

Probability of urinary tract infection in infants with ureteropelvic junction obstruction: is antibacterial prophylaxis really needed?

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Abstract In infants with ureteropelvic junction obstruction (UPJO), the risk of urinary tract infection (UTI) is unknown, and there is a lack of prospective studies showing definitive evidence regarding the benefits and necessity of antibiotic prophylaxis. The aim of this study was to assess the risk of UTI in infants with UPJO and to determine whether the risk varies according to the degree of hydronephrosis. Infants with hydronephrosis detected prenatally or within the postnatal 28th day and who had no previous history of UTI were followed prospectively without antibacterial prophylaxis. Imaging studies were performed according to our Pediatric Uro-Nephrology Study Group protocol. Dimercaptosuccinate (DMSA) scintigraphy was performed in all infants at the end of 1 year of follow-up. Eighty-four infants (56 boys, 28 girls) were included in the study. The distribution of patients in each hydronephrosis grading group was incidentally similar. Within a median follow-up period of 18 (12–24) months, none of the patients had UTI. Furthermore, no pyelonephritic scar was found on DMSA scans in any patient. We conclude that prophylactic antibiotic usage is not indicated in infants with UPJO, regardless of the severity of hydronephrosis, as the risk of UTI is minimal in this population.

Keywords Ureteropelvic junction obstruction · Prenatal hydronephrosis · Prophylaxis · Urinary tract infection · DMSA

Introduction

The wide usage of obstetric ultrasonography (US) since the 1980s has led to prenatal recognition of many congenital malformations. Urinary tract abnormalities constitute 20–30% of these and are mainly upper urinary system dilatations, so-called prenatal hydronephrosis [1–3]. Approximately half of the infants with prenatal hydronephrosis have ureteropelvic junction obstruction (UPJO) [4, 5]. It was suggested by some authors that infants with UPJO had a risk of urinary tract infections (UTI). The incidence of UTI was reported to be 0–15% in retrospective studies [6, 7]. There is a lack of prospective studies showing definitive evidence regarding the benefits and necessity of antibiotic prophylaxis in these patients [7, 8]. Some clinicians prefer to use antibacterial prophylaxis in all patients with hydronephrosis, some only in cases with severe hydronephrosis, yet others in none; besides, the duration of prophylaxis varies between studies [4, 9–12]. In this study, we aimed to determine the risk of UTI in infants with UPJO during the postnatal follow-up and to determine whether the risk varies according to the degree of hydronephrosis.

Patients and methods

This prospective study was performed between January 2007 and June 2009. Infants with unilateral or bilateral hydronephrosis detected prenatally or within 28 days of birth

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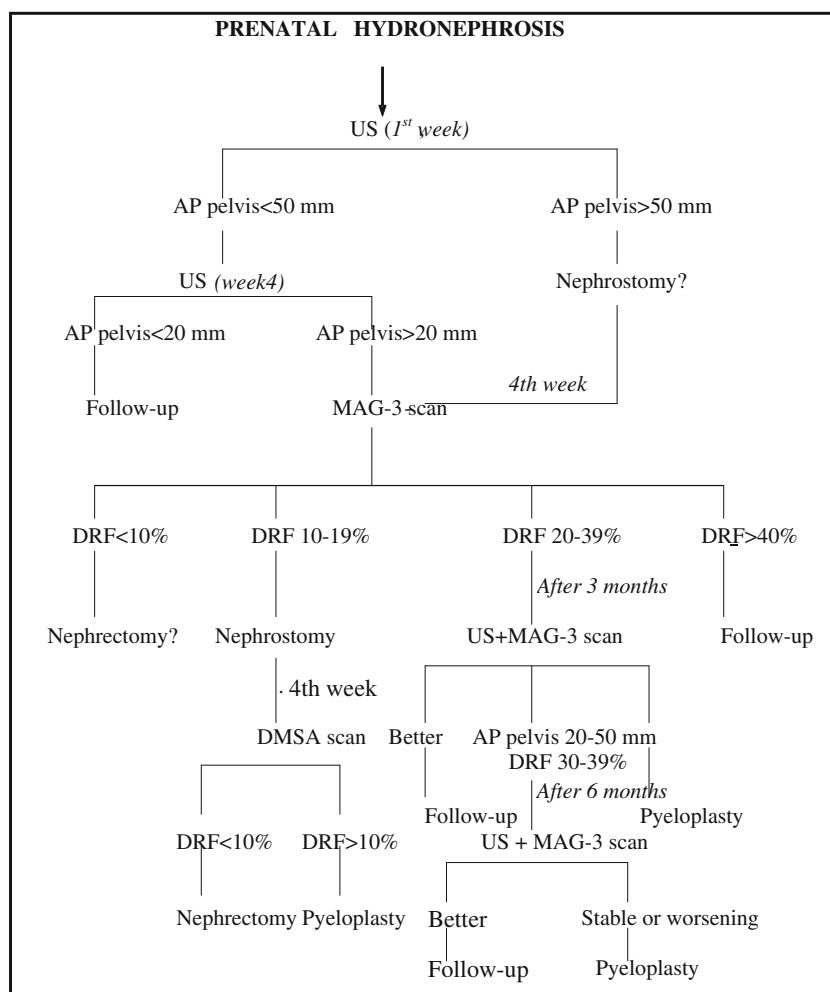
were consecutively included in the study. Hydronephrosis was defined as the dilatation of the anteroposterior pelvic diameter of the renal pelvis >6 mm before 20 weeks of gestation, >8 mm between 20–30 weeks, and >10 mm after 30 weeks. All infants were required to have a history or symptoms of UTI before entering the study. Patients who had no hydronephrosis on renal US in the first month of follow-up or who were diagnosed afterward as having posterior urethral valve, vesicoureteral reflux (VUR), duplex urinary tract, renal hypoplasia, or complex urinary anomalies were excluded. Infants who were lost to follow-up or who failed to complete the 1-year follow-up were also excluded.

Mothers were informed verbally and in written form regarding UTI symptoms. They were also informed regarding infant nutrition, genital hygiene, and preventive measures (avoiding constipation and diaper dermatitis, maintaining proper hydration) for UTI. The study was explained by a physician uninvolved in the study. Infants whose parents provided consent were included. All patients

were followed monthly by a single investigator (AI) during the entire study period without prophylaxis. At each visit, the infants were investigated for signs and symptoms of UTI; urine samples were taken for analysis using a urine bag. In case of significant pyuria [≥ 5 leukocytes/high-power field (HPF)] and/or bacteriuria (≥ 7 bacteria/HPF) on urine microscopy or in febrile infants, urinary catheterization was performed to obtain samples for urine culture. UTI was defined by the presence of $\geq 10^4$ colony-forming units (CFU)/ml bacteria in urine samples collected by catheterization. The radiologic methods were performed according to the protocol generated by our Pediatric Uro-Nephrology Study Group (Fig. 1).

Renal–pelvic US scans were performed by one of two radiologists who were members of the Pediatric Uro-Nephrology Study Group. Grading of hydronephrosis was made according to the Society for Fetal Urology (SFU) classification system [13], with patients being divided into four groups. At the end of 1 year of follow-up, a dimercaptosuccinate (DMSA) scan was performed to

Fig. 1 Protocol for prenatal hydronephrosis generated by the Akdeniz University Pediatric Uro-Nephrology Study Group



AP: Antero-posterior, US: Ultrasonography, DRF: Differential renal function

detect any renal scarring caused by a subclinical UTI. Technetium-99m-mercaptoacetyltriglycine ($^{99m}\text{Tc-MAG-3}$) and $^{99m}\text{Tc-DMSA}$ scans were evaluated by one of the two nuclear medicine specialists of the study group. In case of urinary catheterization for these investigations, a single-dose antibiotic (second-generation cephalosporin, per oral route) was given before the procedure. Surgical intervention was indicated in infants with grade IV hydronephrosis with a differential renal function $<40\%$ on a MAG-3 scan, with persistent renal parenchymal thinning, with progressive increasing of kidney length on US, or no response to diuretics on scintigraphy. The recovery from hydronephrosis was defined as a minimum of two subsequent US scans without hydronephrosis.

Infants with at least 1 year of follow-up were reclassified according to hydronephrosis grading on their first US. For statistical analysis, Student's t test and univariate variance analysis were used. Confidence interval (CI) for the proportion was calculated by Confidence Interval Calculator (v4, November 2002, www.pedro.org.au/wp-content/uploads/Cicalculator.xls) using the Wilson score method without continuity correction at 0.95 confidence level [14].

Results

At the beginning of the study, 134 infants with prenatal hydronephrosis were screened. Five were lost to follow-up because of migration to other regions of the country. Forty-five were excluded due to diagnoses other than UPJO (18 VUR), 13 duplex urinary tract, eight multicystic dysplastic kidney, three vesicoureteral junction obstruction, and three posterior urethral valve). The remaining 84 infants, 56 boys (66%) and 28 girls, were included in the study. The distribution of patients grouped according to hydronephrosis grading were as follows: 23 (27.4%), 23 (27.4%), 20 (23.8%), and 18 (21.4%), for grades I–II–III–IV, respectively (Table 1). Sixty-eight (80%) infants had unilateral hydronephrosis, 46 of whom (67%) had left UPJO. The median follow-up period was 18 (12–24) months. Follow-up periods were similar between groups (group I: 15 months; group II: 18 months; groups III and IV: 24 months; $p=0.079$). The birthweight of infants ranged between 2,750 and 3,980 g (mean 3,290 g for boys,

3,220 g for girls) and weight percentiles at the end of 1 year were between 25 and 90.

Natural course of infants with unilateral hydronephrosis ($n = 68$)

Fifteen of 19 (79%) infants with grade I unilateral hydronephrosis completely recovered, whereas there was no change in the remaining four. Ten of 16 (63%) infants with grade II unilateral hydronephrosis recovered, one regressed to grade I, and five were unchanged. Only three of 16 (19%) infants with grade III unilateral hydronephrosis recovered; five regressed, seven showed no change, and one progressed to grade IV. Of 17 infants with grade IV unilateral hydronephrosis, none recovered, six regressed (five to grade III and one to grade II), five showed no change, and six required pyeloplasty (Table 2).

Natural course of infants with bilateral hydronephrosis ($n = 16$)

Two of four (50%) infants with grade I bilateral hydronephrosis had complete recovery; the remaining two had no change. Of seven infants with grade II, two (29%) recovered, another two regressed, and three showed no change. All four infants with grade III bilateral hydronephrosis regressed (one to grade I and three to grade II). Only one patient had grade IV bilateral hydronephrosis: the left side recovered at the 18th month and the right side required pyeloplasty at the 24th month (Table 1). No UTI was detected in any patient during the entire study period (95% CI 0–4.37), whereas a female infant with grade I hydronephrosis presented with fever to a local hospital at 7 months of age and had 50,000 IU/ml *Escherichia coli* on urine culture collected by urine bag and with normal serum leukocyte count and C-reactive protein level. Diagnosis of UTI was not made in this infant, as urine sample was not collected by urinary catheterization and her serum leukocyte count and C-reactive protein levels were not increased.

Except for three patients who underwent pyeloplasty in the early period (first 3 months), DMSA scintigraphy was performed in 81 infants at the 12th month and was normal in all patients [no photopenic areas; differential renal

Table 1 Patient groups and follow-up periods according to hydronephrosis grading

Groups	No.	Percent	Male/female	Follow-up period (months) (mean)
Grade I	23	27.4	13/10	12–24 (17.2)
Grade II	23	27.4	18/5	12–24 (18.5)
Grade III	20	23.8	13/7	12–24 (21.6)
Grade IV	18	21.4	12/6	12–24 (17.7)
Total	84	100	56/28	12–24 (18.7)

Table 2 Patient prognosis according to hydronephrosis grading

Groups	Surgery	Conservative follow-up				
		Completely recovered	Partially recovered	No change	Progressed	Total
Grade I	-	15	-	4	-	23
		2		2		
Grade II	-	10	1	5	-	23
		2	2	3		
Grade III	-	3	5	7	1	20
			4			
Grade IV	6	-	6	5		18
	1	-	-			
Total	7	32	18	26	1	84

The numbers at the top and bottom of the column indicate the number of unilateral and bilateral hydronephrosis cases, respectively.

functions (DRF) 46–54%]. Voiding cystourethrography (VCUG) was introduced only in patients with severe bilateral hydronephrosis or in those who needed surgery; none of the 17 children that underwent VCUG had VUR.

Discussion

We prospectively evaluated 84 infants with UPJO without antibiotic prophylaxis; no UTI was observed in any of the patients, including those who needed surgery. Antibiotic prophylaxis may be indicated in patients with VUR, recurrent UTI, symptomatic bladder dysfunction, and obstructive uropathy and in those with febrile UTI before 1 year of age [15]. However, in recent reports, the efficacy of antibiotic prophylaxis in patients with VUR has been unclear. Williams et al. [9] reported in their meta-analysis that data are insufficient to form an opinion regarding the effectiveness of low-dose, long-term antibiotics for preventing symptomatic UTI in children. The decision of whether to introduce antibiotic prophylaxis to prevent UTI in patients with prenatal hydronephrosis is controversial. Some authors report that children with physiological dilations or UPJO without VUR are at risk for UTIs, the incidence of which was reported to be 0–15% [6, 7]. However, there has been no consensus regarding administering low-dose, long-term antibiotics in these patients. Conflicting results were reported in the relevant studies [7, 8]. In clinical practice, some clinicians prefer to introduce antibiotics in all patients with hydronephrosis, some only to patients with high-grade hydronephrosis, and others to none of the patients. The duration of prophylaxis also varies between studies; some authors prefer a period of 1 year and others for as long as the hydronephrosis persists [4, 9–12]. The prolonged usage of these antibiotics, usually cotrimoxazole or nitrofurantoin, may lead to both adverse effects and to the development of resistant bacteria. The obligation to undertake daily drug administration may have a negative psychological effect on parents, which should also be considered [16].

Madden et al. [7] found in their retrospective study of 53 infants with UPJO that the frequency of UTI was similar between infants who did and did not receive antibiotic prophylaxis (14% vs 19%, respectively). However, their study had some limitations with respect to its retrospective nature, heterogeneity of patient groups, limited number of patients, and uncertainty regarding indications for antibiotic usage. Roth et al. [8] reported in their study of 92 children (56 with UPJO, 36 with obstructive megaureter) followed without prophylaxis that the frequency of UTI was 4.3%, which was similar to children with intact urinary system, and concluded that antibiotic prophylaxis is unnecessary in this population. Mami et al. [16] reported in their prospective study with 223 infants that UTI risk was similar between patients with mild to moderate hydronephrosis and those without hydronephrosis (3.6% vs 2.5%). Lidelfelt et al. [17] reported that only one of 34 children with mild hydronephrosis experienced UTI without prophylaxis, whereas none of six patients with prophylaxis had UTI in a 2-year follow-up period; the authors concluded that children with mild hydronephrosis do not need antibiotic prophylaxis. On the other hand, Yavaşcan et al. [18] reported that the UTI frequency was higher in 175 patients with urinary tract malformations compared with those without abnormality (1.32 ± 1.66 vs 0.27 ± 0.67 episode/year). Song et al. [19] reported that 30% of 75 infants with grades III and IV hydronephrosis secondary to UPJO developed UTI when followed without antibiotic prophylaxis; the authors concluded that children with severe hydronephrosis should receive antibiotic prophylaxis. Lee et al. [20] declared that antibiotic prophylaxis might be beneficial in obstructive hydronephrosis based on an observation that 39% of their patients with obstructive uropathy had UTI.

In our study, UTI was not detected in any patient, including those with severe hydronephrosis. Moreover, DMSA scans performed for detecting subclinical or unrecognized pyelonephritis were normal in all patients. Only one female infant with grade I hydronephrosis was

diagnosed with unproven UTI at the seventh month of follow-up at another center. The inadequate collection method of the urine sample in this patient may have led to the positive urine culture result; her DMSA scan was also normal. The superiority of this study to similar ones in the literature is its prospective nature, rationality of UTI definition, equal distribution of patients with mild and severe hydronephrosis, and the advantage of having a single responsible investigator during the entire study period. Surprisingly, none of the 84 patients developed UTI, which is a new finding in the literature. Similar results were also reported by Mami et al. [16]. Nutritional status, hydration, and genital hygiene of infants in our study were also followed closely by educating the parents on these issues at each visit.

We conclude that prophylactic antibiotic usage is not indicated in infants with UPJO, regardless of the severity of hydronephrosis, as the risk of UTI is minimal in this population. Parents of such infants should be reminded about the early warning symptoms and risk of UTI, with routine review of signs and symptoms of UTI, which would be an important approach to prevent late complications of UTI, especially in developing countries

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