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Outcomes of intermediate-risk hydronephrosis in pediatric patients

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Summary

Purpose
Hydronephrosis is a common antenatal diagnosis and is present in approximately 1–5% of pregnancies. The urinary tract dilation (UTD) classification system was introduced in 2014 and stratifies post-natal hydronephrosis risk into three groups: low-risk (P1), intermediate-risk (P2), and high-risk (P3). Recommendations for P3 hydronephrosis have been established, whereas those for P1 and P2 UTD are often left to the discretion of providers with P1 considered low-grade and less concerning significant pathology. Given the obscure nature of P2 hydronephrosis, we sought to determine the natural history and outcomes of pediatric patients with P2 hydronephrosis within a single institution.

Materials and methods
Children <18 years old diagnosed with hydronephrosis between January 2015 and December 2018 were identified by ICD-9 and ICD-10 codes. Patients with P1 hydronephrosis, P3 hydronephrosis, known vesicoureteral reflux, complex anomalies (ex. Posterior urethral valve), neurological impairments, neurogenic bladder secondary to spinal abnormalities, and <6 months of follow-up were excluded. The development of urinary tract infection (UTI; ≥100 000 CFU/mL of bacterial growth, UA > 10 WBCs/hpf with fever >38C), need for surgical intervention (impaired renal function, worsening hydronephrosis, and/or delayed drainage on diuretic renography), and stability of hydronephrosis were collected retrospectively.

Results
Eighty-seven patients [105 renal units (RU)] were included. Twenty-six patients (30%) were female and 61 (70%) were male. Of the male patients, 30 (49%) of them were circumcised. The median age at initial evaluation was 1 month, and the median duration of follow-up was 13 months. Thirty-four (32%) RU had complete resolution, 24 (23%) improved to P1 hydronephrosis, 33 (31%) remained stable, and 14 (13%) progressed to P3 hydronephrosis. The median duration to resolution and improvement was 8.5 months and 5 months, respectively. Eleven (11%) RU required surgical intervention, 10 of which underwent pyeloplasty, with a median duration to intervention of 9 months. Fifty-five patients (63%) received antibiotic prophylaxis (amoxicillin or sulfamethoxazole-trimethoprim) for a median duration of 5 months. Nine patients (10%) developed a UTI, 3 of which were taking antibiotic prophylaxis at the time of infection.

Conclusions
Intermediate-risk hydronephrosis diagnosed in the pediatric population will either improve, resolve, or remain stable during 1-year follow-up in 87% of RU. Only 11% of RU required surgical intervention, and 19% of patients developed a UTI in the absence of antibiotic prophylaxis. These findings will assist with counseling parents concerning the importance of follow-up imaging and monitoring for UTI. However, the low risk of surgical intervention is encouraging and should be discussed with the children's caretakers.

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Summary Table

n	87
Male	61 (70%)
Circumcised	30 (49%)
Uncircumcised	29 (48%)
Female	26 (30%)
Median age at Diagnosis (months)	1
Median follow up (months)	13
Prenatal Hydronephrosis	
Yes	69 (80%)
No	18 (21%)
Unilateral Hydronephrosis	69 (80%)
Bilateral Hydronephrosis	18 (21%)
Total Renal Units	105

Introduction

Hydronephrosis, or dilation of the renal collecting system, is a common antenatal diagnosis, present in approximately 1—5% of all pregnancies [1]. Etiologies for pediatric hydronephrosis in order of frequency include transient or physiologic hydronephrosis, ureteropelvic junction obstruction, vesicoureteral reflux, and urinary tract obstructive uropathy [2]. Several classification systems have been used for grading prenatal hydronephrosis. The Society for Fetal Urology (SFU) grading system has been the most frequently used grading system for hydronephrosis. However, concerns with the SFU grading system, including an unclear differentiation of grades 3 and 4 disease prompted the development of the Urinary Tract Dilation (UTD) in 2014 [3].

The UTD classification system has been validated as a unified grading system used across the prenatal and postnatal time period to describe hydronephrosis [3,4]. Classification is based on six ultrasound observations which included bladder status, ureteral status, parenchymal appearance, parenchymal thickness, urinary tract dilation, and anteroposterior diameter of the renal pelvis [5]. The UTD classification system stratifies postnatal risk into three groups: low risk (P1), intermediate risk (P2), and high risk (P3) groups. Although recommendations for evaluation and management of patients with P1 or P3 hydronephrosis have been established, they are less clear for patients with P2 hydronephrosis and often left to the discretion of the clinician [5,6].

The literature has shown that patients with P1 hydronephrosis are more likely to experience resolution (75%) and, therefore, require less surgical intervention in comparison to those with higher risk hydronephrosis [7]. There is a paucity of data in the literature regarding the natural course and outcomes of P2 hydronephrosis. Based on the SFU grading system, approximately 97% of SFU grade 1 and 2 hydronephrosis resolved, improved, or stabilized during the first year of follow-up with only 3% requiring surgery over time, while 30% of SFU grade 3 hydronephrosis and 68% of SFU grade 4 hydronephrosis eventually required surgery [8,9]. Currently, it is unclear if P2 hydronephrosis is more similar to SFU grade 2 or SFU grade 3 hydronephrosis in terms of surgical need.

Historically, risk factors for surgical intervention for hydronephrosis were impaired differential renal function, decrease in renal function over time, urinary tract infection, development of kidney stones with a relative indication of worsening hydronephrosis on ultrasound imaging, and worsening drainage noted on diuretic renography [10]. Based on the literature, there is not a clear cutoff value for differential renal function for an indication for surgery but prior studies have used less than 35—40% of renal function as a criterion for early intervention for treatment of obstruction [11]. To date, risk factors and/or indications for surgery have not been formally established for P2 hydronephrosis. Additionally, high grade hydronephrosis has previously been associated with an increased risk of urinary tract infection (UTI) and antibiotic prophylaxis has been recommended when high grade hydronephrosis is diagnosed [12]. However, little is known regarding the risk of UTI in children with P2 hydronephrosis.

We sought to understand the natural history of P2 hydronephrosis, identify risk factors for surgical correction, and determine the risk of UTI in this patient population to better understand optimal follow-up. We hypothesize that P2 hydronephrosis is not associated with a high risk of UTI and, therefore, antibiotic prophylaxis is not necessary when P2 hydronephrosis is diagnosed. We also hypothesize that the historical indications for intervention in patients with hydronephrosis will apply to patients with P2 hydronephrosis.

Materials and methods

This retrospective study was performed with approval from University of North Carolina's Institutional Review Board (IRB File #18—3018). All patients less than 18 years of age diagnosed with hydronephrosis after January 2015 were identified utilizing ICD-9 diagnosis codes (591.0, 593.5, 753.2) and ICD-10 diagnosis codes (N13.0, N13.10, N13.20, N13.30, N13.39, N13.40, Q62.0). Patients with P1 hydronephrosis, P3 hydronephrosis, neurogenic bladder secondary to spina bifida or other spinal abnormalities, neuro-

logical impairments (ie. Cerebral palsy, Down's Syndrome), ureterocele, posterior urethral valves, known vesicoureteral reflux (VUR), and extensive pelvic surgery were excluded. Patients with less than 6 months of follow-up imaging were also excluded from analysis. Voiding cystourethrograms (VCUG) were available for review in 68 (78%) of the included patients. Clinical indications for VCUG in our cohort included development of urinary tract infection, hydronephrosis and/or hydroureter on prenatal or postnatal ultrasound and voiding dysfunction. In the final analysis, all renal units with isolated P2 hydronephrosis were included.

The grading of the hydronephrosis was determined by the radiology report that accompanied the diagnostic imaging based on the UTD classification system and verified by pediatric radiologist (BS) review. The follow-up interval was defined as the time between the initial diagnostic ultrasound indicating P2 hydronephrosis and the last ultrasound imaging. The change in hydronephrosis status (ie. stable, resolved, worse) was determined by comparing the follow-up images to the initial diagnostic image. Diuretic renography was performed by obtaining dynamic posterior imaging of the urinary tract immediately following administration of technetium 99-Mag3 radiotracer intravenously and then again immediately following the administration of furosemide intravenously. This was based on the well-tempered renogram protocol described in the literature [13]. Urine cultures for the patients included in this study were reviewed to determine the number of UTIs. A UTI was defined as bacterial growth $\geq$100 000 CFU/mL, urine analysis $>$10 WBC/hpf with fever $>$38C.

Statistical analysis was performed using Microsoft Excel. Descriptive statistics were used for all data.

Results

Eighty-seven patients were included in this study. Table 1 summarizes the baseline characteristics of the patients. Twenty-six (30%) patients were female and 61 (70%) were male. Of the male patients, 29 (48%) were circumcised. The median age at diagnosis was 1 month (range 0.03—180) with a median follow-up time of 13 months (range 1—48). Prenatal hydronephrosis was present in 80% of the cohort. Sixty-nine patients presented with unilateral hydronephrosis and 18 patients presented with bilateral hydronephrosis. Eighty-four renal units had a voiding cystourethrogram (VCUG) performed showing no vesicoureteral reflux (VUR). A total of 105 renal units were included in the study for analysis.

Table 1 Patient characteristics.

n	87
Male	61 (70%)
Circumcised	30 (50%)
Uncircumcised	29 (48%)
Female	26 (30%)
Median age at Diagnosis (months)	1
Median follow up (months)	13
Prenatal Hydronephrosis	
Yes	69 (80%)
No	18 (21%)
Unilateral Hydronephrosis	69 (80%)
Bilateral Hydronephrosis	18 (21%)
Total Renal Units	105

The longitudinal outcome of the 105 renal units were evaluated and are summarized in Table 2 and Fig. 1. Thirty-four (32%) renal units had complete resolution, 24 (23%) improved to P1 hydronephrosis, 33 (31%) remained stable, and 14 (13%) progressed to P3 hydronephrosis. The median duration to resolution and improvement was 8.5 months and 5 months, respectively. Fourteen (13%) renal units underwent fluctuation in hydronephrosis status over the course of follow-up. Of these 14 renal units, 8 renal units worsened to P3 hydronephrosis with subsequent improvement to P1 hydronephrosis, 1 renal unit worsened to P3 hydronephrosis with subsequent resolution, 3 renal units improved to P1 hydronephrosis with subsequent worsening to P3 hydronephrosis, and 2 renal units resolved with subsequent worsening to P3 hydronephrosis.

Eleven renal units (11%) required surgical intervention, with a median time to intervention of 9 months (mean 12 months). Of those renal units requiring surgical intervention, 2 (18%) had worsening dilation to P3 hydronephrosis, less than 30% of differential renal function on diuretic renography, and delayed drainage. Four (36%) patients had delayed drainage alone. Three patients (27%) had both delayed drainage on diuretic renography and worsening dilation to P3 hydronephrosis. One patient had worsening dilation to P3 hydronephrosis in the setting of less than 30% of differential renal function. One patient had worsening dilation to P3 hydronephrosis alone. Ten of the 11 renal units requiring surgical intervention, underwent a pyeloplasty procedure. One patient underwent nephrectomy. Overall, 87% of renal units with intermediate-risk P2 hydronephrosis resolved, improved, or stabilized during the first year of follow-up.

Nine patients (10%) in total experienced a urinary tract infection (see Table 3). Of these nine patients, eight

Table 2 Natural history and progression of renal units.

	N
Total Renal Units	105
Improved or Resolved	58 (55%)
Improved to P1	24 (23%)
Complete Resolution	34 (32%)
Median time to improvement (months)	5
Median time to resolution (months)	8.5
Progressed to P3	14 (13%)
Median time to progression (months)	3
Fluctuation in hydronephrosis status	14 (13%)
Resolved with subsequent worsening	2
Improved with subsequent worsening	3
Worsened with subsequent resolution	1
Worsened with subsequent improvement	8
Stable	33 (31%)
Surgical Intervention	11 (11%)
Median time to intervention (months)	9
Development of renal calculi	1 (1%)

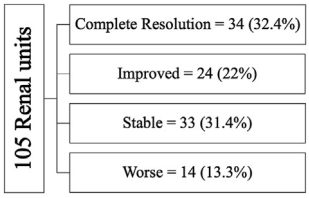

Fig. 1 Progression of renal units.

patients had a VCUG performed showing no VUR. Fifty-five patients (63%) in total received antibiotic prophylaxis for a median duration of 5 months. The antibiotic prescribed was either Amoxicillin or Sulfamethoxazole-Trimethoprim. Of the 55 patients who received antibiotic prophylaxis, 3 patients (6%) developed a urinary tract infection while on prophylaxis. Two of these 3 patients were uncircumcised males. Of the 32 patients (37%) who did not receive antibiotic prophylaxis, 6 patients (19%) developed a urinary tract infection. Three of these patients were female and 3 of these patients were male. Of these male patients, one was circumcised and two were uncircumcised. The collection method of these urinary specimens for cultures was not consistently provided within the chart.

Of the 18 patients with bilateral hydronephrosis, none developed a urinary tract infection or required surgical intervention. Seven of these patients experienced bilateral resolution of their P2 hydronephrosis. Two patients experienced unilateral resolution, with one patient experiencing stability of the contralateral side and the second patient experiencing improvement on the contralateral side. Four patients experienced bilateral improvement to P1 hydronephrosis. Three patients had unilateral improvement to P1 hydronephrosis with stability of their P2 hydronephrosis on the contralateral side. One patient had worsening hydronephrosis bilaterally to P3 hydronephrosis. One patient had unilateral worsening of the hydronephrosis to P3 hydronephrosis with stability on the contralateral side. Overall, for renal units where bilateral P2 hydronephrosis was present, seven patients experienced complete resolution, four patients improved to P1 hydronephrosis, and one patient had worsening P3 hydronephrosis.

Table 3 Antibiotic prophylaxis & development of UTI.

	n
On antibiotic prophylaxis	55 (63%)
Median duration (months)	5
Urinary tract infection	3 (6%)
Female	1 (33%)
Male	2 (67%)
Circumcised	0
Uncircumcised	2 (100%)
No antibiotic prophylaxis	32 (37%)
Urinary tract infection	6 (19%)
Female	3 (50%)
Male	3 (50%)
Circumcised	1 (33%)
Uncircumcised	2 (67%)
Number of children with UTI's	9 (10%)
Female	4 (44%)
Male	5 (56%)
Circumcised	1 (20%)
Uncircumcised	4 (80%)

Discussion

Hydronephrosis affects up to 5% of all pregnancies which requires post-natal evaluation contributing to elevated cost and parental anxiety [1,14]. Classifying the degree of hydronephrosis is important to determine risk of UTI and need for antibiotic prophylaxis, follow up imaging and counseling of risk for parents. Initially evaluated with the SFU grading system, prenatal hydronephrosis is often classified using the UTD classification system which stratifies patients into P1, P2, P3 risk groups. The literature describing the natural outcomes of those patients with P2 hydronephrosis is lacking and decisions are often left to the discretion of the clinician.

When counseling parents, providers often have to make decisions based on the likelihood of progression and need for intervention. The results of this retrospective study demonstrated that the majority of intermediate risk hydronephrosis is transient in nature. Of all the renal units with P2 hydronephrosis, 32% completely resolved within a median follow up time of 1 year and 23% of total renal units improving to P1 hydronephrosis within this time period. In a larger prospective study comparing the predictability of hydronephrosis resolution between the SFU grading system and the UTD classification system, Braga et al. reported a 42% resolution rate of patients with P2 hydronephrosis at 1 year, 69% at 2 years, and 81% at 3 years [15]. However, unlike our study, they included patients with VUR and did not assess rates of improvement in this patient population. Other studies in the literature have reported that higher grades of prenatal hydronephrosis have been associated with longer spontaneous resolution times without specifically looking at the resolution times of P2 hydronephrosis [16—19].

In patients without improvement or resolution of the P2 hydronephrosis, some will require surgical intervention. In our study, 11% of patients required surgery, most commonly a pyeloplasty due to obstruction of the ureteropelvic junction, within a median duration to intervention of 9 months. Those who required surgical intervention were more likely to have either persistent delayed drainage on their diuretic renography (82%) or progression to high grade P3 hydronephrosis. In a study performed by Nelson et al. investigating the clinical outcomes based on UTD risk scores, they showed that surgical intervention was associated with UTD risk, reporting that approximately 6% of patients with P2 hydronephrosis required surgery. This was compared to 1% in patients with P1 hydronephrosis and 43% in patients with P3 hydronephrosis ($p < 0.001$). In their study, one of the most common procedures performed was the pyeloplasty procedure [7]. In a similar study investigating patients with isolated hydronephrosis (without VUR or ureteral dilation), Braga et al. reported that the higher hydronephrosis risk groups were associated with a greater risk of surgery. They report a rate of 31% for both P2 and P3 hydronephrosis combined but did not break this down by subgroup. Additionally, the pyeloplasty procedure was the

most commonly performed surgical intervention in their study [20]. Other studies in the literature also describe an increased risk of surgical intervention in higher hydronephrosis risk groups but do not specifically investigate patients with P2 hydronephrosis [18,21].

In regards to UTI risk, our study found that 10% of patients developed a UTI. Of these patients, 44% were female and 56% were male. One patient in the UTI group did not have a VCUG performed to rule out VUR. Additionally, 19% of the patients not taking antibiotic prophylaxis developed a UTI and 6% were uncircumcised males. The literature varies with regard to the benefit of prophylactic antibiotics in preventing UTIs with moderate hydronephrosis. Braga et al., concluded that children with high grade hydronephrosis may benefit from prophylaxis while there was no benefit for low grade hydronephrosis. They found that children with high-grade hydronephrosis receiving continuous antibiotic prophylaxis had a significantly lower UTI rate versus those not on antibiotic prophylaxis (14.6% vs. 28.9%, $p < 0.01$). The UTI rate for children with low grade hydronephrosis, respectively, showed no difference (2.2% vs 2.8%). The impact of gender, reflux status, and circumcision status were not assessed and no conclusions for moderate grade hydronephrosis were given [12,22]. In an observational study of patients with non-refluxing high grade hydronephrosis not on antibiotic prophylaxis, Song et al. concluded that prophylaxis may benefit these patients. All male patients in this study were uncircumcised [23]. Similarly, Alconcher et al. described a UTI rate of 9% in patients with mild bilateral hydronephrosis and postulated that neither prophylaxis nor lower urinary tract screening is warranted in this population [24]. When specifically looking at how circumcision status affects UTI risk, the literature has shown that being uncircumcised increases the UTI risk, but does not specifically look at risks of those with P2 hydronephrosis [12,25].

Overall, the literature describing the natural course and clinical outcomes of patients diagnosed with P2 hydronephrosis continues to be limited. These findings included in our study may assist practitioners with offering stronger evidence-based guidance and counseling to parents regarding the prognosis of patients with isolated P2 hydronephrosis. The results of our study should be interpreted in light of its limitations. This study is limited by its retrospective nature and single institution experience. Additionally, due to the number of patients lost to follow up and the varied history taking and/or documentation amongst providers, the number of UTI's were likely underreported in this study. Also, the reflux status of approximately 20% of renal units is unknown since a VCUG was not performed in these cases. This includes one patient who developed a UTI who possibly could have had VUR. Lastly, due to the short median follow up time presented, our study does not capture long-term outcomes for this patient population and may under-represent the incidence of UTI's or obstruction after the first year of life.

Conclusions

Intermediate-risk hydronephrosis diagnosed in the pediatric population will either improve, resolve, or remain stable during 1-year follow-up in 87% of renal units. Few renal units required surgical intervention or developed a UTI in the absence of antibiotic prophylaxis. These findings will assist with counseling parents concerning the importance of follow-up imaging and monitoring for UTI.

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