Management of Infants Diagnosed with Antenatal Hydronephrosis and Determining the Need for Surgical Intervention

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ABSTRACT

Antenatal hydronephrosis (ANH) is the most common pathology in the fetal period. The cause of ANH ranges from intrauterine transient hydronephrosis to clinically severe congenital anomalies of the kidney and urinary tract. Coexistence with oligohydramnios, ectopic kidney, and extrarenal anomalies in the prenatal period supports the existence of important pathology. Ultrasonography should be performed on all babies with ANH in the postnatal period, and the follow-up of the patients should be done according to the anteroposterior renal pelvic diameter and the grading recommended by the Society for Fetal Urology. Surgical intervention is vital according to some criteria in patients with progressive hydronephrosis and vesicoureteral reflux.

Key words: Antenatal hydronephrosis, surgical intervention, vesicoureteral reflux

DEFINITION

Hydronephrosis is swelling of one or both kidneys. Hydronephrosis occurs as a result of enlargement of the renal pelvis and/or calyces. In infants diagnosed with hydronephrosis before birth, this condition is defined as antenatal hydronephrosis (AHN).[1]

ETIOLOGY

Many pathological conditions can cause AHN. AHN can occur due to or without a urinary tract anomaly. AHN without urinary tract anomaly has been termed isolated ANH (IAHN). IAHN is the etiology in the majority of infants with hydronephrosis. IAHN is believed to result from a physiological expansion of the developing ureter. The etiology of IAHN has not been fully elucidated, and additional studies are needed for this.[2]

Approximately 60% of AHNs are temporary and physiological hydronephrosis. Although ureteropelvic junction obstruction and vesicoureteral reflux (VUR) the most common urinary tract anomalies, the pathologies shown in Table 1 can be observed.[3]

EPIDEMIOLOGY

Hydronephrosis is the most common pathological finding in the urinary tract in antenatal screening performed by fetal ultrasonography (US) and constitutes 50% of all congenital anomalies. In studies conducted, it was found that 0.6–1.4% of fetuses had AHN. The incidence of a significant uropathy in association with hydronephrosis is 0.2%. Male/female ratio is 2/1 and 20–40% of the cases are bilateral. There is a positive family history of up to 8% (renal agenesis, multicystic kidney, polycystic kidney, and reflux nephropathy) in affected fetuses. It is stated that the rate of urological diseases requiring surgical intervention is between 4.1 and 15.4%. Studies have also shown that the timing of hydronephrosis is important. Early onset of hydronephrosis in fetal development is directly related to the prognosis.[1,4-10]
PATHOPHYSIOLOGY

The ureter begins development as a solid cord of tissue that lengthens and canalizes during embryological development. The urogenital sinus undergoes differentiation to form the bladder and urethra at 10 weeks’ gestation and 12 weeks’ gestation, respectively. Current technology does not allow renal imaging before completion of nephrogenesis. After the fetus is formed, the placenta acts as a fetal hemodializer, maintaining salt, and water homeostasis. The fetal kidney begins to produce hypotonic urine between the 5th and 9th weeks of pregnancy.\(^{[11,12]}\)

A deficiency at any point along the urinary tract after fetal kidney begins to function may present as ANH, causing temporary or permanent partial or complete obstruction of urine flow, and causing proximal expansion of the collection system. A deficiency at any point along the urinary tract after fetal kidney begins to function can lead to transient or permanent partial or complete obstruction of urine flow, causing proximal dilation of the collecting system that manifests as ANH. This obstructive process is mostly temporary and may not be pathological. However, if there is significant obstruction and is permanent, nephrogenic tissue may be affected, resulting in varying degrees of cystic dysplasia and renal failure.\(^{[13]}\)

Most anomalies of the urinary tract detected during prenatal period are characterized by hydronephrosis or enlargement of the upper urinary tract due to their obstructive nature. Furthermore, ANH can be the result of non-obstructive processes, such as VUR, non-refluxing non-obstructed megaureter, and prune belly syndrome. Urine produced in the kidneys is the main component of amniotic fluid, which is necessary for normal lung development and prevention of compression deformities. Obstructive lesions, especially bilateral lesions, are harmful to the developing kidneys and lungs.\(^{[14,15]}\)

Josephson reported that obstruction is associated with decreased renal blood flow, glomerular filtration, and potassium excretion, and only a small percentage of this damage is benefited by early intervention. Although there has not been much success in the current studies, we think that future studies will allow fetal surgical interventions to prevent obstruction in pathological ANH detected in the prenatal period.\(^{[16,17]}\)

Prenatal Diagnosis and Follow-Up

Routine use of fetal US enables early detection of many intrauterine anomalies. Two methods are used to detect ANH. The first is the anteroposterior renal pelvic diameter (APRPD) measurement and the second is the grading system developed by the Society of Fetal Urology (SFU). SFU has developed a grading based on the US image of the long axis of the renal parenchyma and pelvocalyceal system \([\text{Tables 2 and 3}].^{[18]}\)

SFU grading system in ANH measurements is very valuable for an academic evaluation. However, the SFU grading system cannot be used much in practice in the detection of hydronephrosis in the intrauterine period due to its application and evaluation difficulties. For this reason, APRPD measurement is the most frequently used method and its value is high in practical application. Values with prognostic significance determined in the measurements made in the 2nd and 3rd trimesters of pregnancy using APRPD are shown in \(\text{Table 2}.^{[21,22]}\)

AHN should be diagnosed using APRPD in the prenatal period and graded by the same method. APRPD, values that are 4 mm and above in the second trimester and 7 mm and above in the third trimester are considered abnormal and require postpartum evaluation. In cases with unilateral hydronephrosis, US should be performed once in the third trimester. In cases with bilateral hydronephrosis, US should be performed once a month until delivery, depending on the presence of symptoms suggestive of the lower urinary tract obstruction (progressive hydronephrosis, oligohydramnios, dilated, or thickened wall bladder) \([\text{Figure 1}].\) Diagnostic and therapeutic intervention in the

<table>
<thead>
<tr>
<th>Table 1: Urinary system anomalies observed in pediatric hydronephrosis</th>
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<tbody>
<tr>
<td>• Ureteropelvic junction obstruction</td>
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<tr>
<td>• Vesicoureteral reflux</td>
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<tr>
<td>• Ureterovesical stricture</td>
</tr>
<tr>
<td>• Urethral atresia</td>
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<td>• Anterior urethral valve</td>
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<td>• Fetal folds</td>
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<tr>
<td>• Extrarenal pelvis</td>
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<tr>
<td>• Multicystic dysplastic kidney</td>
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<tr>
<td>• Peripelvic cysts</td>
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<tr>
<td>• Primary non-obstructive megaureter</td>
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<tr>
<td>• Megacalycosis</td>
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<td>• Neurogenic bladder</td>
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<tr>
<td>• Ectopic ureter</td>
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<tr>
<td>• Ureterocele</td>
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<tr>
<td>• Posterior urethral valve</td>
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<tr>
<td>• Prune-belly syndrome</td>
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<tr>
<td>• Tumors</td>
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<td>• Congenital urethral stricture</td>
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| Table 2: AHN definition and staging according to APRPD measurement\(^{[19]}\) |
|--------------------------|----------------|----------------|----------------|
| **Classification of AHN** | **Second trimester APRPD (mm)** | **Third trimester APRPD (mm)** | **Postnatal (mm)** |
| Mild                     | 4–6            | 7–9            | 7–9            |
| Moderate                 | 7–10           | 10–15          | 9–15           |
| Severe                   | >10            | >15            | >15            |

AHN: Antenatal hydronephrosis, APRPD: Anteroposterior renal pelvic diameter
prenatal period should only be considered in the presence of the lower urinary tract obstruction. If there is no life-threatening problem outside of the kidney in any AHN case after the 20th week of pregnancy, the pregnancy is not terminated. Infants with a high probability of detecting severe urological anomalies should be referred to a Pediatric Nephrology-Urology Center immediately after birth.[7,21-36]

**POSTNATAL EVALUATION AND MANAGEMENT**

Physical examination plays an important role in the evaluation of a baby with hydronephrosis. Undescended testis, association of anterior abdominal wall defects (Prune-Belly syndrome), presence of abdominal mass (ureteropelvic junction obstruction or multicystic dysplastic kidney), and palpation of the bladder (posterior urethral valve) are important findings.[3]

Figure 2 depicts the management of the follow-up and treatment of an infant with ANH.[21,22] The first step of ANH evaluation is urinary system US. Relative oliguria is seen in newborns at 24–72 h and hydronephrosis may not be observed in USG performed at this time. In patients with suspected posterior urethral valve, history of oligohydramnios, hydronephrosis of the solitary kidney, and bilateral severe hydronephrosis evaluation the first US should be performed within 24–48 h. In other patients, the first US should preferably be done within 3–7 days [Figure 2].[21,22] In the postnatal period, it is more appropriate to monitor infants with the SFU staging system, in which APRPD measurement, calyceal dilatation degree, and parenchymal involvement are evaluated in more detail [Table 3].[21] In addition, kidney echogenicity, ureter dilatation, and bladder wall problems should be evaluated.

Voiding cystourethrogram (VCUG) should be performed in cases with suspected bladder outlet obstruction and SFU Grade 3-4.[1] Hydronephrosis is defined as SFU ≥Grade 1 or APRPD ≥7 mm in a newborn baby. In babies with APRPD <10 mm in the antenatal third trimester, Grade 1-2 hydronephrosis is usually detected in the postnatal period according to SFU. It is reported that hydronephrosis in these babies is probably not associated with obstruction, and the recovery rate is 98%.[34,35] Although it is not certain in cases with Grade 3-4 hydronephrosis or APRPD >12 mm according to SFU, it is likely to be a urological problem requiring surgical correction.[22,37]

US performed in the 1st week of life is insufficient to detect all abnormalities of the kidney and urinary system due to the low urine amount due to dehydration and low glomerular filtration rate. US performed in the 4th week is more sensitive and specific in detecting obstructive problems. Even if their first US is normal, all infants with AHN should be re-evaluated by US at the 4th week. The fact that these two USs performed in the first 4 weeks are normal is quite successful in excluding obstructive kidney diseases and severe dilated VUR. Patients with SFU Stage 0 and APRPD <7 mm as a result of US performed at the 4th week should not be considered as hydronephrosis and these cases need not be followed up.[21,29,37]

Patients who are evaluated as unilateral or bilateral, isolated (without ureter enlargement, bladder problem, and kidney parenchyma problem) mild hydronephrosis (APRPD <10 mm or SFU Grade 1-2) in the first two US can be monitored only by US. The frequency of follow-up can be performed every 3–6 months, and then every 6–12 months, provided that it is evaluated according to the severity indicators of hydronephrosis. Most babies with mild hydronephrosis (SFU Stage 1-2, APRPD <10 mm) generally do not pose a significant problem for long-term follow-up. Hydronephrosis regresses spontaneously in the first 2 years of life in the
Table 3: Society of Fetal Urology grading system in antenatal hydronephrosis\[20\]

<table>
<thead>
<tr>
<th>Grade</th>
<th>Figure</th>
<th>Central renal complex</th>
<th>Renal parenchyma thickness</th>
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<tbody>
<tr>
<td>0</td>
<td><img src="image" alt="Normal" /></td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>I</td>
<td><img src="image" alt="Urine in pelvis barely splits sinus" /></td>
<td>Urine in pelvis barely splits sinus</td>
<td>Normal</td>
</tr>
<tr>
<td>II</td>
<td><img src="image" alt="Evident splitting of pelvis and major calyces" /></td>
<td>Evident splitting of pelvis and major calyces</td>
<td>Normal</td>
</tr>
<tr>
<td>III</td>
<td><img src="image" alt="Wide splitting of pelvis, major and minor calyces" /></td>
<td>Wide splitting of pelvis, major and minor calyces</td>
<td>Normal</td>
</tr>
<tr>
<td>IV</td>
<td><img src="image" alt="Further splitting of pelvis, major and and minor calyces" /></td>
<td>Further splitting of pelvis, major and and minor calyces</td>
<td>Reduced</td>
</tr>
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majority of patients, and non-US radiological examination or antibiotic prophylaxis is not required for these babies. Infants with moderate hydronephrosis with an APRPD of 10–15 mm can be followed up safely with US only, provided that the family is informed about urinary tract infection (UTI) and follow-up for UTI. Infants with APRPD >15 mm at baseline and SFU Stages 3-4 should be followed more closely. For these patients, it is extremely important to reveal the enlargement of the renal pelvis, calices, or ureters, or increased thinning of the cortical parenchyma. These patients should be imaged with VCUG between 4 and 6 weeks. According to the VCUG result, act as in the algorithm.[38-42]

VCUG INDICATIONS[43-45]
- Within 1–3 days of life in babies with signs of the lower urinary tract obstruction
- Infants with SFU Grades 3-4 on first postnatal US
- VCUG should be withdrawn after the urine becomes sterile in babies with AHN and febrile UTI during follow-up
- In USGs, VCUG should be withdrawn within 4–6 weeks in infants with APRPD> 15 mm, SFU Stage 3-4 or one of the criteria of ureter enlargement.

99MTC-MERCAPTOACETYLTRIGLYCINE INDICATIONS
- Patients with moderate to severe hydronephrosis (APRPD> 10 mm and SFU Grade 3-4) but without VUR
- Regardless of the grade, patients with a dilated ureter, and no VUR should be evaluated with diuretic renography.

UTI AND CONTINUOUS ANTIBIOTIC PROPHYLAXIS
The families of all babies with AHN should be informed about the subjective UTI findings of this age group and the necessity of absolute routine urine analysis and correct urine culture test in cases with fever. Routine urinalysis and urine culture can be taken in infants and until the family becomes conscious, monthly/2-month periods. Afterward, when a UTI clinic is suspected or after a fever, a routine urinalysis should be performed. Urine culture should be done in case of nitrite and/or leukocyte esterase positive. Circumcision may be recommended for boys. The diagnosis of febrile UTI in the follow-up changes the follow-up plan in terms of VUR. Preventive antibiotic treatment should be initiated in patients with moderate to severe hydronephrosis (APRPD>= 10 mm and SFU Grade 3-4) or dilated ureter until the diagnosis is completed or in patients with febrile UTI during the follow-up period and all patients with VUR.[9,22,46] Trimethoprim-sulfamethoxazole should not be used as a prophylactic antibiotic in newborns, as it prevents the binding of bilirubin to albumin. Instead, oral amoxicillin should be started at a dose of 10 mg/kg/day as a single daily dose.

SURGICAL INTERVENTION INDICATIONS[22,43,47]
- Cases with VUR causing recurrent UTIs and developing new scar in renal parenchyma
- Infants with signs of lower urinary tract obstruction (progressive hydronephrosis, bilateral hydronephrosis, dilated or thickened-walled inadequate emptying bladder, and dilated posterior urethra)
- Cases who remained as 4th and 5th degree VUR at the end of the 1st year
- Cases with a radionuclide half-life ($t_{1/2}$) > 20 min in diuretic renography, not allowing flow and/or having differential kidney function lower than 40% on the side with obstruction
- Cases with posterior urethral valves should be performed early urethral catheterization, electrolyte abnormalities should be corrected and referred to pediatric urology centers for treatment of possible complications and surgical intervention
- Other indications for surgery are pain, palpable renal mass in the flank, and recurrent febrile UTIs.

CONCLUSION
When looking at the current studies in the literature, it was observed that there was no consensus on the evaluation and management of patients with AHN. In the light of the reviewed literature, AHN management algorithms were created according to the current data in the prenatal and postnatal period. The criteria for surgical treatment in AHN are still unclear. Thanks to the basic and clinical studies to be carried out in the future, the appropriate approach to these patients or the criteria to be selected for the cases to be operated will become clearer. Antibiotic prophylaxis and, if necessary, surgical intervention are vital for the follow-up of patients with AHN and to prevent renal failure with renal scarring after VUR.

REFERENCES
Engin: Antenatal hydronephrosis
