Published in final edited form as:

J Pediatr Urol. 2014 August ; 10(4): 639–644. doi:10.1016/j.jpuro.2014.07.004.

Resolution rate of isolated low-grade hydronephrosis diagnosed within the first year of life

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Abstract

Objective—Diagnosis of low-grade hydronephrosis often occurs prenatally, during evaluation after urinary tract infection (UTI), or imaging for non-urologic reasons within the first year of life. Its significance in terms of resolution, need for antibiotic prophylaxis, or progression to surgery remains uncertain. We hypothesized that isolated low-grade hydronephrosis in this population frequently resolves, UTIs are infrequent, and progression to surgical intervention is minimal.

Patients and methods—Children <12 months old diagnosed hydronephrosis (Society for Fetal Urology [SFU] grade 1 or 2) between January 2004 and December 2009 were identified by ICD9 code. Patients with other urological abnormalities were excluded. Stability of hydronephrosis, UTI (> 100,000 CFU/mL bacterial growth) or need for surgical intervention was noted.

Results—Of 1496 infants with hydronephrosis, 416 (623 renal units) met inclusion criteria. Of 398 renal units with grade 1 hydronephrosis, 385 (96.7%) resolved or remained stable. Only 13 (3.3%) worsened, of which one underwent ureteroneocystostomy. Of 225 renal units with grade 2 hydronephrosis, 222 (98.7%) resolved, improved or remained stable, three (1.3%) worsened, of which one required pyeloplasty. Only 0.7% of patients in the ambulatory setting had a febrile UTI.

Conclusions—Low-grade hydronephrosis diagnosed within the first year of life remains stable or improves in 97.4% of renal units. Given the low rate of recurrent UTI in the ambulatory setting, antibiotic prophylaxis has a limited role in management.

Keywords

Hydronephrosis; Urinary tract infection; Infants

Introduction

Hydronephrosis is the most common anomaly diagnosed on fetal screening ultrasounds with detection in 1–5% of pregnancies [1]. Hydronephrosis may be diagnosed during evaluation after UTI or when imaging is obtained for non-urolological reasons. For high-grade hydronephrosis, the presence of vesicoureteral reflux (VUR), and severe abnormalities, aggressive evaluation and intervention, including antibiotic prophylaxis, is often indicated. However, there is currently no established algorithm in terms of surveillance and use of antibiotic prophylaxis for isolated low-grade (Society for Fetal Urology [SFU] grades 1 and 2) hydronephrosis. Currently, the literature suggests that resolution is common, with resolution rates ranging from 46% to 80% [2,3]. UTIs are also reportedly infrequent with an incidence of 1.3–12% [3–5].

The available literature demonstrates great variability in measured outcomes. In an effort to aid treating physicians, the SFU published a consensus statement in 2010 regarding the management of antenatal hydronephrosis. For mild hydronephrosis, it is recommended to repeat an ultrasound at 1 month of age, given that a single ultrasound within 7 days of life is insufficient to rule out obstruction. These children are recommended to undergo repeat imaging at 1 year, at which point the decision can be made regarding further follow-up. The use of antibiotic prophylaxis is debated given the lack of robust evidence of benefit [6]. In the setting of evaluation for VUR, the AUA guidelines on VUR state that for prenatally identified SFU 1 or 2, screening voiding cystourethrogram is optional [7]. Despite these publications management strategies such as surveillance and antibiotic prophylaxis for UTI prevention continue to vary [8].

Studies evaluating outcomes in patients with hydro-nephrosis do not uniformly describe hydronephrosis and the definition may incorporate either the SFU grading criteria or the anterior–posterior diameter measurement [2,9]. The heterogeneity of diagnosis criteria coupled with variation in surveillance methods has interfered with the development of standard guidelines [8]. In order to more clearly understand the natural history of low-grade hydro-nephrosis, we used strict criteria to review our experience with isolated low-grade hydronephrosis and determined the resolution rate of hydronephrosis within a year of diagnosis and at last ultrasound imaging, surgical intervention rate and UTI rate.

Methods

Patient selection and review

After obtaining Institutional Review Board approval, all infants (<12 months of age) diagnosed with hydronephrosis between January 1, 2004, and December 31, 2009, were identified utilizing ICD-9 codes (591.0, 593.5, 753.19, 753.20, 753.21, 753.22, 753.29). Patients with known VUR, spina bifida, ureterocele, posterior urethral valves, or prior corrective surgery were excluded. Patients with no imaging available for review were also excluded. In the early post-natal period, only renal ultrasounds performed after the seventh day of life were included for review. Patients with at least one follow-up renal ultrasound were included in the analysis. All renal units diagnosed with isolated SFU grades 1 and 2 hydronephrosis were included in the final analysis. Comparison of first post-natal ultrasound

to follow-up ultrasounds was performed to determine stability, resolution, or worsening hydronephrosis. Grading of hydronephrosis was based on initial radiology grading with subsequent verification by one of three pediatric urologists (JW, JR, SR). The date of renal ultrasound acquisition was noted in order to determine time from diagnosis to resolution or the end of follow-up. The interval between initial diagnostic ultrasound to last ultrasound was considered our follow-up interval. Voiding cystourethrograms (VCUGs) were available for review in 65% (270) of the included children.

The number of urinary tract infections in the included cohort was determined by reviewing urine culture microbiological data. A urinary tract infection was defined as bacterial growth 100,000 CFU/mL. If available, symptoms associated with UTI were noted. Nosocomial infections were considered UTIs which occurred while the patient was hospitalized in the neonatal intensive care unit (NICU). Ambulatory UTI occurred in those patients outside of the hospital setting diagnosed either in our system or reported by the primary physician or parent during a clinic visit.

Statistical analysis

Statistical analysis was performed using STATA 11.2 (College Station, TX, USA) and GraphPad Prism 4.00 for Windows (San Diego, CA, USA). Chi-square analysis was performed to compare resolution rates between groups. Descriptive statistics were used for all other extracted data.

Results

Patient identification and demographics

There were 1496 infants with a diagnosis of hydronephrosis. Six hundred forty-one patients were excluded due to VUR (528), spina bifida (65), ureterocele (31), and posterior urethral valves (17). Of the remaining 855 infants, 193 were excluded due to absence of hydronephrosis on post-natal ultrasound, 167 due to lack of follow-up imaging, 76 due to moderate or high-grade (SFU grades 3 and 4) hydronephrosis, and three due to prior corrective surgery for hydronephrosis. The three patients who had undergone prior corrective surgery were diagnosed with UPJ (ureteropelvic junction) obstruction and underwent pyeloplasty prior to presentation to our clinic. The initial degree of their hydronephrosis was not available in our records. The remaining 416 (124 females and 292 males) infants were analyzed.

Pre-natal hydronephrosis was present in 171 patients. Post-natal renal ultrasound confirming persistent hydro-nephrosis was done at a mean age of 1.1 months. The mean follow-up for this group was 19.4 months. For the 245 patients with post-natal diagnosis of hydronephrosis, the mean age at diagnosis was 1.2 months and mean follow-up was 11.5 months. The rationale for ultrasonography in these patients was variable, including congenital abnormalities in 115 (46.9%), UTI in 36 (14.7%), acute kidney insufficiency in 27 (11%), unknown indication in 25 (10.2%), hypertension in 19 (7.8%), intra-abdominal process in 13 (5.3%), and hematuria in 10 (4.1%). Mean follow-up for the entire cohort was 14.6 months (median 8 months). Unilateral hydronephrosis was present in 164 patients and

bilateral hydronephrosis in 252 patients. Of the patients with bilateral hydronephrosis, 45 had SFU grade 3 or 4 in one renal unit. Renal units with high-grade hydronephrosis were excluded, leaving a total of 623 renal units with SFU grades 1 and 2 hydronephrosis for analysis (Table 1).

Longitudinal outcome of renal units

The 623 renal units were evaluated for worsening, stable, improved, or resolved hydronephrosis on follow-up renal ultrasound. Of 398 renal units with SFU grade 1 hydronephrosis, 266 had complete resolution (66.7%), 119 remained stable (30%), and 13 developed higher-grade hydronephrosis (3.3%). Of these 13 renal units, eight had SFU grade 2, four SFU grade 3, and one SFU grade 4 hydronephrosis at the end of follow-up. Of 225 renal units with SFU grade 2 hydronephrosis, 107 resolved (47.6%), 46 remained stable (20.4%), 69 improved to SFU grade 1 (30.7%), and three worsened (1.3%). Of these three renal units, two had SFU grade 3 and one SFU grade 4 hydronephrosis. Overall resolution rates for SFU grades 1 and 2 hydronephrosis was 59.9% with improvement or stability in 37.6%, and worsening in 2.6%. Of all renal units, two ultimately required surgical intervention (Table 2). A change in degree of hydronephrosis was noted at 1 month and 10 months after the first ultrasound in the units that required surgical intervention. One renal unit progressed from SFU grade 2 hydronephrosis to SFU grade 4 requiring pyelo-plasty. A MAG3 renal scan was obtained once worsening hydronephrosis was noted and a differential function of 55%, and 45% associated with delayed drainage was reported. The second renal unit progressed from SFU grade 1 to SFU grade 4 with ureterectasis. A MAG3 renal scan demonstrated a differential function of 27% and 73%. This patient ultimately required a ureteroneocystostomy. Of the 16 units that had worsened hydronephrosis, changes were noted within the first 12 months (median 2.5 months, range 1–12 months). Evaluation of renal ultrasounds within the first 12 months after diagnosis demonstrated an overall resolution rate of 53.8%, improvement in 12.6%, stability in 28.2%, worsening from SFU grade 1 to grade 2 in 3%, and worsening above SFU grade 2 in 2.4%. Overall, 94.6% of renal units with low-grade hydronephrosis, resolved, stabilized, or improved within the first year of follow-up. These rates are similar to the overall rates of resolution, improvement, stability, and worsening at the end of follow-up (Table 2).

Comparison of renal units diagnosed with hydronephrosis before and after birth failed to demonstrate a difference in the complete resolution rate (prenatal 58% vs. post-natal 62%, $p = 0.62$; Table 2). Similarly, no significant differences were noted on the rate of improvement, stability, or worsening hydronephrosis between the groups. Interestingly, the median time to resolution of low-grade hydronephrosis was 10 months for the renal units diagnosed prenatally and 3 months for the units diagnosed after birth ($p = 0.01$; Fig. 1).

Of the patients included for analysis, VUR was ruled out by a VCUG in 65% (270/416) of patients. The remaining patients did not undergo VCUG. Comparison of renal unit outcomes between these two groups demonstrated no significant differences. In the group of renal units evaluated by VCUG, resolution occurred in 58%, stability in 26.1%, improvement in 13.1%, and worsening in 2.8%. In the group of renal units not evaluated by VCUG,

resolution occurred in 63.4%, stability in 27.2%, improvement in 7.6%, and worsening in 1.8%.

Urinary tract infections

Urinary tract infections after diagnosis of hydronephrosis were defined as urine culture growth of $\geq 100,000$ CFU/mL. Owing to limited documentation for hospitalized patients, information concerning symptoms and indications for urine collection was limited. Collection method of these specimens was not consistently provided in the chart. In our cohort, prophylactic antibiotics were started by a primary provider in 36/416 patients (8.6%). These were discontinued in all patients at a median time of 3 months. There were a total of 43 UTIs in 37 infants (8.9%). Of 37 infants, 24 were males (circumcised $n = 8$) and 13 females. A total of 28 UTIs were nosocomial and 15 occurred in the ambulatory setting. Enteric pathogens were identified in 29 of 43 infections (67.5%), gram positive in nine (20.9%), and yeast in five (11.6%). Of the UTIs occurring in the ambulatory setting, four were febrile UTIs ($>101.5^{\circ}\text{F}$ (38.6°C)) and all were due to enteric pathogens (Table 3). Thus, only 0.7% of patients with low-grade hydronephrosis were noted to have a febrile UTI in the ambulatory setting.

Discussion

The recognition of urologic anomalies in the perinatal period has increased due to routine prenatal sonography and the accessibility of ultrasound after birth. Anomalies of the urogenital tract are the most common diagnoses made on prenatal ultrasound. Prenatal hydronephrosis has been reported to occur in 1–5% of pregnancies, and 12–89% of these patients have underlying urologic pathologies [1,10]. The rationale supporting early diagnosis is the vital role that management of underlying conditions has on renal preservation. Unfortunately, early identification of anomalies is also accompanied by parental anxiety and concern. Understanding the natural history of hydronephrosis is a critical step in not only understanding the pathologies requiring treatment but also in counseling parents.

To our knowledge, this is the largest cohort of renal units with isolated SFU grades 1 and 2 hydronephrosis reported in the literature as it pertains to resolution rates, UTIs, and progression to surgical intervention. Of 623 renal units with isolated low-grade hydronephrosis (SFU grade 1 or 2), nearly all renal units resolved, improved, or remained stable, suggesting that isolated low-grade hydronephrosis has a very low risk for progression and loss of the renal unit. Only 16 of 623 (2.6%) of the renal units worsened, requiring prolonged follow-up and only two of 623 (0.3%) ultimately required surgery. These data are commensurate with other studies. Tombesi and Alconcher [11] evaluated infants diagnosed prenatally and demonstrated a resolution rate of 73% and progression of 1% in a cohort of 277 renal units with mild hydronephrosis. In a cohort of 144 infants with mild hydronephrosis on first post-natal ultrasound, Barbosa et al. [2] reported resolution of mild hydronephrosis in 46.5% of children and stability in 47.2% and progression to surgical intervention in 6.3%. However, their surgical cohort included patients requiring intervention for VUR and neurogenic bladder. Only three of 144 patients (2%) had UPJ obstruction

requiring pyeloplasty. Yang et al. [3] demonstrated that SFU grade 1 and SFU grade 2 hydronephrosis resolved in 67.8% of children and progression to surgery occurred in 4.8% of patients. In this study, the mean time to resolution was 13.4 months (range 2 weeks–5.6 years).

The reported intervals to resolution of low grades of hydronephrosis have been variable largely due to differences in follow-up regimens and criteria. Alconcher et al. [12] reported that 80% of units resolved within the first 12 months of life. Others have reported intervals to resolution of 13.4 months–17 months [2,3]. In our study, resolution of low-grade hydronephrosis occurred in 373 of 623 (59.8%) renal units at a median of 5 months (range 0 months–91 months; pre-natal median 10 months, post-natal median 3 months), and at maximum follow-up of 93 months 607 of 623 (97.4%) renal units improved or remained stable. When comparing those units diagnosed prenatally to those diagnosed after birth, resolution rate was higher in the post-natal diagnosis group (pre-natal 58%, post-natal 62%), but this was not statistically significant. Overall, the rates of stability, improvement or resolution were essentially equal between the groups.

Progression of hydronephrosis and need for surgical intervention is a constant concern for the managing physician. In the current cohort, 16 out of 623 (2.6%) of renal units had progression of hydronephrosis. However, only two of 623 (0.3%) renal units required surgical intervention. Most importantly all units progressed within the first 12 months after initial diagnosis. Our findings suggest that surveillance within the first year after diagnosis is likely to capture renal units at risk for deterioration. However, late progression of hydronephrosis has been reported to occur in 1–5% of patients. Since the current study does not have a long enough follow-up interval to report outcomes years after diagnosis, the appropriate long-term follow-up of improving or stable renal units with isolated low grade hydronephrosis remains debatable. Data chronicling the behavior of isolated hydronephrosis in a fixed follow-up protocol to assess for late progression would be appropriately answered with prospective long-term studies.

Reported UTI rates in patients with low-grade hydro-nephrosis are variable ranging from 1.3% to 12% [10,11,13,14]. UTIs in our cohort were similarly uncommon in patients diagnosed with isolated low-grade hydro-nephrosis. We report a nosocomial UTI rate of 6.2% and an ambulatory UTI rate of 2.6% (0.7% febrile UTI). In the current study, 8.9% of patients with low-grade hydronephrosis followed conservatively developed a UTI. VCUG was performed in 81% of those patients (30/37) and in all cases, VCUG was negative. While 19% in this subgroup did not undergo VCUG, these patients did well clinically, requiring no imaging other than follow-up ultrasounds. Our findings suggest a limited role of prophylactic antibiotics in patients with isolated low-grade hydronephrosis [15].

Our study is limited by its retrospective nature and all problems associated with this study type. Identification of patients based on ICD-9 code relies heavily on accurate coding and may have missed patients with hydronephrosis. In addition, given that our mean follow-up was 14.6 months, the overall long-term outcome of patients remains unknown and thus our data, including resolution/improvement/worsening hydronephrosis rates, must be interpreted within the context of this short mean follow-up period. The absence of a standardized re-

imaging protocol to access resolution in frequent intervals limits our ability to broadly apply our time to resolution to the general population. Additionally, while universally utilized, the SFU grading system is subjective and there can be variability in grading among physicians, which could have influenced our reported outcomes. Unfortunately, our retrospective review did not reveal accessibility to prenatal ultrasounds or official reports describing radiographic APD (Anterior–Posterior Diameter) measurements thus limiting our ability to report this information. Additionally, 35% of our cohort did not undergo evaluation with a VCUG, so VUR may have been missed in these children. However, given the low rate of febrile UTIs in this study, the significance of undiagnosed VUR in this cohort is questioned.

Lastly, the lack of accurate, detailed history regarding the indications for some of the urine cultures obtained and the method used for collection is pervasive and limits our ability to have an accurate representation of UTI rates in our cohort. We attempted to minimize underreporting by capturing all urine cultures with >100,000 CFU/mL of bacterial growth. Our information database accesses all outpatient, inpatient, and affiliated clinic results allowing us to capture a significant number of positive urine samples. This approach may lead to over reporting of UTI rates. Alternatively, in patients who do not seek routine care in one of our system's affiliated clinics, true urinary tract infections may be missed unless properly documented by a physician within the system. Thus, the possibility of underreporting of UTIs is also present in our cohort.

These limitations support the need for prospective multi-centered studies that can address these issues and provide more accurate data. However, in spite of these limitations, this study does support the need for follow-up with more aggressive and long-term evaluation in units that worsen early during evaluation.

Conclusion

Low-grade hydronephrosis diagnosed within the first year of life remained stable or improved in 97.4% of renal units. For isolated low-grade hydronephrosis in children <12 months of age, observation for 12 months after diagnosis is necessary, unless hydronephrosis completely resolves. More aggressive, long-term follow-up is necessary in those units with worsening hydronephrosis. Given the low rate of UTI in this and other studies, antibiotic prophylaxis has a limited role in management. Long-term, prospective studies are necessary to validate these findings and allow development of refined guidelines for infants diagnosed prenatally or incidentally with low-grade hydronephrosis.

Acknowledgments

Funding

None.

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Figure 1.

Time to resolution in complete resolved renal units. Comparison of the resolution curves between prenatally diagnosed and post-natally diagnosed hydronephrosis demonstrate a statistically significant difference in time to resolution. Median time to resolution of prenatally diagnosed renal units was 10 months versus 3 months in post-natally diagnosed units. Resolution rates were similar at the end of follow-up.

Table 1

Patient characteristics.

	<i>n</i>
Patients (total)	416
Male	292 (70%)
Female	124 (30%)
Age at Diagnosis (months)	1.2
Mean Follow-up (months)	14.6
Prenatal Hydronephrosis	
Yes	171
No	245
Unilateral Hydronephrosis	164
Bilateral Hydronephrosis	252
Total Renal Units	668
Grade 1 and 2	623
^a Grade 3 and 4	45

^aThese are excluded from analysis.

Table 2

Renal units and longitudinal outcome by SFU grade.

Overall		<i>n</i>	%
Grade 1 and 2		623	
	Resolved	373	59.9%
	Stable	165	26.5%
	Improved	69	11.1%
	Worse	16	2.6%
Progressed to Surgery		2	0.3%
<i>Prenatal hydronephrosis</i>			
Grade 1 and 2			
	Resolved	145	57.8%
	Stable	67	26.7%
	Improved	33	13.1%
	Worse	6	2.4%
<i>Postnatal hydronephrosis</i>			
Grade 1 and 2			
	Resolved	228	61.3%
	Stable	98	26.3%
	Improved	36	9.7%
	Worse	10	2.7%
<i>Median time to resolution</i>			
Prenatal		10 months	
Postnatal		3 months	

Table 3

Urinary tract infections in patients after diagnosis with SFU 1 or 2 hydronephrosis.

Occurrence (UTIs)	<i>n</i> (patients)	% (patients)	
Urinary tract infections	43	37	8.9%
Nosocomial	28	26	6.2%
Ambulatory	15	11	2.6%
Febrile (>101.5 °F)	4	3	0.7%