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Received: 2012.07.18 Accepted: 2012.12.06 Published: 2013.02.19		Clinical importance of pyelocalyceal dilation diagnosed by postnatal ultrasonographic screening of the urinary tract	
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Background: Material/Methods:		Ultrasonographic (US) screening of the urinary tract (UT) in infants was used to determine if there is a connec- tion between the frequency of pyelocaliceal dilation (PCD) in asymptomatic infants with normal antenatal US screening and occurrence of congenital anomalies of kidney and urinary tract (CAKUT) and urinary tract infec- tions (UTI). US screening of the UT was performed on 1000 healthy infants, 7 days to 6 months old. Two subgroups of kid- neys were described: subgroup 1 contained kidneys with anterior posterior pelvic diameter (APPD) of 5–9.9 mm, and subgroup 2 with APPD over 10 mm. US examinations and methods for detection of UTI and CAKUT were used.	
Results:		PCD was found in 74 infants (7.4%): 1.9% of infants had CAKUT, and 8.4% had UTI. In subgroup 1, CAKUT was found in 4 (6.3%) and UTI in 9 (14.3%) infants. In subgroup 2, CAKUT was found in 6 (54.5%), and UTI in 4 (36.4%) infants.	
Conclusions:		Mild PCD significantly increases the risk for CAKUT but not for UTI. Moderate to severe PCD significantly in- creases risk for both CAKUT and UTI. The postnatal US screening of UT is recommended for improved detec- tion of PCD and associated CAKUT. Indirectly, postnatal US screening of UT can help in detecting people at risk for UTI in the first year of life, and therefore help prevent possible kidney damage.	
Key words:		urinary tracthydronephrosiscongenital anomalies of kidneys and urinary tracturinary tract infectionmass ultrasound screening	
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## Background

Hydronephrosis is the dilation of the renal collecting system, which is often, but not always, associated with an obstruction, a vesicoureteric reflux, or an abnormal development of the ureteric morphology. Any underdevelopment of the urinary tract can cause its temporary or permanent dilation. Thus, finding a difference between a transitory and permanent dilation of the renal collecting system could be a real diagnostic challenge [1,2]. US (ultrasound) screening is a very sensitive method for the detection of hydronephrosis. There are several common methods used for grading the intensity of hydronephrosis, which is based either on a structural illustration of the renal collecting system, or on measuring the anterior posterior pelvic diameter (APPD). According to the Society of Fetal Urology (SFU), there are 4 grades of hydronephrosis, ranging from grade 0 to grade 4 [3-8]. Other grading systems for determining the intensity of hydronephrosis include measuring APPD, such as the Grignon (1986) grading system [7] or the Blachar (1994) grading system [8]. Grignon's grading system discriminates 5 degrees of hydronephrosis, and Blachar's grading system classifies hydronephrosis from grades 0 to 3 [7,8]. In fetuses, renal pelvic diameter greater than 10 mm may suggest an obstructive uropathy or an unusual extrarenal pelvis [9]. However, even a narrower renal pelvic diameter can be clinically significant if it is connected to the enlargement of renal calyces [3]. Because the enlargement of the renal collecting system may indicate various associated congenital anomalies of kidneys and urinary tract (CAKUT), in some countries prenatal and postnatal US screening of the urinary tract is regularly performed [3,10-14]. Antenatal hydronephrosis is positively diagnosed in 1-5% of pregnancies, but about 20% of the anomalies that are recorded during intrauterine development are not present after birth [15]. Children with prenatal hydronephrosis of any grade had a greater risk of an associated CAKUT than children with normal prenatal US of the urinary tract. Moreover, the risk for a postnatal pathology increased significantly with the grade of antenatal hydronephrosis [16]. Capolicchio et al. (1999) suggested that patients with prenatally diagnosed hydronephrosis using US screening had less chance of having kidney damage and a better chance for early surgical intervention than patients with postnatally diagnosed hydronephrosis [17]. On the other hand, 10%-20% of the hydronephrosis detected postnatally was not seen during the prenatal US screening [15]. According to various authors, postnatal US screening should be done between the third and tenth day after birth in order to avoid a state of relative dehydration and physiologic oliguria within the first days of life. This can cause an underestimation of the degree of hydronephrosis, resulting in a false-negative diagnosis [18-20]. Hydronephrosis and obstruction of the urinary system seem to be closely connected, although hydronephrosis can occur without a clinically significant obstruction. Nonetheless,

hydronephrosis certainly represents an abnormal state and its presence can lead to kidney damage. Therefore, prenatally or postnatally diagnosed hydronephrosis must be followed up in order to detect those infants with severe obstructive dilation and, if necessary, treat them by surgical or endoscopic procedures before any irreversible kidney damage or deterioration of renal function occurs [18,21-26].

The aim of our study was to detect the number of hydronephroses, diagnosed by postnatal US screening, that remained unrecognized by prenatal US screening, as well as to explore their possible connection with other CAKUT and urinary tract infection (UTI).

## **Material and Methods**

In this prospective study, US screening of the urinary tract was performed on a group (main group) of 1000 healthy newborns and infants (511 males and 489 females) ranging in age from 7 days to 6 months (average 77±46 days, median 62 days). These children were patients at the Pediatric care unit of an out-patient clinic in Solin, Croatia, and were included in the study after their parents gave written consent. The inclusion criterion was that all children had a normal prenatal US screening of the urinary system, declared as "normal" by a gynecologist. The exclusion criteria were a history of "positive" prenatal US screening for anomalies and clinical signs of urinary tract illness, especially of UTI, before postnatal US screening. Every US screening was done in the same clinic and performed by the same doctor. Screening was performed using a Siemens Sonoline Prima ultrasound machine. All the children were examined with a semi-convex probe of 5 MHz or a linear probe of 7.5 MHz, if necessary. At the time of US examination, all the patients were well hydrated and were not receiving diuretics. First, a sonogram of the bladder was done in the supine position. Then, the screening continued on to the right and left kidney lengthwise and transverse in the supine position, and then in the prone position. Apart from examining the position and outline of both kidneys, echogenicity of cortex and medulla, corticomedullary differentiation or possibly dilated calyces were described. APPD were measured in transverse section (Figure 1). Children who had a collecting system diameter of 5 mm or greater were observed with special attention, and put into 1 of 2 subgroups. Subgroup 1 consisted of kidneys whose APPD ranged from 5 to 9.9 mm, and kidneys in subgroup 2 had an APPD of 10 mm or greater. The children whose pyelocaliceal system was less than 5 mm were put into the control group. After confirming PCD, infants were not given an antibiotic prophylaxis, but were further observed by ultrasound every 2–3 months. Moreover, regular urine analyses were taken every 2 months. In the case of fever, an additional urine sample was taken. Urine cultures were taken in the case of leukocyturia or if the child showed clinical signs of UTI. Changes in PCD during the observed period were recorded as follows: PCD completely



Figure 1. Transverse ultrasound scan of the right kidney in prone position in one 45-days old female infant shows a right uretero-pelvic junction obstruction with dilated calyces and renal pelvis. The distance between cross 1 and cross 2 represents APPD.

disappeared if APPD decreased to less than 5 mm in both subgroups, PCD decreased in subgroup 2 if APPD decreased to less than 10 mm), and PCD increased in both subgroups if APPD increased to values that were larger than basic ones. In the next 6-54 months (average value 23±12 months, median 20 months), all the children from the main group had follow-ups in case of a UTI or CAKUT. UTI was diagnosed by clinical signs of high fever, chills, flank pain, dysuria, irritability, or abdominal pain with vomiting and by laboratory parameters of elevated ESR and CRP, proteinuria and leukocyturia, leucocytosis, and significantly positive urine culture of 10<sup>5</sup> or more colony-forming units of a single organism per milliliter of urine. In addition to US, CAKUT was also diagnosed by direct radionuclide cystography, voiding cystoureterography, dynamic renal scan, DMSA scan, IVU, and CT scan, if necessary. Children with PCD were screened for the first time at the average age of 71.6±46 days (51 days median, 21 days minimum, 180 days maximum). The average duration of observation of these children was 26±12 months (24 months median, 6 months minimum, 53 months maximum). The control group children were on average evaluated for the first time at the age of 77.4±46 days (62.5 days median, 7 days minimum, 180 days maximum). The average age of these children at the time of their follow up was 22.5±12 months (20 months median, 6 months minimum, 54 months maximum). There were no statistically significant differences in the age at first US screening between the group with PCD and the control group (Mann-Whitney test: z=1.26; p=0.209), but that difference was significant regarding duration of followup period between those 2 groups (Mann-Whitney test: z=2.8; p=0.005). None of the children were lost to follow-up.

### Statistical analysis

The statistical package STATISTICA 7.0 was used in analyzing data. We used  $\chi^2$  test, Fisher exact test and the Mann-Whitney test. We interpreted the results with a significance level of p<0.05.



Figure 2. The incidence of urinary tract infections in the *main* group, control group, subgroup 1 and subgroup 2, all examined by postnatal US screening. This figure shows that incidence of urinary tract infections in the main examined group was 8.4% (N=84), in control group 7.7% (N=71), in the subgroup 1 14.3% (N=9), and in the subgroup 2 36.4% (N=4).



Figure 3. The incidence of congenital anomalies of kidneys and urinary tract (CAKUT) in the *main group, control group, subgroup 1* and in *subgroup 2* examined by postnatal US screening. Figure shows that the incidence of CAKUT in the *main group* was 1.9% (N=19), in *control group* 1.0% (N=9), in *subgroup* 1, 6.3% (N=4), and in *subgroup* 2, 54.5% (N=6).

### Results

#### Main group

In the *main group* of 1000 infants tested by postnatal US screening, PCD was detected in 74 (7.4%) children (46 males, 28 females); 3 had bilateral PCD. Out of 511 examined males, 46 had PCD, and 28 out of 489 females had PCD ( $\chi^2$ =3.91; p=0.048). In this group, UTI was detected in 84 (8.4%) children (44 males, 40 females) (Figure 2). There were no significant difference for UTI between sexes ( $\chi^2$ =0.06; p=0.806). Associated CAKUT were also detected in 19 (1.9%) children (12 males, 7 females) (Figure 3). There were no significant difference for CAKUT between sexes ( $\chi^2$ =1.13; p=0.289).

#### PCD group

From this group of 74 patients with PCDs, 13 children (17.6%) had a UTI during the observed period, while 10 children (13.5%) were diagnosed with an associated CAKUT.



Figure 4. The natural history of the 65 PCDs from the *subgroup 1* (APPD 5–9.9 mm). Figure shows that 54 PCDs (83.1%) from *subgroup 1* disappeared during the observed period while 11 PCDs (16.9%) of them remained unchanged.



Figure 5. The natural history of the 12 PCDs from the subgroup 2 (APPD ≥10 mm). It shows that 7 PCDs (58.3%) from subgroup 2 disappeared or decreased, while 5 (41.7%) of them remained unchanged during the observed period.

Out of 77 PCDs, 49 PCDs were positioned on the left side and 28 on the right side. This data showed that left side was significantly more affected by PCD than the right side ( $\chi^2$ =5.7; p=0.017). Out of them, 16 remained the same (20.8%), 3 PCDs (3.9%) decreased, and 58 PCDs (75.3%) had their collecting systems normalized during the observation period.

Subgroup 1 consisted of 63 children (35 males and 28 females). Two children from this group had PCD on both sides, and the others had unilateral PCDs. PCD on the left side was 1.7 times significantly ( $\chi^2$ =4,45;p= 0.035) more frequent than on the right side (41:24). In this subgroup, 9 (14.3%) had a UTI during the observed period, and 4 (6.3%) children had associated CAKUT (1 hydrocalyses, 1duplication of the renal collecting system, 1 vesicoureteric reflux grade 3, and 1 renal hypoplasia) (Figures 2 and 3). In the follow-up screenings, 11 PCDs (16.9%) remained the same, and in the remaining group of 54 (83.1%), PCDs had disappeared. No patient from that group had any surgical intervention (Figure 4).

Subgroup 2 consisted of 11 children (all males). One of the observed patients had PCD on both sides, and the others had PCD on only 1 side. Even though the enlargement was

dominant on the left side (8:4), there was no statistical significance regarding affected sides ( $\chi^2$ =1.3; p=0.248). In this subgroup, 4 (36.4%) children acquired a UTI during the observation period, and 6 children (54.5%) had an associated CAKUT (Figures 2 and 3). During the period of our study, 5 (41.7%) collecting systems remained unchanged, 3 (25%) had a decrease of PCD, and 4 (33.3%) collecting systems had normalized (Figure 5). Altogether, only 3 children underwent surgery.

## **Control group**

In the *control group* of 926 children, UTI was detected in 71 (7.7%) children, and CAKUT was discovered by US screening in 9 (1.0%) children (Figures 2 and 3).

#### Comparison between the groups

In the group of patients with PCD, UTI was 2.3 times more frequent than in the *control group* ( $\chi^2$ =8.73; p=0.003), and CAKUT was 15 times more frequent ( $\chi^2$ =58; p<0.001).

In the *subgroup1*,UTI was not significantly more frequent than in the *control group* ( $\chi^2$ =3.46; p=0.063), but UTI was significantly more frequent in *subgroup 2* than in the *control group* ( $\chi^2$ =44.5; p<0.001). CAKUT was significantly more frequent in *subgroup 1* ( $\chi^2$ =13.1; p<0.001) and in *subgroup 2* ( $\chi^2$ =198; p<0.001) than in the *control group*.

#### Comparison between subgroups 1 and 2

A statistically significant difference was found between *sub*group 1 and subgroup 2 regarding sex ( $\chi^2$ =7.9; p=0.005) due to the fact that subgroup 2 consisted of males only. Although the children in subgroup 2 had 2.5 times greater occurrence of UTI than children in subgroup 1, it was statistically insignificant (Fisher exact test: p=0.094) due to the small sample size in subgroup 2. At the same time, a statistically significant difference in the number of associated CAKUT between the 2 subgroups was noted. Children in subgroup 2 had an 8.6 times greater occurrence of CAKUT than in subgroup 1 ( $\chi^2$ =18.6, p<0.001). Normalization of the renal collecting system was 2.5 times more frequent in subgroup 1 than in subgroup 2 (Fisher exact test: p=0.037) ( $\chi^2$ =13.5, p<0.001).

## Discussion

Even though some classifications of PCDs differ regarding the measures of APPD [1,13,14], we found that *subgroup 1* from our study correlated with SFU's, Blachar's, and Grignon's grade 1; *subgroup 2* correlated with SFU's grades 2, 3, and 4, with Grignon's grades 2,3,4, and 5, and with Blachar's grades 2 and 3 [3–5,7,27]. Our study shows that PCDs were more frequent in males and on the left side, especially their higher grades, and associated CAKUT and UTI-s were evenly distributed among sexes, which is in accordance with the findings of Ilić et al. (2011), who found an equal prevalence of UTI in both sexes in the first 2 years of life [28].

## Recovery rates of PCD during the observation time

An analysis of a number of studies has shown that the majority of mild degree hydronephroses at first stabilized and eventually disappeared. This especially refers to those from SFU's first and second degrees, in contrast to hydronephrosis of third and fourth degree [4]. Dremsek et al. (1997) concluded that an APPD less than 10 mm on a neonatal sonogram does not necessarily mean a pathological change, because the size of the urinary tract often spontaneously retracts to normal within the first year of life [29]. Our study showed that overall recovery rate of PCD was 79.2%, and Padovani's study showed that 72.3% of all PCDs spontaneously disappeared (90% in G I, 73% in G II and 58% in G III). Only 1 GIII patient showed a progressive dilation. Out of 17 newborns,15 displayed severe hydronephrosis (G IV–G V) and had regular follow-ups. Among them, 7 spontaneously recovered and 4 achieved complete resolution [27]. Regarding the recovery rate of mild PCD (subgroup 1), our study showed an 83.1% resolution, compared to 90% from Padovani's study. Moderate and severe PCDs from our study (subgroup 2) had a lower percentage of normalization (58.3%) in contrast to Padovan's study [27]. Bereczki et al. (2004) observed that 49.8% of the recorded dilations completely disappeared, 42.2% remained the same, and 7.4% increased (more than 30 mm) [30]. This recovering tendency of PCD was also noted by Lee et al. (2004), who showed that dilations of the collecting system are often likely to decrease, and very rarely become enlarged [31]. Sidhu et al. (2006) found that 98% of infants who had prenatal idiopathic hydronephrosis with a lower degree of dilation (APPD less than 12 mm), decreased their dilation to a normal level over time. This was not the case in infants with greater degrees of dilation (APD greater than 12 mm), in whom only 51% of cases normalized over time [4]. Some of the controversial results regarding the percentage of disappearing dilations might be the result of different criteria for hydronephrosis, expertise of pediatricians and gynecologists performing the US examination, and precision level of US screening equipment.

## CAKUT in children with PCD

Our results suggest that all children from our study with PCDs, regardless of grade, need further CAKUT observation, because we discovered a 15 times higher risk for associated CAKUT in that group than in the rest of the population. In children with mild PCD (*subgroup 1*) that risk was 6.3 times greater. Special

attention should be paid to children with higher grades of PCDs because they had 8.6 times higher risk for associated CAKUT than those with mild PCD. Similar to our study, Coelho et al. (2007), Tsai et al. (1998), and Grazioli et al. (2010) showed that the percentage of associated CAKUT positively correlated with the degree of hydronephrosis [10,32,33].

## UTI in children with PCD

It has already been well documented that infants with postnatal PCD have an increased risk of UTI [34,35].

In our study, the occurrence of UTI in children with PCD, regardless of grade, was 17.6%. Our results also point out that children having mild dilation of the pyelocaliceal system (*subgroup 1*) actually do not need further observation regarding UTI, because we did not discover significantly greater occurrence of UTI in this group than in the rest of the population, which is in accordance with results of Dremsek et al. (1997) and Tabel et al. (2010) [29,36].

Mami et al. (2009) did not find any significant difference in UTI frequency between infants with moderate PCD (APD 10–15 mm) and infants of the control group [13]. However, another study by the same authors showed a significantly higher incidence of UTI in infants with isolated severe renal pelvic dilation (APD >15  $\leq$ 20 mm) than in infants of the control group [14].

Higher grades of PCDs from our study positively correlated with number of UTIs, what is in accordance with findings of Tabel et al. (2010) and Coelho et al. (2007) [10,36]. That data indicate that postnatally screened children with high grade of PCD should be carefully monitored for UTI and should be protected by long-term uroantiseptic prophylaxis in their first year of life, but those with mild PCD-s should be treated like other healthy children. In addition to the fact that the children in our study were likely to have a UTI proportionate to their intensity of PCD, we recommend further diagnostic treatment in the case of constant or increased PCD during examinations. All data from our study indicate that patients with high grades of PCDs have to be carefully monitored for UTI and associated CAKUT, but patients with lower grades of PCDs have to be monitored for associated CAKUT only.

## Necessity of postnatal US screening of urinary system

In the past, patients with hydronephrosis were often diagnosed postnatally, but only when a palpable mass was discovered in the abdomen or when patients had already been affected by UTI and had to undergo a diagnostic procedure. Today, the use of ultrasonographic imaging has allowed great progress in diagnosing urinary system anomalies. Prenatal US screening of the urinary system proved not to be sensitive enough due to many subjective and objective factors [29,36,37]. Nevertheless, this method successfully diagnosed many cases of hydronephrosis in utero. To date, several studies on postnatal US screening have been performed. Among all CAKUT diagnosed by postnatal US screening, only 15.2% and 39% were found prenatally [29,30,38]. German authors computed the sensitivity of prenatal US screening to be 36%, and the accuracy rate was 99% [37]. This data suggests that every infant could benefit from both a prenatal and postnatal US screening of the urinary tract, as it enables prompt detection of any CAKUT.

Our experience with prenatal US screening has also shown an insufficiency in diagnosing urinary tract dilations, and shows the importance of screening children postnatally as well. Our investigation has proven that postnatally screened children showed an additional 7.4% more PCDs, even though their prenatal sonograms were declared normal. Padovani et al. (1996) found 7.1% PCDs (APPD >5 mm) in a group of 1881 healthy newborns, which is similar to our findings [27]. Contrary to our results, Tsai et al. (1998) found 17.7% PCDs (9.6% mild dilation and 8.1% hydronephrosis) in a group of 2384 healthy asymptomatic newborns, which is a much higher percentage than in our study. This is probably due to differences in criteria of each study, such as the fact that they assumed every visible collecting system to be pathologically enlarged [32]. The

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results of all these studies lead to the conclusion that prenatal US screening of the urinary tract is insufficient for a good diagnosis of PCD and needs to be complemented with a postnatal US screening.

# Conclusions

The postnatal US screening of the urinary system is a useful and valuable method for detecting PCDs. It can uncover additional instances of PCDs, which were not seen in prenatal US screening. Our results indicate that mild cases of PCD in infants significantly increase the risk for CAKUT, but not for UTI. Moderate and severe cases of PCD raise the risk for CAKUT and for UTI. Early diagnosis and early treatment of CAKUT, as well as watchfulness for possible UTI should be the final goal in kidney damage prevention. Therefore, we recommend that postnatal US screening of the urinary system should be done in all children in the first months of life, preferably together with ultrasonographic screening of the hips.

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