



# Incidence of urinary tract infections in infants with antenatally diagnosed hydronephrosis—A retrospective single center study



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## ABSTRACT

**Objective:** To evaluate the incidence of urinary tract infections (UTIs) in infants with antenatal hydronephrosis (AHN). **Materials and Methods:** A cohort of AHN patients admitted to our institution between 2003 and 2013 were identified. Altogether 192 patients with nonrefluxing hydronephrosis (HN, n = 135), nonrefluxing hydroureteronephrosis (HUN, n = 21), or vesicoureteral reflux (VUR, n = 36) were identified. Patients with complex anomalies or neonatal decompression of the urinary tract were excluded. Information about UTIs diagnosed among the AHN patients was collected and compared with data from 58 controls.

**Results:** During the median follow-up time of 2.6 (0.3–11.2) years, 24 (13%) patients (15 (10%) males and 9 (19%) females) and 2 (3%) controls experienced at least one UTI ( $p = 0.033$ ). Eighteen (69%) UTIs were febrile. The males had the first UTI at significantly younger age than the females (0.3, 0.0–1.7 years vs. 1.0, 0.4–4.8 years,  $p = 0.010$ ). UTI was detected in 15 (63%) patients with grade 4–5 VUR, in 8 (6%) patients with HN, and in one (5%) patient with HUN ( $p$ -values  $<0.001$ , 0.726 and  $>0.999$  against the controls). None of the patients with grade  $\leq 3$  VUR had UTI. Fifty-eight percent of the patients with UTI were on antimicrobial prophylaxis. In five (12%) cases UTI appeared within one week after voiding cystourethrography (VCUG).

**Conclusions:** Infants with AHN and grade 4–5 VUR had the highest risk of UTI. UTIs tended to be more common in females than in males; however, males experienced UTI at younger age than females. VCUG caused UTI in 2.3% in our material.

**Level of Evidence:** III.

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The prevalence of fetal hydronephrosis (HN) in antenatal ultrasonography (US) is approximately 1% [1]. Antenatal hydronephrosis (AHN) may be caused by a variety of urological abnormalities from transient dilatation of the renal collection system to severe urinary tract obstruction and vesicoureteral reflux (VUR) [2,3]. Urinary tract abnormalities, particularly pyeloureteral obstruction (PUO), nonrefluxing hydroureteronephrosis (HUN), and vesicoureteral reflux (VUR), have been connected to increased risk of UTIs [4,5,6,7,8].

In this study, we evaluated retrospectively the frequency of UTI in a cohort of children with antenatally detected hydronephrosis. We aimed primarily to study (1) the risk of UTIs in children with different causes of AHN (VUR grades 1–3, VUR grades 4–5, nonrefluxing HUN, and HN alone) compared to children without any abnormality that is supposed to associate with UTIs, and (2) bacterial etiology and resistance in UTIs. Secondly we analyzed the impact of surgical intervention on UTI risk in AHN patients.

**Abbreviations:** AHN, antenatal hydronephrosis; HN, hydronephrosis; HUN, hydroureteronephrosis; PUO, pyeloureteral obstruction; US, ultrasonography; UTI, urinary tract infection; VUR, vesicoureteral reflux; VCUG, voiding cystourethrography.

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## 1. Materials and methods

All patients with urinary tract abnormalities (ICD-10: Q60.0–Q64.9 and N13.0–N13.9) diagnosed between January 2003 and December 2013 were identified from the database of the Helsinki University Hospital using electronic search tools. We further selected manually all patients who had antenatally detected hydronephrosis to exclude patients who were diagnosed after UTI or other symptoms appearing postnatally. The ethics committee of the Helsinki University Hospital approved the study protocol.

A total of 192 patients with persistent HN (the postnatal anteroposterior diameter (APD) of renal pelvis  $>7$  mm), nonrefluxing HUN (distal ureter visible on ultrasound examination), or VUR system were identified and included in the study (Table 1). None of the patients were circumcised. Renal US examination was performed on all patients, renal scintigraphy on 161 patients and voiding cystourethrography (VCUG) on 150 (78%) patients. VCUG was performed to a selected patient group according to our standard protocol: patients with (1) visible ureter in US or (2) pelvis APD  $\geq 10$  mm, (3) HN in association with reduced size kidney, or (4) bilateral hydronephrosis.

VUR was classified according to international classification [9]. In the case of bilateral VUR, the patient was classified according to the higher

**Table 1**

Total number of patients and gender distribution in AHN patients and controls.

Diagnostic group	Boys	Girls	Total
VUR gr 1–3, n (%)	8 (67)	4 (33)	12
VUR gr 4–5, n (%)	20 (83)	4 (17)	24
Nonrefluxing HUN, n (%)	16 (76)	5 (24)	21
HN, n (%)	100 (74)	35 (26)	135
All patients, n (%)	144 (75)	48 (25)	192
Controls, n (%)	38 (66)	20 (34)	58

VUR, vesicoureteral reflux; HUN, hydroureteronephrosis; HN, hydronephrosis.

grade. We excluded syndromic patients and patients with complex urogenital abnormalities, ureteroceles, or urethral obstructions.

The control group consisted of 58 patients with suspected urinary tract abnormality and either normal postnatal renal US or abnormality supposedly not exposing to UTI (renal agenesis ( $n = 16$ ), dysplastic or multicystic dysplastic kidney ( $n = 20$ ), simple renal or ovarian cysts ( $n = 4$ ), renal or adrenal cystic tumor ( $n = 2$ ), ectopic kidney ( $n = 5$ ) or adrenal hemorrhage ( $n = 1$ )). All patients with dysplastic kidneys were investigated with US, VCUG, and scintigraphy to exclude contralateral pathology.

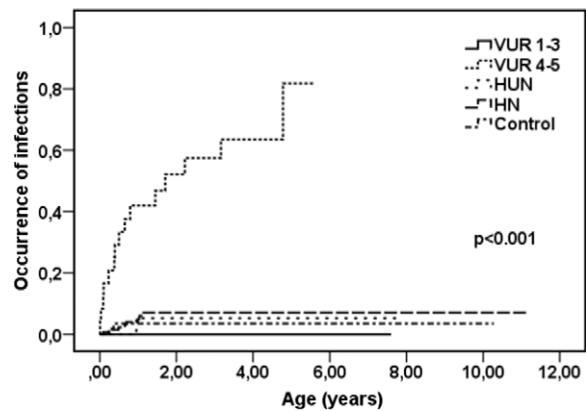
Information about age, gender, antimicrobial prophylaxis, results of imaging studies and possible urological surgery was collected. Antimicrobial prophylaxis was started according to our current protocol: (1) in patients with grade 3–5 VUR until they were toilet trained, (2) in patients with HN  $\geq 10$  mm of APD, or (3) in patients with dilated ureter without VUR until the first year of life. Occurrence of UTI was collected retrospectively from the patient journals and laboratory database. The diagnosis of UTI was defined as growth of a single pathogen on urine culture and significant pyuria ( $>60 \times 10^6/\text{L}$ ) in urinalysis. A bacterial count of 100,000 or more colony forming units (CFU)/mL in voided samples (clean catch urine, urine bag),  $\geq 50,000$  CFU/mL in a catheter sample, and any bacterial growth in suprapubic aspiration were considered significant. Bacterial growth in bag sample was confirmed by either suprapubic aspiration or catheter sample. In 13 patients the diagnosis was based on two consecutive bag urine samples and in two patients in one bag sample. Both of these two patients had clinical symptoms suggesting UTI, significant bacterial growth in urine and pyuria ( $>250\text{--}2063 \times 10^6/\text{L}$ ). Febrile UTI was defined as verified UTI together with fever ( $>38.5^\circ\text{C}$ ), or CRP  $>35$  mg/L [10]. The risk for UTI was calculated in each patient group during the follow-up time in our hospital. UTIs after surgery were analyzed separately in patients requiring surgical intervention.

The occurrence of UTIs is presented with Kaplan–Meyer curves. Patients' age and gender at the outset of the first UTI were compared between different diagnostic groups with Mann–Whitney test. Categorical variables were compared with Fisher's exact test. Statistical analyses were done with SPSS statistical package (IBM SPSS statistics 22).

## 2. Results

### 2.1. General findings

The median follow-up time for the AHN patients was 2.6 years (range 0.3–11.2 years) and that for the controls was 3.3 years (range 0.2–10.3 years) ( $p = 0.533$ ). Two (3%) out of the 58 controls and 24 (13%) of the 192 patients had UTI before any operative intervention ( $p = 0.051$ ). Females tended to have more UTIs than males (9/48 (19%) vs. 15/144 (10%),  $p = 0.243$ ). The vast majority of the first-time UTIs (17/24 (71%)) were diagnosed during the first year of life (Fig. 1). The males had their first UTI at significantly younger age than the females (median 0.3 years; range 0.0–1.7 years vs. 1.0 years; range 0.4–4.8) years,  $p = 0.010$ ). Nineteen (79%) of the 24 AHN patients and the other control patient with UTI had pyelonephritis.

**Number of patients at risk**

Age (years)	0.00	2.00	4.00	6.00	8.00	10.00
VUR 1-3	12	9	5	1	0	0
VUR 4-5	24	9	4	0	0	0
HUN	21	13	8	5	0	0
HN	135	55	25	11	5	1
Control	58	41	20	12	4	1

VUR, vesicoureteral reflux; HUN, hydroureteronephrosis; HN, hydronephrosis

**Fig. 1.** The occurrence of UTI in controls patients and AHN patients in different diagnostic groups.

### 2.2. UTIs in AHN subgroups

Patients with grade 4–5 VUR had significantly more UTIs than the patients with HUN, HN, or the control patients ( $p < 0.001$ ,  $<0.001$ ,  $<0.001$  and  $<0.001$  respectively). The UTI occurrence did not differ between the control patients and other patient groups except patients with gross VUR (Table 2). Female gender was a nonsignificant risk factor for UTI.

In our study 13 patients with HN had APD of renal pelvis between 7 and 10 mm. The UTI occurrence of patients with HN did not differ from controls when those particular patients were excluded ( $p = 0.720$ ).

### 2.3. UTI bacteriology, recurrence and antimicrobial prophylaxis

Altogether 161 patients had initially continuous antibiotic prophylaxis. Twenty infections occurred during antibiotic prophylaxis. In 16 (80%) cases, the bacteria were resistant to the prophylactic antibiotic (Table 3). *Escherichia coli* caused 17 (71%) of the 24 first-time infections and only 4 (40%) of the 10 recurrent infections in the patients. In the controls, both infections were caused by *E. coli*, which was sensitive to all tested antibiotics.

Six of the 24 (25%) patients with UTI had recurrent infection without or before any operative intervention. Four (67%) of them had grade 4–5 VUR, one (17%) had HUN, and another had HN. Two patients with grade 4–5 VUR had two UTI recurrences and one child had three recurrent infections. There were no verified UTI recurrences in the control patients.

Altogether 215 VCUGs were done for the patients and controls. In five cases (2.3%), UTI was detected within one week after VCUG had been performed. From all three of these VCUG-related infections were first-time UTIs and two were recurrences. Four out of five patients had grade 4–5 VUR and one of them had HN. The patients with grade 4–5 reflux had pyelonephritis and the patient with HN had cystitis. All five patients were on antibiotic prophylaxis during VCUG before the UTI. According to our VCUG protocol patients receive therapeutic dose of antibiotics for three days. The prophylaxis starts in the morning of the examination day.

### 2.4. UTIs in AHN patients with surgical intervention

Forty-three (22%) patients underwent surgical intervention. Twelve (28%) of these patients had had at least one UTI before the first

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