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CLINICAL STUDY

Evaluation and Outcome of Antenatal Hydronephrosis: A Prospective Study

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Abstract

Antenatal hydronephrosis (AHN), defined as dilatation of renal pelvis and/or calyces, is the most frequently detected antenatal abnormality. However, postnatal management of AHN is controversial. The purpose of this study was to describe the clinical outcomes of infants with AHN and to contribute to the definition of the postnatal evaluation of these patients. One hundred and thirty-six infants with AHN were prospectively followed up to 18 months. Patients were divided into two groups according to the degree of sonographic hydronephrosis (HN) on days 5–7: group I ($n = 87$, 64%) included patients who had grades 1 and 2 (64%) and group II ($n = 49$, 36%) included patients who had grade 3 and above HN. The grade of HN was found to be correlated with the increased risk of urologic pathologies. Frequency of vesicoureteral reflux was found to be significantly lower in patients with mild HN (6%) as compared to patients with severe AHN (29%) ($p = 0.005$). In addition, the risk of urinary tract infection increases with increasing grades of HN (10% vs. 29%, $p = 0.006$). The frequency of spontaneous resolution in patients with mild AHN (64%) was also significantly higher than in patients with severe HN (29%) ($p < 0.001$). The degree of AHN can be used for making decision about further diagnostic imaging and treatment. Our results strongly suggest that low-grade HN is a relatively self-limited condition and needs minimal investigation. In contrast, the outcome of more severe degrees of AHN needs clarification.

Keywords: antenatal hydronephrosis, prospective follow-up, vesicoureteral reflux, ureteropelvic junction obstruction

INTRODUCTION

Antenatal hydronephrosis (AHN), defined as dilatation of the renal pelvis and/or calyces, is the most frequently detected antenatal abnormality and the number of fetuses identified with AHN has been reported more frequently with the increasing use of ultrasonography (US) for fetal–maternal screening. However, usage of different grading systems for evaluating hydronephrosis (HN), different criteria for therapeutic intervention, and variable methods of assessments of renal function have contributed to a lack of uniformity in clinical approach.^{1–6} No associated abnormality is detected in the majority of the cases, and AHN stabilizes or resolves. Still, these infants might be referred for urological and/or nephrological consultations and radiological imaging and monitoring, in addition to long-term follow-up protocols and unnecessary antibiotic prophylaxis. On the other hand, in a few patients, minimal HN that can be considered as a negligible abnormality may be the first indicator of the

underlying important findings such as vesicoureteral reflux (VUR) or high-grade urinary tract obstruction.^{2,3,7} The urgency with which to undertake imaging depends on the suspected antenatal diagnosis. Clinical scenarios with bilateral HN, posterior urethral valves (PUVs), and complicated duplex systems take a high priority. The aim of this prospective study was to describe the clinical outcomes of infants with AHN and to contribute to the definition of the postnatal evaluation of these patients.

MATERIALS AND METHODS

Patients

The study group included all recently diagnosed (from November 2008 to January 2010) infants who were referred to our Pediatric Nephrology Department with the diagnosis of AHN from different centers and in whom the diagnosis of AHN was confirmed in the early postnatal period by the same radiologist. Exclusion

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criteria were as follows: (1) patients referred with the diagnosis of AHN but with unsatisfactory data (i.e., timing of US, severity of dilatation); (2) patients who did not have dilatation on US performed on the fifth to seventh postnatal days; and (3) patients who did not come for follow-up visits. HN was graded in accordance with the Society of Fetal Urology (SFU) study that categorized renal pelvic dilatation, the number of calyces seen, and parenchymal atrophy within five grades of increasing severity.⁸ Patients were divided into two groups according to their degree of sonographic HN on days 5–7: group I included patients who had grades 1 and 2 and group II included patients who had grade 3 and above HN. Infants were followed prospectively at 1-month intervals up to the sixth month, then at 3-month intervals up to 18 months of life. On admission and in all follow-up visits, body weights and lengths were measured; urinalysis and urine culture tests were performed. Postnatal diagnosis, urinary tract infection (UTI), and surgical requirements of the patients in each group were evaluated.

Methods

Data collected were side and grade of HN, associated urinary tract abnormalities, frequency and outcome of imaging studies, incidence of UTIs, frequency of surgical interventions, and initiation of antibiotic prophylaxis. An ultrasound scan was performed by the same pediatric radiologist using an Aplio scanner (Toshiba Medical Systems, Tokyo, Japan) with 3.5 MHz convex and 7.5 MHz linear transducers on days 5–7, on weeks 4–8, at the sixth month, and at the first year of life. The following US parameters were recorded: HN severity and laterality, presence of ureter dilatation, increased renal echogenicity, parenchymal thinning, duplicate system, and bladder thickening, with a full and empty bladder. The configuration of the pelvis was added to ultrasonographic assessment for clinical use as grade of dilatation and AP diameter of the pelvis. Extrarenal pelvis is a term that describes the renal pelvis placement outside of normal pelvis axis on renal ultrasound.

A voiding cystourethrography (VCUG) was performed in the infants who had bilateral HN, dilatation of the ureter, PUV, multicystic dysplastic kidney (MCDK), and proven UTI. VUR was graded according to the classification of the International Reflux Committee study.⁹ On follow up, we performed VCUG to the patients with VUR after 12 months of diagnosis. A technetium-99m (^{99m}Tc) dimercaptosuccinic acid (DMSA) scintigraphy was performed in all patients with VUR and in patients who had UTI on follow-up. A ^{99m}Tc mercaptoacetyl triglycine-3 (MAG-3) scintigraphy was performed in patients who had grade 3 and above HN to evaluate renal obstruction. A potential unilateral ureteropelvic junction obstruction (UPJO) that might need surgery was defined as prolonged excretion of tracer after administration of furosemide in combination with significant calyceal dilatation and associated renal pelvic dilatation.

UTI was defined as a urine specimen collected by transurethral catheterization containing at least 10,000 colony-forming organisms per milliliter of a single bacterial pathogen. Parents were informed about possible UTI and asked to come to our clinic if they had fever (38°C or more) and/or clinical symptoms such as anorexia, vomiting, and weight stasis. Postnatally all infants with grade 3 and above HN, VUR, PUV, and proven UTI were given prophylactic amoxicillin (10 mg/kg/day), which was replaced by single-night dose of trimethoprim (2 mg/kg/day)–sulfamethoxazole (TMP/SMX) at 3 months.

Indications for surgery were impaired renal function (one-sided <40%), deterioration of relative renal function (>5%), persistence or increase of the HN, and recurrent UTIs.

Informed consent was obtained from the parents of each patient and the study was approved by the institutional ethics committee.

Statistical Analysis

Statistical analysis was performed using SPSS 11.5 (SPSS Inc., Chicago, IL, USA) program. Frequency was used to describe the data. Chi-squared test or Fisher's exact chi-square (χ^2) test was used to determine the relationship between the grade of HN, urinary tract abnormalities, incidence of UTIs and surgical interventions, frequency of imaging studies, and antibiotic prophylaxis. $p < 0.05$ was considered as statistically significant.

RESULTS

The study group consisted of 136 recently diagnosed infants (109 males) with AHN. Group I included 87 patients (64%) and group II included 49 patients (36%).

Bilateral HN was detected in 43 patients (49%) in group I and 27 patients (55%) in group II. In group I there were five patients with VUR, four patients with ureterovesical junction obstruction, one with horseshoe kidney, one with duplex system, and one with megacolon. In group II there were 14 patients with VUR, 7 patients with severe UPJO, 1 with PUV, 1 with polycystic kidney disease, and 1 with MCDK. Seventy-six patients in group I and 25 patients in group II were considered as "nonspecific AHN." Extrarenal pelvis/extrarenal extension of pelvis was detected in 15 patients. Although AP diameters of the patients with extrarenal pelvis/extrarenal extension of pelvis ranged from 7 to 30 mm, none of these patients had UTI and/or surgical requirement, and HN resolved spontaneously in all except one who is still on follow-up without any complication.

VCUG was performed in 85 (63%) patients (Table 1). VUR was detected in 19 (22%) (bilateral in 10) patients. One patient had grade 1, six patients had grade 3, nine patients had grade 4, and three patients had grade 5 VUR. Frequency of VUR was found to be significantly lower in group I as compared to the patients in group II

Table 1. Imaging findings and clinical outcome of patients according to the grade of hydronephrosis.

	Number of patients		<i>p</i>
	Group I (<i>n</i> = 87)	Group II (<i>n</i> = 49)	
Sex			
Female	16 (18)	11 (23)	
Male	71 (82)	38 (77)	
Bilateral hydronephrosis (<i>n</i> = 70)	43 (49)	27 (55)	
Left-sided hydronephrosis (<i>n</i> = 52)	35 (40)	17 (35)	
Indications of VCUG (<i>n</i> = 85)			
Bilateral hydronephrosis	43	27	
Urinary tract infection	6	4	
Ureter dilatation	3	2	
Vesicoureteral reflux (<i>n</i> = 19)	5 (10)	14 (42)	<0.001
DMSA scintigraphy (<i>n</i> = 32)	12	20	
Abnormality (<i>n</i> = 11)	1	10	
MAG3 scintigraphy (<i>n</i> = 38)	0	38	
Abnormality (<i>n</i> = 6)	0	6	
Urinary tract infection (<i>n</i> = 23)	9 (10)	14 (29)	0.006
Surgical treatment	1 (1)	11 (22)	
Spontaneous resolution	56 (64)	14 (29)	<0.001

Notes: VCUG, voiding cystourethrography; DMSA, dimercapto-succinic acid; MAG3, mercaptoacetyltriglicine-3.

Values within parentheses indicate percentage values with respect to the total number of patients in each group.

($p < 0.001$). VUR resolved spontaneously in four and after subureteric injection in one patient who had grade 4 VUR in group I. In 3 patients VUR was not resolved and VCUG was not performed in 11 patients yet.

DMSA scan was performed in 32 (24%) children. Of these 32 children, renal scarring and/or dysplasia were detected in 11 (34%); all were found to have grade 3 and above VUR. MAG-3 renal scan was performed in 38 (28%) patients. Obstruction was detected in 6 (16%) children. Five of them were operated with increasing degree of HN and one was operated because of repeated UTI.

UTI was observed in 23 (17%) patients. UTIs were more frequent in group II (Table 1). Antibiotic prophylaxis was given to 58 (43%) patients. Fourteen (29%) patients with grade 3 and above HN had recurrent UTIs on antibiotic prophylaxis.

Surgical treatment was performed in 12 (9%) patients. Surgical intervention was performed in 11 (22%) children in group II, whereas just 1 patient (1%) (who had grade 4 VUR) needed operation in group I. Ultrasonographic appearance of HN improved spontaneously in 70 (52%) patients, at the end of the follow-up. Spontaneous resolution was more frequently observed in group I (Table 1).

DISCUSSION

The current literature includes retrospective reviews of children with AHN. There are a limited number of prospective studies¹⁰⁻¹² and meta-analyses^{2,3} that allow some conclusions regarding the natural history of

AHN. Recently, the SFU consensus statement on the evaluation and management of AHN was published which suggested that the optional schedule for pre- and postnatal evaluation of children with AHN is unclear and individualized approach may be more appropriate.¹³ The prospective nature of our study with a relatively large group of patients disclosed important issues that deserve attention.

Compatible with the literature the grade of HN correlated with the increased risk of urologic pathologies.¹³⁻¹⁵ The frequency of UTIs and surgical treatment was lower and spontaneous resolution rate was higher in patients with low-grade HN as compared to patients with high grade. A quite heterogeneous distribution of urological abnormalities in this group of patients is a striking finding. These abnormalities should be followed up for UTI and other complications.

US is the most common and important imaging technique utilized in monitoring AHN. Its ease of use and absence of radiation make it an excellent instrument to follow renal dilatation. In addition to the severity of HN and other proposed criteria, renal pelvis configuration was used as a new parameter for ultrasonographic evaluation of AHN in our study. Fifteen patients were found to have extrarenal pelvis/extrarenal extension of the pelvis. Contrary to the results of Katzir et al.¹⁶ none of these patients (including the ones who had severe AHN) had UTI and/or surgical requirement, during the follow-up period. We suggest that as pelvis of the kidney serves as a reservoir, pressure and parenchymal involvement reduce in infants who have extrarenal pelvis even if they seem to have obstruction.

Numerous studies have demonstrated that VUR occurs in 10–20% of patients with AHN and is associated with significant morbidity. Although it was reported that the incidence of reflux increases with the degree of sonographic dilatation postnatally¹⁴⁻¹⁹ Lee et al.² noted that the incidence of VUR between groups of children with mild, moderate, and severe AHN is not significantly different. In addition, a normal postnatal US does not exclude VUR.^{16,20} Despite these conflicting data our study showed that the frequency of VUR in infants with low-grade HN is low and the consequences are minor when performed with our criteria. Currently, the management protocol for antenatal HN remains undefined. Many authors recommended performing a VCUG to all children with AHN regardless of the degree of postnatal dilatation.^{16,18} On the contrary, it remains unproven whether the identification and treatment of all children with VUR confers any clinical benefit. Another problematic aspect is that bilateral HN, a proposed indication of VCUG, was found in nearly half of the patients of our study group. However, merely 5 of the 43 patients with bilateral HN in group I (12%) had VUR. Only one of them (with grade 4 VUR) had renal scarring, namely dysplasia, and none had recurrent UTIs. In other words, we have performed VCUG with the indication of bilateral HN to two in every three patients and

detected asymptomatic VUR in one of the seven patients in group I. These data show that indications of VCUG for infants with low-grade HN should be discussed. Eleven (41%) of the 27 patients with bilateral HN in group II had VUR. Compatible with our findings a recent study by Kort et al.²¹ showed that the frequency of the VUR is 4 times more in high-grade HN than in low-grade HN. Moreover, radiologic investigation is costly, can be invasive, is associated with radiation risk, and causes significant parental anxiety. Consequently, we recommend a VCUG in children with moderate-to-severe degrees of HN, while a VCUG should be considered in those with mild HN on a case-by-case basis, such as in those with increased echogenicity, calyceal and/or ureteral dilatation, and dilated bladder or who has UTI.

The decision to place all children with AHN on prophylactic antibiotics because of the risk of VUR or UPJO before postnatal diagnostic imaging is controversial. Coelho et al.²² found that female gender and presence of uropathy were independent predictors of UTI in patients with AHN. Consistent with the literature, the risk of UTI increases with increasing grade of HN in our study. We suggest that antibiotic prophylaxis is not necessary in asymptomatic newborns with mild AHN. Parents must be informed of the possibility of VUR and the necessity to perform bacteriological urine examination in case of unexplained fever. On the other hand, prophylaxis should be given to patients with any grade of VUR because of the risk of UTI and renal damage.

In conclusion, the degree of AHN can be used as a guide for making decision about diagnostic imaging and treatment. Our results strongly suggest that mild HN (SFU grades 1–2) is a relatively self-limited condition and needs minimal investigation. In contrast, the outcome of severe degrees of AHN (SFU grades 3–4) needs clarification. We believe that VCUG is not mandatory in asymptomatic newborns with mild AHN. Clinical and US follow-up is advised during the first year of life. However, due to limitations such as small sample size and short follow-up time of our study we could not determine the strict follow-up criteria for patients with AHN. Further multicenter, prospective, long-term follow-up studies with large number of patients are clearly needed to determine which parameters of prenatal and postnatal ultrasound are predictive, especially in infants with severe AHN.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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