Vesicoureteral Reflux in Neonates with Hydronephrosis; Role of Imaging Tools

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Abstract

Objective: Neonatal Hydronephrosis is a common abnormality diagnosed ante- or postnatally. The aim of this study was to determine the prevalence and severity of vesicoureteral reflux (VUR) in neonates with antenatal or postnatal hydronephrosis and the value of ultrasonography as a noninvasive tool for VUR prediction.

Methods: In a prospective study, 202 infants with neonatal hydronephrosis were studied. Two successive renal ultrasound examinations were performed at 1 and 4-6 weeks after birth in neonates with antenatal hydronephrosis or immediately after presentation. Voiding cystourethography (VCUG) was performed in all infants.

Findings: The incidence of VUR was 29.7%, of which 17.8% had severe (grade IV-V) reflux. 27% of 133 neonates with unilateral and 34.8% of 69 cases with bilateral hydronephrosis had VUR. Although a significant association was observed between severity of hydronephrosis and VUR, 5.9% of normal appearing and 7.8% of grade 1 hydronephrotic neonates had high-grade reflux.

Conclusion: VUR was observed significantly in hydronephrotic neonates. A normal or mildly hydronephrotic urinary tract on ultrasound scan cannot exclude presence of severe VUR. We recommend performing VCUG in all hydronephrotic newborns.


Key Words: Vesicoureteral reflux; Hydronephrosis; Voiding cystoureterography; Ultrasound

Introduction

The routine fetal ultrasonography is widely used for diagnosis of many fetal anomalies including upper urinary tract dilation [1]. Neonatal hydronephrosis is a common abnormality that could be diagnosed ante- or postnatally. The incidence
of antenatal hydronephrosis is 2-9 per 1000 infants\[2,3\]. Although most cases of antenatal hydronephrosis are due to renal pelvis dilatation with or without obstruction, vesicoureteral reflux (VUR) is a common cause occurring in 10 to 15 percent of them \[4,5\].

Some neonates that were not diagnosed prenatally may present with neonatal infection or other nonspecific signs and symptoms. Early detection of VUR in neonates and infants is critical due to inducing higher risk of renal scarring in very young children \[6\].

Nephropathy induced by vesicoureteral reflux is one important cause of the end stage renal failure in children\[7\]. There are several controversial studies on optimal length of follow up of these neonates after birth \[8,9\]. Whereas VUR is detected in voiding cystourethrography (VCUG) in a substantial proportion of sonographically normal kidneys, many children with incidentally detected mild renal pelvic distention have no VUR \[10\].

The traditional algorithm for the evaluation of hydronephrosis is to perform VCUG in the first week of the baby’s life, as the value of VCUG to detect reflux would potentially save asymptomatic children from future renal damage \[11\]. Some authors question the custom need for VCUG, because unlike ultrasound, VCUG is invasive and distressful to the child and carries a significant radiation burden \[12,13\].

In spite of these concerns with VCUG, many physicians still perform VCUG in all infants with prenatal hydronephrosis \[14-17\].

With regard to the importance of application of VCUG in neonatal dysfunction, the aim of this study was to determine the prevalence of VUR in neonates with antenatal and neonatal hydronephrosis and to assess the value of ultrasonography scan as a noninvasive tool for VUR diagnosis.

Subjects and Methods

After obtaining the permission from the Research Committee at Mazandaran University of Medical Sciences, this descriptive study was carried out in Booali Sina Hospital, Sari, Iran, from September 2004 to March 2008. All newborns referred to the pediatric nephrology clinic with antenatal or postnatal diagnosis of hydronephrosis (renal pelvis anteroposterior diameter ≥4 mm before 33 weeks gestational age or ≥7 mm after 33 weeks and in neonatal period) were enrolled in this study.

Abdominal ultrasonography was performed to determine the presence and severity of hydronephrosis on the first week of infant life or immediately after admission of patients.

All patients received Cephalexin 10 mg/kg daily. Renal ultrasonography was repeated at 4th-6th week. The postnatal ultrasonography scans were performed by the same trained examiner using a General Electric machine. VCUG was performed in early admission for all infants that had bilateral hydronephrosis, dilated urethra, a thick walled bladder or urinary tract infection (UTI). In other infants VCUG was performed at 4th-6th week of age. Reflux was defined according to the international classification of reflux (grade 1–5)\[18\] and hydronephrosis was defined according to the Society for Fetal Urology (grade 1-4)\[19\]. If postnatal ultrasonography showed renal pelvis dilatation equal to or more than 10 mm, the renal scintigraphy with 99mTc-DTPA (technetium-99m diethylene triamine penta-acetic acid) was performed after the second month of age.

The data are shown as mean ± standard deviation (SD) and analyzed with using Chi-square and non-parametric Mann Whitney U test. The significance level was determined as less than 0.05 (SPSS 11.5 software, USA).

Findings

A total of 202 patients were enrolled in this study. Demographic characteristics and the presentation of patients are demonstrated in table 1. One hundred and sixty eight patients (83.2%) have been diagnosed prenatally and other patients were referred with postnatal symptoms. Unilateral hydronephrosis was more common than bilateral one (65.8% vs. 34.2%).
**Table 1:** Demographic data and presentation of neonates with hydronephrosis (n=202)

<table>
<thead>
<tr>
<th>Presentation</th>
<th>Frequency (%)</th>
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<tbody>
<tr>
<td>Male (%)</td>
<td>171 (84.7%)</td>
</tr>
<tr>
<td>Unilateral/Bilateral involvement</td>
<td>133/69 (66%/34%)</td>
</tr>
<tr>
<td>Prenatal diagnosis</td>
<td>168 (83.2%)</td>
</tr>
</tbody>
</table>

**Clues for postnatal Diagnosis:**
- Infection: 15 (7.4%)
- Voiding problems: 5 (2.5%)
- Accidental: 3 (1.5%)
- Auricular defects: 2 (1%)
- Associated anomalies: 2 (1%)
- Positive family history: 1 (0.5%)
- Others: 6 (3%)

**Presence of Reflux:** 60 (29.7%)

VUR was identified in 60 (29.7%) of newborns including 48 males (28% of all males) and 12 females (38.7% of all females). The rate of VUR was 27.1% in unilateral hydronephrosis and 34.8% in bilateral involvement. Table 2 shows the grades of VUR. Pathological findings of hydronephrosis are given in table 3. Three most common findings were ureteropelvic junction obstruction (UPJO) (43.6%), transient mild hydronephrosis (20.3%) and VUR (17.8%).

The severity of reflux was classified in mild (equal to grade I or II), moderate (grade III) and severe (grade IV or V). A percentage of 14.3% of patients with unilateral hydronephrosis and 24.5% of patients with bilateral hydronephrosis had severe VUR (Table 4). The ultrasonography finding was normal in seven patients at first week; three of these 7 patients had VUR; one unilateral grade III, one bilateral grade I, and one bilateral grade III. The ultrasonography finding was normal in nine patients at sixth week, three of them had VUR, while two patients had bilateral grade III (one with bilateral grade III left and grade 1 right and the other with left grade IV) VUR. Two patients had in the first as well as in the sixth week normal ultrasound with normal VCUG.

Seventy seven renal units of the 271 units with hydronephrosis detected by ultrasonography had VUR, this was grade I in 6, Grade II in 10, grade III in 16, grade IV in 22, and grade V in 23 cases. There was significant correlation

**Table 2:** Grade of vesicoureteral reflux in unilateral and all hydronephrotic neonates

<table>
<thead>
<tr>
<th>Grade of VUR</th>
<th>Unilateral hydronephrotic infants with VUR (n=36 of 133)</th>
<th>Bilateral hydronephrotic infants with VUR (n=24 of 69)</th>
<th>All infants with VUR (n=60 of 202)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3 (2.3%)</td>
<td>1 (1.5%)</td>
<td>4 (2%)</td>
</tr>
<tr>
<td>2</td>
<td>8 (6%)</td>
<td>0 (0%)</td>
<td>8 (4%)</td>
</tr>
<tr>
<td>3</td>
<td>6 (4.5%)</td>
<td>6 (8.7%)</td>
<td>12 (5.9%)</td>
</tr>
<tr>
<td>4</td>
<td>13 (9.8%)</td>
<td>7 (10%)</td>
<td>20 (9.9%)</td>
</tr>
<tr>
<td>5</td>
<td>6 (4.5%)</td>
<td>10 (14.5%)</td>
<td>16 (7.9%)</td>
</tr>
</tbody>
</table>

*VUR: vesicoureteral reflux*
Table 3: Pathologies diagnosed in hydronephrotic neonates (n=202)

<table>
<thead>
<tr>
<th>Pathologies</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ureteropelvic junction obstruction</td>
<td>88 (43.6)</td>
</tr>
<tr>
<td>Transient hydronephrosis</td>
<td>41 (20.3)</td>
</tr>
<tr>
<td>Vesicoureteral reflux</td>
<td>36 (17.8)</td>
</tr>
<tr>
<td>Ureterovesical junction Obstruction</td>
<td>9 (4.5)</td>
</tr>
<tr>
<td>Multicystic dysplastic kidney</td>
<td>7 (3.5)</td>
</tr>
<tr>
<td>Posterior urethral valve</td>
<td>7 (3.5)</td>
</tr>
<tr>
<td>Duplication</td>
<td>5 (2.5)</td>
</tr>
<tr>
<td>Others</td>
<td>9 (4.5)</td>
</tr>
</tbody>
</table>

between grade of hydronephrosis in postnatal ultrasonography and presence and severity of VUR ($P=0.025$). The frequency of VUR in hydronephrotic neonates was 21.1%, 25%, 32% and 40.1% at grade 1, 2, 3 and 4, respectively. It is important to note that 7.8% of neonates with grade 1 postnatal hydronephrosis, 13% of grade 2 and 5.9% of neonates with normal postnatal ultrasonography had severe (grade IV-V) reflux.

Complication occurred in six patients undergoing VCUG: 3 cases of acute pyelonephritis shortly after performance of VCUG while on chemoprophylaxis, 2 cases of failure of urethral catheterization and one patient with gross hematuria.

Discussion

Currently an increasing number of neonatal uropathies including VUR are detected by ultrasonography. Prior to application of the prenatal ultrasonography, hydronephrosis was often observed symptomatically with infection or pain[20].

Hydronephrosis has much variation in its etiology and clinical outcome[3]. They are focused mainly on work up and management of prenatal hydronephrosis [21-24]. In our study, 29.7% of neonates with a history of prenatal or postnatal hydronephrosis had VUR, which was similar to other studies [25]. We observed no significant difference in degree of VUR with gender of patients, presentation and laterality of hydronephrosis.

One important and not fully answered question is whether it is necessary to use VCUG for all neonates with hydronephrosis. Three important points should be considered in this regard. First, does VUR have adequate prevalence in hydronephrotic neonates? Second, what are the importance and severity of reflux diagnosed in these infants? Third, would other what are the importance and severity of reflux

Table 4: Severity of VUR diagnosed in hydronephrotic neonates

<table>
<thead>
<tr>
<th>Severity of VUR</th>
<th>Neonates with unilateral HN‡ (n=133)</th>
<th>Neonates with bilateral HN (n=69)</th>
<th>All neonates (n=202)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No VUR*</td>
<td>97 (72.9%)</td>
<td>45 (65.2%)</td>
<td>142 (70.3%)</td>
</tr>
<tr>
<td>Mild</td>
<td>11 (8.3%)</td>
<td>1 (1.4%)</td>
<td>12 (5.9%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>6 (4.5%)</td>
<td>6 (8.7%)</td>
<td>12 (5.9%)</td>
</tr>
<tr>
<td>Severe</td>
<td>19 (14.3%)</td>
<td>17 (24.6%)</td>
<td>36 (17.8%)</td>
</tr>
</tbody>
</table>

* VUR: vesicoureteral reflux / HN: hydronephrosis
diagnosed in these infants? Third, would other noninvasive imaging studies (e.g., ultrasonography) be helpful for detection of VUR in neonatal hydronephrosis instead of VCUG? Our study showed that one out of three neonates with hydronephrosis has VUR which is consistent with the reported incidence in the literature. Brophy et al. observed VUR in 21% of infants with antenatal hydronephrosis. Zerrin showed that 38% of neonates with hydronephrosis had VUR. Similar findings were reported by other studies. The main difference between our study and the previous similar studies is that we enrolled both antenatally as well as postnatally diagnosed neonates with hydronephrosis, whereas only prenatally diagnosed infants were included in other studies. In our study, 26.8% of 168 patients diagnosed antenatally, had VUR, a rate that was similar to those of other studies.

Similar to some reports, our results demonstrate the importance of VUR diagnosed in these neonates. 17.8% of the neonates had severe degree (grade IV and V) reflux. Farhat reported that 48% of neonates with antenatal hydronephrosis have high grade (IV to V) reflux. Similarly, Ismaili et al. showed that 36% of 43 infants with primary VUR identified from a cohort of 497 infants with fetal renal pelvis dilatation had high grade (IV-V) VUR. Other studies also reported the importance of VUR in infants.

The use of neonatal renal US in screening infants for VCUG is controversial. Several studies suggested that ultrasonography is not a suitable tool to be used instead of VCUG, because it detected only small numbers of patients with VUR. However, Ismaili suggested that ultrasonography signs related to VUR should not be limited to renal pelvis diameter, and ultrasonography has significant ability to select patients who do not need to undergo a VCUG. They included 190 infants with neonatal hydronephrosis, when two successive neonatal ultrasonography at day 5 and one month after birth were normal (74 infants), VCUG showed abnormalities in only 5 (6.7%) patients, and concluded that VCUG should not be used routinely in patients with two successive normal renal neonatal ultrasonograms. We found only two neonates with normal ultrasound both in first and sixth week, in whom VUR has not been observed.

Berrocal showed that VUR occurred in 25.7% of mild hydronephrotic kidneys and 26.3% of undistended kidneys contralateral to hydronephrotic ones. There was a poor correlation between VUR and mild hydronephrosis and the latter should not be considered in itself an indication for VCUG in asymptomatic neonates. In our study, there was a significant association between ultrasonogram findings and VUR, but it was interesting that a considerable portion of neonates with normal postnatal ultrasonography or low grade hydronephrosis had severe reflux. Therefore, ultrasound is not a suitable replacement imaging tool for VCUG. Therefore, we recommend to perform later imaging for all neonates referred with hydronephrosis.

One limitation of our study was that we have not presented the outcome of patients (e.g., renal scarring, hypertension, renal failure, and need to surgery) due to reflux. It should be noted that we are following patients enrolled in this study to assess the impact of pre- and postnatal hydronephrosis on the long-term renal function.

**Conclusion**

VUR is a relatively common finding in neonates referred for hydronephrosis. A large portion of these patients has severe VUR that could not be desirably diagnosed with ultrasonography. We recommend VCUG for even a low grade hydronephrosis.

**Acknowledgment**

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References


