that there is a strong correlation between severe pathology and surgical intervention, and similarly between hydronephrosis worsening and increasing fUTI risk.<sup>10</sup> The current practice regarding the management of

non-refluxing HGH varies significantly on an institutional, national, and international basis. Some may raise the point that we compared two different diagnoses. However, our aim was to evaluate the impact of dilated ureter on the HGH management, as the management protocol is usually the same for all HGH units. In order to study that impact, we divided all non-refluxing HGH units into two main categories: those with dilated ureter, “HUN group,” and the remaining units with HGH were categorized as “IH group.” In their study, Braga et al compared the fUTI incidence between units with dilated ureter (32%) and those without dilated ureters (6%).<sup>11</sup>

In our study, we focused on patients with non-refluxing HGH, given that VUR is a known risk factor for fUTI and disease progression and, consequently, well-discussed in previous studies.<sup>12,13</sup>

In Coelho et al, 51% of IH units with moderate to high hydronephrosis underwent pyeloplasty during a two-year followup.<sup>14</sup> In our study, only 25.3% of IH had initial surgical management. This difference may be related to different indications of surgery and our preference for a trial of conservative management. Braga et al had a 28.8% of HGH patients with HUN who underwent surgical interventions, which was similar to 23.5% (8/34) of our HUN units (two units initially and six units after failed conservative management).<sup>15</sup> Despite the fact that there was no difference in the percentage of units that had surgical interventions, we noted that 50% of HUN units that had surgical interventions (4/8) had >1 procedure while all of the IH units underwent one procedure. This reflects the complexity of surgical intervention in this group of patients.

Some studies have shown that there is potential for IH cases to resolve spontaneously over time and there has been an attempt to stratify patients based on their likelihoods for resolution.<sup>1</sup> Ulman et al published a prospective study of 104 infants with unilateral non-refluxing IH.<sup>16</sup> In their cohort, 22% of patients underwent pyeloplasty, 54% had resolution to grade 0 or 1, and 24% had improvement to grade 2 or 3 at five years, with a mean time to complete resolution of 19 months.<sup>16</sup> The current study produced similar results, with

complete resolution in 52.3% of IH units, downgrading in 26.6%, no change in 10.1%, and surgical management in 11% at a median followup of 42.4 months, with a median age at resolution of 31.8 months. The differences in time to resolution and the percentage of cohort with complete resolution were likely due to our strict definition of resolution. It is interesting to note that even though 26.2% of our conservatively managed patients had bilateral hydronephrosis, only 11% required further surgical management in comparison with 22% in Ulman study. This could be explained by the fact that 63.1% of our IH patients with failed conservative management had either preoperative obstructive or equivocal renograms in comparison to 91% of Ulman's surgical sub-cohort.<sup>16</sup>

In consideration of the HUN cohort, our results were consistent with the trends seen in the current literature, which recommend initial conservative management for HUN in the absence of significant obstructive uropathy.<sup>4</sup> During conservative management, 18.7% of our HUN units were resolved, with a median time to complete resolution of 41.1 months. Nineteen percent of our HUN group required operative management after failed conservative management. Interestingly, HUN and IH units that underwent surgical intervention after failed conservative management had similar age at surgery (12.6 vs. 15.2 months, respectively) ( $p=0.9$ ). DiRenzo et al found that in patients with HGH, there was resolution 12.2% of units in the first year of life.<sup>2</sup> Despite the similarity in the resolution rate, our cohort had a longer time to resolution. That can be explained by the different definition of resolution in either studies.

In the current study, we found that IH units that underwent surgical interventions had significant worsening of APD while HUN units that had failed conservative management had no significant worsening of either APD or ureteral diameter. More prospective studies with larger numbers of patients would be needed to confirm the HUN findings.

In another study, 80 patients with primary HUN were prospectively followed for a mean time of 26.3 months, of which 82% had HGH. Researchers found that, with respect to their entire cohort, 76% of patients experienced spontaneous resolution at a median followup of 19 months.<sup>15</sup> The difference in the resolution rate is likely due to their resolution definition as an APD of  $<10$  mm, SFU  $<2$ , or ureter diameter  $<8$  mm, while we required a ureteral diameter  $\leq 4$  mm. This is compounded by the inclusion of both high- and low-grade hydronephrosis, while our cohort consisted only of HGH.<sup>15</sup>

An issue of particular controversy in the management of non-refluxing HGH is the use of CAP. Although the SFU consensus recommends CAP in cases of HGH, with or without hydroureter, it is not universally echoed in the field.<sup>10</sup> A systematic review suggested there is value in offering CAP to infants with HGH.<sup>17</sup> This notion is supported by other groups, who have found that the UTI risk approaches 30–40% with

non-refluxing HGH.<sup>18,19</sup> Lee et al identified HGH, hydroureter, and obstructive uropathy as independent risk factors for fUTI, separate from the presence of reflux.<sup>19</sup> This is consistent with the findings in our study, as fUTI was diagnosed in 30% of HUN patients compared to 10.7% of IH patients who had conservative management ( $p=0.009$ ). Further, during conservative management, HUN patients required a significantly longer duration of CAP than IH patients ( $p=0.001$ ). As supported by our previous results, the hydroureter itself increases the fUTI risk.<sup>20</sup>

To our knowledge, no comparative study has evaluated the conservative management of HGH regarding the presence of dilated ureter. Collectively, we found that the associated hydroureter worsens the prognosis of HGH in terms of lower resolution rate, higher chance to change to surgery, and more fUTI susceptibility. Dilated ureter negatively impacts complete resolution ( $p=0.004$ ), with longer median time to resolution. A possible explanation for this is that the natural history of HUN trends toward a slow disease improvement, especially when our resolution criteria are quite strict. This notion is supported by Arena et al, who suggest that the time of spontaneous resolution of a primary HUN may exceed 3.6 years.<sup>21</sup>

The limitations of this study lie in it being a retrospective review. Although a conservative approach was used throughout the study, individual practice preferences of different surgeons and patients lead to discrepancies in the prescription of antibiotics and change to surgical intervention. However, our indications for surgical intervention or CAP are similar to the British Association of Pediatric Urologists and the SFU recommendations.<sup>4,10</sup> In addition, a small number of patients with HUN was included in our study; however, it is comparable to the numbers of patients with high-grade HUN in other studies.<sup>2,21</sup> Indeed, prospective, controlled studies are needed to truly examine CAP effectiveness and utility.

## Conclusions

Renal units with IH had four times more initial surgical interventions than those with HUN. The rate of fUTI was almost triple in association with hydroureter, even under antibiotics coverage. None of the circumcised patients experienced fUTI. The presence of dilated ureter decreased the resolution rate by almost 50%. HUN was associated with a higher rate of failed conservative management and more complexity of surgical intervention.

**Competing interests:** The authors report no competing financial or personal interests related to this work.

This paper has been peer-reviewed

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