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Original Article

Postnatal follow-up results of antenatally diagnosed hydronephrosis: A single-center experience

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Abstract

Aim: The incidence of antenatal hydronephrosis (AHN) has also increased with the raised use of ultrasonography (US); however, there is no consensus on how to approach the babies who were diagnosed prenatally with AHN. The present study aims to investigate the postnatal examination, treatment, and results of babies diagnosed with AHN.

Material and Methods: In this study, 276 infants who were followed-up with the diagnosis of AHN between January 2012 and December 2015 in the pediatric nephrology outpatient clinic were evaluated retrospectively. Two hundred and fifty babies with AHN (196 males and 54 females) included in our study. Babies with and without abnormality were compared and etiological causes and treatment modalities of babies with AHN were investigated in the postnatal follow-up.

Results: Despite no abnormality detected in 144 (57.6) AHN patients, 106 babies (42.4%) had urinary system abnormality in the postnatal US. As the underlying anomalies, ureteropelvic junction obstruction (UPJO) was the most common in 67 kidneys (63.2%); vesicoureteral reflux (VUR) was found in 29 kidneys (%27.3), ureterovesical junction obstruction (UVJO) in 5 kidneys (4.7%) and posterior urethral valve (PUV) in 3 kidneys (2.8%).

Conclusion: Evaluation of babies with AHN starting from postnatal first week will provide early diagnosis of urinary system pathologies and early treatment of babies diagnosed with obstructive pathology.

Keywords: Antenatal hydronephrosis; children; prenatal diagnosed; postnatal follow

INTRODUCTION

Antenatal hydronephrosis (AHN), known as the expansion of the fetal kidney collector ducts, occurs in approximately 1-5% (50% transient or physiological) of all pregnancies. One of the most widespread renal anomalies is in the prenatal ultrasonography (US) (1-3). Early recognition of urinary tract/renal congenital anomalies in the intrauterine period allows the monitoring and treatment of these anomalies in the postpartum period. Although the attempt does not lead to a risk to the mother and the fetus, it may improve perinatal survival (4). However, the use of different measures for therapeutic intervention, different grading systems for the assessment of AHN, and variable methods for assessing renal function are leading to discrepancies in this clinical approach (5,6). In addition, all prenatal findings of the US do not necessarily reflect pathology, as most of them are of a transient and no clinical significance (7).

Although AHN is generally regarded as a mild abnormality in some patients, AHN may sometimes be the first manifestation of diseases like vesicoureteral reflux (VUR) or urinary tract obstruction (4-6). To sum up, there is no definitive protocol for follow-up of patients with AHN, and surveillance and treatment approach is contradictory to these patients. Thus, this study aims to identify the clinical consequences of AHN babies and to conduce to the identification of postpartum assessments of these patients.

MATERIAL and METHODS

Two hundred and seventy-six children evaluated in the outpatient clinic of Pediatric Nephrology, between January 2012 and December 2015, were initially screened for AHN. Finally, 250 patients meeting the inclusion criteria, whose antero-posterior renal pelvis diameters (APPD) in the intrauterine period were higher than 7 mm, were included in this study (Figure 1). AHN was defined as the antenatal US measurement of APPD and more than 4 mm in the second trimester and 7 mm in the third trimester were considered to be AHN, according to the Society of Fetal Urology (SFU) (8). (1) Babies with unilateral or bilateral

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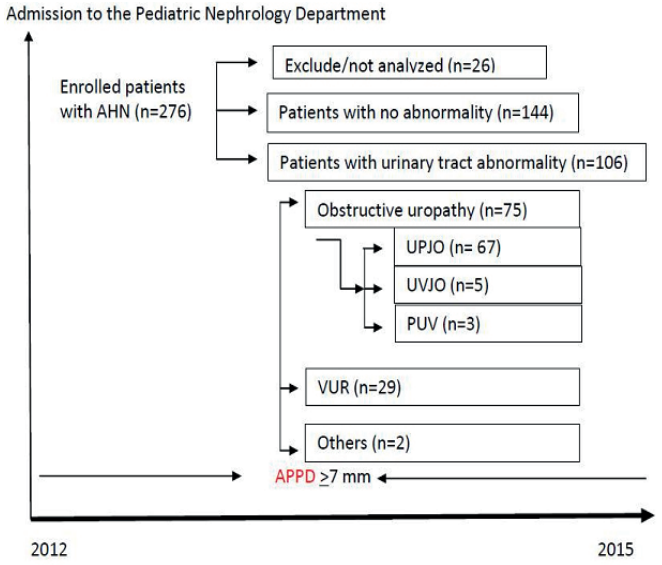
AHN, (2) babies who had kidney US in the first 4-6 weeks of life, (3) babies following at least one year were included in this study. (1) Patients with a diagnosis of AHN but with the insufficient US or other data (2), patients who have improved dilatation in the postpartum US (3), babies who did not follow up (4) babies with diseases, such as spinal dysraphism, neurological abnormalities, or neurogenic bladder findings (5), and babies with kidney malformation affecting at least one kidney, such as kidney agenesis/dysplasia/ectopia, cystic kidney diseases, were excluded from this study.



APPD:Antero-posterior pelvic diameter, AHN: Antenatal hydronephrosis; UPJO: Uretero pelvic junction obstruction; UVJO: Uretero vesical junction obstruction; VUR: Vesicoureteral reflux; PUV: Posterior urethral valve

Figure 1. Clinical outcomes of the 276 children with AHN

AHN was categorized in accordance with the SFU opinion classification (9). Patients were divided into two groups according to postnatal US findings as follows: Babies without pelvic dilatation on the first 4-6 weeks on the life were taken to group I and babies with stage I and above pelvic dilatation were included in Group II. In the course of the first admission and in all applications visits, gestational AHN diagnosis age (weeks), degree of AHN (mm, grade I-IV), or bilateral AHN (left-sided, right-sided or bilateral) degree of AHN in the 1 and 4-6 weeks on the life were measured; urinary tract infections (UTI) were screened. Postnatal final diagnosis, UTI, and surgical needs were evaluated for each patient in each group.

All data evaluated were laterality and size of AHN, accompanying congenital anomalies of the kidney and the urinary tract (CAKUT), timing and findings of imaging methods, the presence and number of UTIs and timing of surgical interventions and antibiotic prophylaxis is started or not.

US parameters, such as kidney sizes, parenchymal thicknesses, increased renal echogenicity, severity and frequency of AHN, presence of ureteral dilation, double collecting system and thickening of the bladder wall thickness, were recorded.

While the first US examinations of the patients were performed in the first week after birth, voiding cystourethrography (VCUG) was performed in infants with signs of lower urinary tract obstruction (bilateral AHN, progressive AHN, bladder with dilated or thickened walls, insufficient emptying and dilated posterior urethra), single or double sided APPD > 15 mm and SFU stage 3-4 or ureteral dilation in postnatal US, and febrile UTI during follow-up.

In cases with bilateral AHN secondary to the presence of PUV, the US was performed within the first 1-2 days of postnatal. In patients with unilateral or bilateral AHN with ureteral dilatation, VCUG was performed between postnatal 4-6 weeks; however, VCUG was performed in the first week after birth in patients with findings suggesting urinary outflow obstruction in addition to bilateral AHN in the US. VUR is rated according to the classification of the International Reflux Committee (10). Control VCUG was performed after 6 or 12 months to investigate whether reflux regressed in only high grade (above grade 3) VUR patients. A technetium-99m (99mTc) dimercaptosuccinic acid (DMSA) scintigraphy was performed for all VUR patients and follow-up patients with proven and/or recurrent UTI. Tc-99m DTPA scintigraphy was performed to evaluate kidney obstruction in children older than three months and in patients with AHN without VUR grade 3 and above. All babies with grade 3 and above AHN, VUR, PUV, and proven UTI were protected with a single dose of amoxicillin (10 mg/kg/day) overnight for the first three months or with trimethoprim (2 mg/kg/day) after the third month. The evaluation criteria with the surgery were as follows: 1) Infants with signs of lower urinary tract obstruction (bilateral AHN, progressive AHN, dilated or thickened bladder wall, inadequate bladder, dilated posterior urethra). 2) Infants who have four and five degree VUR at the end of the first year. 3) Infants with VUR causing recurrent UTI and developing a new scar in the kidney parenchyma. 4) In diuretic renography, babies with a radionuclide half-life > 20 minutes, non-flowing and/or obstructed kidney function less than 40%. Infants who have these findings but cannot be decided, who have aggravated US findings or show 5-10% further deterioration in differential function. 5) Infants with bilateral HN, whose dilatation is worsening or whose function continues to deteriorate, or with HN in the solitary kidney.

Statistical analysis

The data were evaluated using the SPSS Statistics Package (SPSS) (SPSS Inc., Chicago, IL, USA) for Windows version 16.0. Shapiro-Wilk test was used to analyze whether the sample was normally distributed. Normal distribution was expressed as mean and standard deviation (SD), and slope distribution was expressed in median and quarter

intervals. Two groups were compared using paired t-test or the Mann-Whitney U test and; the proportion or percentage of categorical variables was analyzed by the Chi-square test or Fisher's exact test. It was regarded as statistically significant when the P-value was below 0.05.

RESULTS

Two hundred fifty newborns with AHN (196 males and 54 females) were evaluated according to postnatal diagnosis. The mean gestational age at the time of AHN diagnosis was 30.2±12.0 weeks. The median duration of postnatal follow-up was 24 months (3-36). The mean APPD of the fetal renal pelvis was 11.9±6.6. Left-sided and bilateral AHN was observed in 139 (55.6%) patients and 83 (33,2%) patients, respectively. Clinical characteristics of babies with AHN are shown in Table 1.

Neonates with no abnormality (Group I) included 144 patients (57.6%) and neonates with urinary tract anomalies (Group II) included 106 patients (42.4%). Comparative

Table 1. Demographic data of the study group

Patient number (n)	**n=250 (333)[a]**	**%**
Male/Female	196/54	78.4/21.6
Left-sided AHN	139	55.6
Right-sided AHN	28	11.2
Bilateral AHN	83	33.2
Gestational age of AHN diagnosis (weeks)	30.2±12.0	-
<30 weeks (n)	81	32.4
30-35 weeks (n)	88	35.2
>35 weeks (n)	42	16.8
Unknown weeks (n)	39	15.6
Median duration of postnatal follow-up (months)	24 (3-36)	-
APPD of the renal pelvis (mm)	11.9±6.6	-
Mild (5-9 mm) (right-sided/left-sided) (total)	72/108 (180)	54.0
Moderate (10-15 mm) (right-sided/left-sided) (total)	19/58 (77)	23.2
Severe (>15 mm) (right-sided/left-sided) (total)	20/56 (76)	22.8

AHN: Antenatal Hydronephrosis, APPD: Antero-Posterior Pelvic Diameter

Table 2. Data of the infants with and without AHN in the postnatal follow-up

Parameters	Patients with no abnormality (n=144)	Patients with urinary tract abnormality (n=106)	p
Patient number (n, %)	144 (57.6)	106 (42.4)	-
Gender (Male/Female) (n, %)	110/34 (76.4/23.6)	86/20 (81.1/18.9)	0.37
Age of diagnosed (week)	30.3±7.7	30.7±8.2	0.5
UTI prevalence (year)	0.47±0.7	1.13±1.7	**<0.001**
APPD of the renal pelvis (mm)			
Right	7.71±3.3	12.0±5.2	**<0.001**
Left	9.55±4.0	13.3±5.2	**<0.001**
APPD in the first 4-6 weeks in the postnatal life (mm)			
Right	9.31±3.3	13.9±5.6	**<0.001**
Left	11.1±3.4	15.1±5.0	**<0.001**

APPD: Antero-Posterior Pelvic Diameter, UTI: Urinary Tract Infection

data on infants with and without AHN during the postnatal follow-up period are given in Table 2.

In our study, we detected urinary tract abnormality in 106 patients (42.4%) in postnatal US. The anomalies found were as follows: UPJO in 67 kidneys (63.2%), VUR in 29 kidneys (%27.3), ureterovesical junction obstruction (UVJO) in five kidneys (4.7%) and PUV in three kidneys (2.8%). Etiologic classification of neonates with urinary tract abnormality is given in Table 3.

The comparison of data in the groups of surgery and follow-up group with urinary tract abnormality was evaluated. Male/female ratio, mean age of IU diagnosed of AHN and UTI prevalence was found to be significantly higher in the surgery group than in the follow-up group (p=0,010, p=0,050, p= 0,002, respectively) (Table 4).

Table 3. Classification of patients with urinary tract abnormality

	Patient number (n=106)	Surgery	Follow-up	Improved
Obstructive uropathy (n, %)	75 (70.7)			
UPJO (n, %)	67 (63.2)	19 (17.9)	16 (15.0)	32 (30.1)
UVJO (n, %)	5 (4.7)	1 (0.9)	4 (3.7)	-
PUV	3 (2.8)	3 (2.8)	-	-
VUR (n, %)	29 (27.3)	10 (9.4)	-	19 (17.9)
Others (n, %)	2 (1.25)	-	2 (1.8)	-
Patient number (n, %)		33 (31.1)	22 (20.7)	51 (48.1)

AHN: Antenatal Hydronephrosis; UPJO: Uretero Pelvic Junction Obstruction; UVJO: Uretero Vesical Junction Obstruction; VUR: Vesicoureteral Reflux; PUV: Posterior Urethral Valve

Table 4. Data of the patients with urinary tract abnormalities

Parameter	Surgery	Follow-up	p
Patient number (n, %)	33 (31.1)	73 (68.9)	-
Kidney unit number (n, %)	50 (33.3)	100 (66.7)	-
Gender (Male/Female) (n, %)	31/2 (94/6)	55/18 (74.4/24.6)	**0.010**
Age of diagnosed (week)	31.6±6.2	29.1±5.6	**0.050**
UTI prevalence (year)	1.90±2.1	0.79±1.4	**0.002**
AHN (unilateral/bilateral)(n, %)	16/17(48.5/51.5)	46/27(63/37)	0.13
APPD of the renal pelvis (mm)			
Right	12.5±6.1	11.8±4.8	0.64
Left	14.5±5.7	12.7±4.9	0.12
APPD in the first 4-6 weeks in the postnatal life (mm)			
Right	14.9±5.9	13.4±5.4	0.34
Left	16.4±5.8	14.3±4.5	0.060

AHN: Antenatal Hydronephrosis, APPD: Antero-Posterior Pelvic Diameter UTI: Urinary Tract Infection

DISCUSSION

There are many debates about the clinical importance, postnatal evaluation and management of infants with AHN regardless of constant improvements in understanding the genetic basis and outcomes of CAKUT (1-8). AHN is a general definition that describes many urological events in a wide range from temporary expansion of the urinary pelvic system to clinically significant urinary tract obstruction, such as UPJO, UVJO, PUV or VUR. With routine clinical use of the prenatal US, children with urinary tract obstruction or VUR are detected before complications, such as urinary tract infections (UTIs),

kidney stones and renal dysfunction or renal insufficiency (7). Such complications that can be prevented by early diagnosis directly affect mortality and morbidity. The aim of the evaluation of children with AHN is to detect these possible complications early, to prevent their development and to maintain renal function at normal limits.

It has been reported that most mild AHN resolves spontaneously and renal APPD returns to normal level (11). Consistent with the previous studies, the findings obtained in our study showed that 144 (57,6%) patients were detected to be normal.

The clinical significance of AHN depends on the degree/ severity of renal dilatation, and clinically more significant pathologies are seen at more severe enlargements (12). A meta-analysis reported that AHN decreased or improved in 98% of patients with mild AHN (6). When the literature is examined, the risk of urological pathology in patients with mild AHN is 11.9%; in severe cases of AHN, this rate increases to 88.3% (5). Our study showed that 106 (42,4%) infants were detected to be pathological. There was UPJO, the most frequently detected pathology, in 67 (63,2%) patients. The second most frequently detected pathology was VUR in 29 (27,3%) patients. The rate of spontaneous resolution of our patients was 48.1%; the rate of those who remained at follow-up was 20.7%, and the rate of surgery was 31.1% in patients with urinary abnormalities, in accordance with the previous studies (5-7,12).

Studies have reported a higher detection rate of APPD among male infants (13-15). The overall male-to-female (M: F) ratio in our review was 3.6, which is consistent with previous studies (13-15).

Previous studies suggested that AHN might be unilateral or bilateral, but unilateral AHN was more common. Besides, left-sided AHN is more frequent than right-sided AHN (13-15). In our study, consistent with the literature, left-sided and bilateral AHN was observed in 139 (55.6%) patients and 83 (33.2%) patients, respectively.

Many studies have pointed out that 10-20% of the patients with AHN occur in VUR and are associated with significant morbidity. In a prospective study, Braga et al. (16) defined that female gender; hydroureteronephrosis, VUR and lack of continuous antibiotic prophylaxis were independent risk factors for febrile UTI in infants with AHN. Similarly, Hertz et al. (17) demonstrated that ureteral dilatation, high-grade VUR, and UVJO were the risk factor for UTI in infants with AHN. Lee et al. (5) stated that the frequency of VUR did not differ significantly between children with mild, moderate and severe AHN. Also, a normal postnatal US does not exclude VUR (17). Kort et al. (18) showed that the frequency of VUR in high-grade AHN is four times higher than that of low-grade AHN. Sencan et al. (19) retrospectively evaluated 760 mild AHN patients and stated that only 13 patients (1.7%) had VUR.

Currently, the management protocol for AHN is not clear. Some authors recommend performing VCUG to all children with AHN irrespective of the degree of postnatal dilation (19). Other routine VCUG screening for and long-term continuous antibiotic prophylaxis was not necessary for children with mild AHN (16-19). In our study, compatible with previous findings, UTI frequency and mean APPD values diameter (both left and right diameter) were significantly (16-19) higher in children with VUR compared to both patients with no abnormality and obstructive uropathy group ($p<0,05$, for each). Also, bilateral AHN prevalence in children with VUR is higher than patients with no abnormality group ($p=0,030$).

CONCLUSION

In conclusion, most of the urological abnormalities which are noted during infancy will not lead to diseases, such as pyelonephritis, hypertension or even end-stage renal failure later in life if AHN is followed up with proper management. The course of the disease is linked to the underlying pathology for AHN diagnosed cases, but a normal postnatal US scan does not indicate that there is no urinary system anomaly. Therefore, postnatal investigations of infants whose birth is 7 mm or higher in the kidney pelvis are necessary. The evaluation of the infants with urinary system dilatation with the serial US and other radiologic evaluation methods beginning from the postnatal first week will provide early diagnosis of urinary system pathologies. Also, the babies diagnosed as obstructive pathology with AHN are easily understood with the US, but it is difficult to say for the diagnosis of VUR. Therefore, we think that the postnatal urinary system infection follows up of AHN cases is important at the early diagnosis of VUR and decrease of unnecessary radiation containing radiologic examinations. However, we should note that we could not establish clear follow-up criteria for AHN patients due to limitations, such as small sample size, single centeredness and short follow-up period. Thus, especially in severe AHN babies, multicenter, prospective, long-term follow-up studies with a large number of patients are clearly needed to investigate which parameters are predictive of prenatal and postnatal US findings.

Competing interests: The authors declare that they have no competing interest.

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REFERENCES

1. Oliveira EA, Oliveira MC, Mak RH. Evaluation and management of hydronephrosis in the neonate. Curr Opin Pediatr 2016;28:195-201.
2. Rheault MN, Greenbaum LA. Renal and urologic abnormalities in the perinatal period. Clin Perinatol 2014;41:19-20.
3. Quirino IG, Diniz JS, Bouzada MC, et al. Clinical course of 822 children with prenatally detected nephrouropathies. Clin J Am Soc Nephrol 2012;7:444-51.

4. Smith-Harrison LI, Hougen HY, Timberlake MD, et al. Current applications of in utero intervention for lower urinary tract obstruction. J Pediatr Urol 2015;11:341-7.
5. Lee RS, Cendron M, Kinnamon DD, et al. Antenatal hydronephrosis as a predictor of postnatal outcome: A meta-analysis. Pediatrics 2006;118:586-93.
6. Grazioli S, Parvex P, Merlini L, et al. Antenatal and postnatal ultrasound in the evaluation of the risk of vesicoureteral reflux. Pediatr Nephrol 2010;25:1687-92.
7. Nguyen HT, Herndon CD, Cooper C, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. J Pediatr Urol 2010;6:212-31.
8. Nguyen HT, Benson CB, Bromley B, et al. Multidisciplinary consensus on the classification of prenatal and postnatal urinary tract dilation (UTD classification system). J Pediatr Urol 2014;10:982-98.
9. Fernbach SK, Maizels M, Conway JJ. Ultrasound grading of hydronephrosis: Introduction to the system used by the Society for Fetal Urology. Pediatr Radiol 1993;23:478-80.
10. Lebowitz RL, Olbing H, Parkkulainen KV, et al. International system of radiographic grading of vesicoureteric reflux. International Reflux Study in Children. Pediatr Radiol 1985;15:105-9.
11. Sairam S, Al-Habib A, Sasson S, et al.Natural history of fetal hydronephrosis diagnosed on mid-trimester ultrasound. Ultrasound Obstet Gynecol 2001;17:191-6.
12. Pates JA, Dashe JS. Prenatal diagnosis and management of hydronephrosis. Early Hum Dev 2006 ;82:3-8.
13. Gokaslan F, Yalcinkaya F, Fitoz S, et al. Evaluation and outcome of antenatal hydronephrosis: a prospective study. Ren Fail 2012;34:718-21.
14. Kaspar CDW, Lo M, Bunchman TE, et al. The antenatal urinary tract dilation classification system accurately predicts severity of kidney and urinary tract abnormalities. J Pediatr Urol 2017;1477-5131:30155-9.
15. Dos Santos J, Parekh RS, Piscione TD, et al. A New Grading System for the Management of Antenatal Hydronephrosis. Clin J Am Soc Nephrol 2015;10:1783-90.
16. Braga LH, Farrokhyar F, D'Cruz J, Pemberton J, Lorenzo AJ. Risk factors for febrile urinary tract infection in children with prenatal hydronephrosis: a prospective study. J Urol 2015;193:1766-71.
17. Herz D, Merguerian P, McQuiston L. Continuous antibiotic prophylaxis reduces the risk of febrile UTI in children with asymptomatic antenatal hydronephrosis with either ureteral dilation, high-grade vesicoureteral reflux, or ureterovesical junction obstruction. J Pediatr Urol 2014;10:650-4.
18. De Kort EH, Bambang Oetomo S, Zegers SH. The long-term outcome of antenatal hydronephrosis up to 15 millimetres justifies a noninvasive postnatal follow-up. Acta Paediatr 2008;97:708-13.
19. Sencan A, Carvas F, Hekimoglu IC, et al. Urinary tract infection and vesicoureteral reflux in children with mild antenatal hydronephrosis. J Pediatr Urol 2014;10:1008-13.