Frequency of urinary tract infection in children with antenatal diagnosis of urinary tract dilatation

Marco Pennesi,[1] Stefano Amoroso,[2] Giulia Bassanese,[3] Stefano Pintaldi,[2] Giulia Giacomini,[2] Egidio Barbi[1,2]

[1]Department of Pediatrics, Institute for Maternal and Child Health-IRCCS "Burlo Garofolo", Trieste, Italy
[2]Department of Medicine, Surgery and Health Sciences, University of Trieste, Trieste, Italy
[3]Center for Pediatrics and Adolescent Medicine, University of Heidelberg, Heidelberg, Germany

Correspondence to
Dr Stefano Amoroso, Universita degli Studi di Trieste, Trieste 34127, Italy; stefanoamoroso1234@gmail.com

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ABSTRACT

Background Neonates with congenital urinary tract dilatation (UTD) may have an increased risk of urinary tract infections (UTI). At present, the management of these patients is controversial and the utility of continuous antibiotic prophylaxis (CAP) remains uncertain as the literature presents contradicting evidence. The aim of this observational study was to assess UTI occurrence in children with prenatal diagnosis of urinary collecting system dilatation without antibiotic prophylaxis.

Methods Between June 2012 and August 2016, we evaluated the incidence of UTI and the clinical and ultrasonography evolution in 407 children with a prenatally diagnosed UTD. All subjects underwent two prenatal ultrasounds scans (USs) at 20 weeks and 30 weeks of gestation and within 1 month of birth. Patients with a confirmed diagnosis of UTD underwent US follow-up at 6, 12 and 24 months of life. According to the UTD classification system stratify risk, after birth UTD were classified into three groups: UTD-P1 (low risk group), UTD-P2 (intermediate risk group), and UTD-P3 (high risk group). Voiding cystourethrogram was performed in all patients who presented a UTI and in those with UTD-P3. No patient underwent CAP.

Results Postnatal US confirmed UTD in 278 out of 428 patients with the following rates: UTD-P1 (126), UTD-P2 (95) and UTD-P3 (57). During postnatal follow-up, 6.83% patients presented a UTI (19 out of 278). Eleven out of 19 had vesicoureteral reflux (VUR), and other four were diagnosed with obstructive uropathy and underwent surgical correction. Five patients presented a UTI reinfection.

Conclusion The occurrence of UTI in patients with urinary collecting system dilatation was low. The recent literature reports an increased selection of multirestistant germs in patients with VUR exposed to CAP. This study constitutes a strong hint that routine continuous antibiotic prophylaxis could be avoided in patients with UTD.

What is already known on this topic?

- Several studies recommended long-term antibiotic prophylaxis to prevent urinary tract infection in newborns with antenatal ultrasound detection of urinary tract dilatation. The efficacy of continuous antibiotic prophylaxis has however been challenged: the issue is if antibiotics are effective in preventing renal damages.

What this study adds?

- This study showed a low occurrence of urinary tract infection in patients with urinary collecting system dilatation that not underwent continuous antibiotic prophylaxis. Antimicrobial prophylaxis could be an unnecessary routine practice in these children.

INTRODUCTION

Urinary tract dilatation (UTD) detected on antenatal ultrasound examination is one of the most common congenital urological anomalies found during prenatal ultrasonography (US) and occurs in 1%–5% of all pregnancies.[1–4] In the great part of cases, the prenatal finding of UTD is mostly transient and carries limited clinical significance. In some patients, it denotes the presence of an obstructive condition or of a vesicoureteral reflux (VUR) that may lead to an increased risk of UTI and renal damage.[1 5] The aetiology of UTD is poorly predicted by prenatal US and is usually diagnosed in the postnatal setting with additional imaging. Prenatal UTD is mainly caused by a transient or chronic obstruction localised at the ureteropelvic junction, less frequently at the ureterovesical junction or it may be due to a posterior urethral valve in males. In other cases, the cause of a prenatal UTD may be due to the presence of VUR.

Braga *et al*[6] suggested the benefit of selective use of prophylactic antibiotics in children with prenatal detection of UTD with an intermediate or high risk of complications such as UTI and renal dysfunctions. The multidisciplinary consensus on the classification of prenatal and postnatal UTD states that the use of continuous antibiotic prophylaxis (CAP) should be left to the discretion of the clinician.[1] This reflects in the wide heterogeneity of clinical behaviour and in the fact that over the last few years the efficacy of CAP has been challenged.[7–11] The main issues are whether antibiotics are effective in preventing recurrent acute pyelonephritis and if they can modify the natural history of the disease by limiting renal damage and chronic kidney failure.

The aim of this observational study was to assess the occurrence of UTI in a well-defined cohort of children with a prenatal diagnosis of UTD confirmed at a postnatal US in which no CAP was carried out.

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PATIENTS AND METHODS

Study setting

This study was conducted at the Institute of Maternal and Children Health – *Burlo Garofolo*, Trieste, Italy, in collaboration between the Paediatric Renal Department and the Prenatal Diagnosis Clinic. All parents gave their informed written consent to the anonymous use of data, according to the policy of the Research Institute.

All children with a UTD detected by prenatal US made from June 2012 to August 2016 were enrolled and underwent US follow-up until 24 months of age. None of the cohort's patients started a CAP.

Inclusion criteria and study design

All the fetuses with detection of UTD at 20 weeks and 30 weeks of gestation independently from maternal age, ethnic origin or social status were included. Transabdominal ultrasounds were performed with 4–8 MHz 3-D arrays using a VOLUSON TM E8 Expert ultrasound system. The threshold values for the diagnosis of UTD on sonographic imaging were stratified based on gestational age at presentation detection. To avoid bias, all US examination and UTD classification were made by the same trained gynaecologist, supported by the same paediatric nephrologist (MP). All children with antenatal detection of UTD underwent the first postnatal US evaluation from 2 days to 4 weeks after birth. The postnatal US was made by a well-trained paediatric radiologist supported by the same paediatric nephrologist (MP). Patients without confirmed UTD at the first postnatal US and/or evidence of posterior urethral valve, neurogenic bladder or ureterocele were excluded, while patients with confirmed postnatal UTD continued US follow-up at 6, 12 and 24 months of life. Once a UTD diagnosis had been established, patients were classified into three groups by using the stratification method of risk, in accordance with the multidisciplinary consensus on the classification of prenatal and postnatal tract dilatation (UTD classification system)[1] (table 1).

All patients with severe hydronephrosis (UTD-P3), underwent voiding cystourethrogram (VCUG) at 1 month of life, showing a VUR in six patients. All children who presented a febrile UTI during the follow-up period underwent VCUG.

All patients with UTD-P2 or UTD-P3 underwent to MAG3 renography to evaluate the differential renal function (DRF) and the urine excretion capabilities. The split of the renal function (DRF <40%) and/or a half-time greater than 20 min were considered suggestive of the presence of a urinary collecting system obstruction and thus prompted a surgical evaluation. No data on dimercaptosuccinic acid (DMSA) are reported since the number of infection were low and DMSA studies are not routinely performed unless specific risk factors are present. Moreover, DMSA investigation of the infections was not an objective of the study.

According to UTI Italian guidelines,[11] acute pyelonephritis was defined as fever of unknown origin (rectal temperature ≥38.5°C), together with evidence at optical microscopy of bacteriuria with the presence of abnormal numbers of leukocytes in the urine specimen. In addition, the urine culture had to be positive with colony forming units/mL greater than 100 000. The bacteria type should be the same in two different urine samples. Urine specimens were collected by midstream or bladder catheterisation in the case of septic patients (midstream 83% of cases and bladder catheterisation in 17% of cases). No male child in this series had a history or eventually underwent through a circumcision procedure.

RESULTS

From June 2012 to August 2016, 428 children (291 males and 137 females) with a prenatal diagnosis of UTD were enrolled. Male-to-female ratio was 2.5:1 (71.4% males, 28.6% females). One hundred and twenty-nine children (90 males and 39 females) with prenatal diagnosis of UTD presented a normal postnatal US or ureterocele and were excluded from the study. Twenty-one patients were lost at follow-up (figure 1). The remaining 278 patients with a UTD confirmed after birth were classified into three groups of risk: UTD-P1 (126), UTD-P2 (95) and UTD-P3 (57). At 1 month of life, all 57 UTD-P3 patients underwent VCUG that identified a VUR in six patients (two girls with I grade VUR, one boy and one girl with II grade VUR, one boy with III grade VUR and one girl with IV grade VUR) of which two had UTI. All 278 patients with a confirmed postnatal UTD continued US follow-up evaluations at 6, 12 and 24 months of life.

The UTI in 19 of 278 children with postnatal UTD diagnosis were observed, resulting in an overall incidence of 6.83% (table 2). *Escherichia coli* was the most common cause of UTI (64.7%), while *Enterococcus faecalis* was found in four UTI, and *Klebsiella* and *Morganella morganii* in one UTI each (table 3). All patients who presented a UTI underwent VCUG: nine patients had VUR, other four children were diagnosed with obstructive uropathy based on MAG3 renography (figure 1). Five patients presented a UTI reinfection all with a III or IV grade VUR.

DISCUSSION

This study showed a low occurrence of UTI (6.83%) in patients with a prenatal diagnosis of UTD confirmed by postnatal US in which no CAP was carried out. This incidence is similar to that reported by previous studies on the same topic.[12 13] The prevalence of UTI was slightly higher to that reported by Hoberman *et al*[14] in healthy febrile infants without risk factors in the first 2 years of life (5.3%).

Newborns with UTD are reported to be more likely to develop pyelonephritis within the first year of life, with a risk of permanent renal damage in up to 15% of cases when compared with children without UTD.[15 16] For this reason, the American Urological Association suggested the use of CAP in this population for the first year of life because of the increased risk of

Table1 The UTD classification system stratify risk

UTD-P1 (low risk)	Anterior-posterior renal pelvic diameter (APRPD) between 10 mm and 15 mm. Central calyceal dilatation may be present but not peripheral calyceal dilatation. Renal parenchyma with normal thickness and appearance. The ureter is not seen, and the bladder is normal.
UTD-P2 (intermediate risk)	APRPD >15 mm, calyces may be dilated centrally and peripherally or a dilated ureter is visible. The renal parenchyma has normal thickness and appearance. The bladder is normal.
UTD-P3 (high risk)	The renal parenchyma is thinned, with an increased echogenicity and/or a decreased corticomedullary differentiation or the bladder is abnormal (wall thickening, ureterocele and posterior urethral dilatation).

UTD, urinary tract dilatation.

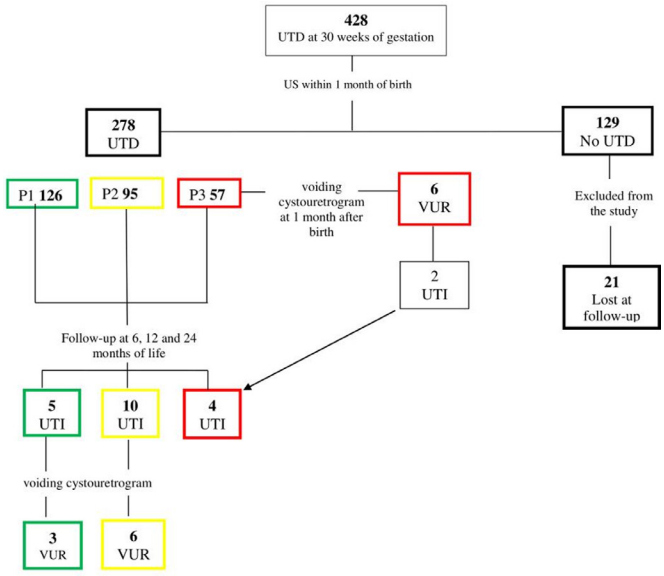

Figure 1 Study flow chart. US, ultrasonography; UTD, urinary tract dilatation; UTI, urinary tract infection; VUR, vesicoureteral reflux.

UTI. The use of CAP for prevention of UTI is being questioned, because of growing concerns regarding the unknown long-term effects of CAP and selection of resistant bacteria.[17 18 19] To date, one systematic meta-analysis showed that there is no difference in UTI rates for patients with low-grade dilation of renal pelvis receiving CAP compared with those receiving no treatment (2.2% vs 2.8%; p=0.15).[9] However, in patients with high-grade (III–IV°) dilation of renal pelvis, a significant decrease in UTI rates was observed in those receiving CAP vs those not receiving it (14.6% vs 28.9%; p<0.01).[6]

The use of CAP is not recommended in patients with UTD P1 (low-risk group).[1] The choice to use CAP in children in the UTD-P2 intermediate risk and P3 high risk is left to the discretion of the clinician.[1]

Our data showed that 63.2% of UTI occurred in the first 6 months of life confirming that this is the period at greatest risk, especially if they are males and affected by hydroureteronephrosis due to VUR, as suggested also by Castagnetti and colleagues.[19] Frequency of VUR in our study was 5.4% of all patients with UTD, similar to that reported by Lee *et al*.[20] Our study possibly underestimates the effective rate of VUR because not all patients underwent indiscriminately VCUG that was performed only in those with severe hydroureteronephrosis (UTD-P3) and in those with UTI.

Table 2 Characteristics and outcomes of patients based on risk group

	UTD-P1	UTD-P2	UTD-P3	Total
Patients	126	95	57	278
Male/female ratio	2.2:1	4.9:1	1.6:1	2.6:1
Bilateral UTD, n (%)	10 (7.9)	8 (8.4)	7 (13.7)	25 (8.9)
Overall rate of UTI, n (%)	5 (4)	10 (10.5)	4 (7)	19 (6.83)
Rate of UTI in the first 6 months, n (%)	3 (60)	5 (50)	4 (100)	12 (63.2)
Rate of VUR in patients with UTI, n (%)	3/5 (60)	6/10 (60)	2/4 (50)	11/19 (57.9)
Rate of UTI in patients with no VUR, n (%)	2/123 (1.6)	4/89 (4.5)	2/51 (3.9)	8/263 (3%)

UTD, urinary tract dilatation; UTI, urinary tract infection; VUR, vesicoureteral reflux.

Table 3 Type of bacteria found in urineculture

Bacteria (first UTI)	Number of UTI		Antibiotic sensitivity/ resistance
Escherichia coli	13	68.4%	Polysensitive
Enterococcus faecalis	4	21%	Polysensitive
Klebsiella	1	5.3%	Polysensitive
Morganella morganii	1	5.3%	Polysensitive
Total events	19		
Bacteria (recurrence)	**Number of UTI**		**Antibiotic sensitivity/ resistance**
Escherichia coli	6		Polysensitive
Klebsiella	1		Polysensitive
Pseudomonas	1		Polysensitive
Total events	8 (in five patients)		

UTI, urinary tract infection.

Data analysis showed that 58% of UTI (11 out of 19) occurred in patients with VUR. However, UTI occurred in only 3% of patients without VUR (8 out of 263), a lower frequency to that reported by the meta-analysis of Easterbrook *et al*.[5] Furthermore, despite in our cohort there were no circumcised patients, the rate of UTI was not as high as that reported in previous studies.[20 21]

This analysis suggests that the risk of UTI in children with UTD is low and similar to the normal population and that the risk of recurrence of UTI is even lower. As a matter of fact, in our 24-month follow-up, a UTI reinfection was demonstrated only in patients with VUR. In addition, all of the UTI that was observed, in absence of CAP, were caused by pathogens with antibiotics poly-sensitivity, like *E. coli* and *E. faecalis*, and none of our patients presented complications such as bacteraemia, sepsis or renal abscess. On the contrary, the meta-analysis by Selekman *et al*[18] on antibiotic prophylaxis in children with VUR showed that CAP significantly increases the risk of UTI from multiresistant germs.

A limitation of this study was that kidney damage was not evaluated with renal scintigraphy. In this perspective, the Randomized Intervention for Children with Vesicoureteral Reflux (RIVUR) trial showed that antimicrobial prophylaxis reduces the risk of recurrent UTI but not of renal scarring in patients with VUR[22] with a difference between the prophylaxis (14.8 %) and no prophylaxis (27.4 %) groups in patients with VUR slightly above the 10% threshold (12.6 %).[23] Furthermore, several randomised controlled trials showed that antibiotic prophylaxis was not effective in reducing the rate of UTI recurrence or renal scarring in patients with VUR.[24 25] For these reasons, the American Academy of Pediatrics (AAP) that VCUG should not be performed routinely after the first febrile UTI.[26]

CONCLUSION

In this study, the occurrence of UTI in patients with urinary collecting system dilatation in the absence of CAP was low. While further randomised studies with a longer follow-up and a cost-effective analysis are needed to confirm these results, this non randomised report is a strong hint that routine prophylaxis treatment could be safely avoided in children with UTD without recurrent infections.

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