

# Simplified Diagnostic Algorithm for Evaluation of Neonates With Prenatally Detected Hydronephrosis

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**Introduction.** The management of neonates with congenital hydronephrosis (CHN) diagnosed antenatally is still controversial. **Materials and Methods.** A prospective study was performed in all newborn infants with CHN born over a 2-year period in order to identify which neonates require a full radiologic investigation including investigation with invasive tests such as voiding cystoureterography (VCUG) and diuretic-enhanced renography. Data on kidney ultrasonography, VCUG, and diuretic renography were collected. The ultrasound grading of hydronephrosis was determined according to Society of Fetal Urology criteria.

**Results.** Sixty-one neonates (47 boys and 14 girls) with CHN were enrolled. All underwent kidney ultrasonography within 72 to 96 hours after birth. Four (7%) had no residual CHN, 34 (56%) had and 23 (38%) unilateral CHN. Of the 41 newborns exposed to diuretic renography, 18 (44%) had ureteropelvic junction obstruction (UPJO). Of the 34 infants that underwent VCUG, 8 (24%) had vesicoureteral reflux (7 bilateral grade 2 or higher, 1 unilateral grade 1 CHN SFU classification). None of the unilateral grade 1 or 2 CHN due to UPJO had vesicoureteral reflux and none with vesicoureteral reflux had UPJO. Twelve patients required surgery (7 had UPJO and 3 high-grade vesicoureteral reflux).

**Conclusions.** These data suggest that mild to moderate unilateral or bilateral CHN rarely coexists with severe obstruction or vesicoureteral reflux. Therefore, systemic VCUG and renography in such patients do not seem justified. Postnatal ultrasonography in combination with renography and VCUG is warranted in the routine examination of neonates presenting with severe unilateral or bilateral CHN.

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## INTRODUCTION

Congenital hydronephrosis (CHN) is the most common urinary tract anomaly, comprising 50% of all urogenital system malformations.<sup>1-4</sup> Early diagnosis and initiation of the treatment are vital to preserve kidney function and to retard the progression of chronic kidney disease.

Technical advances in obstetrical ultrasonography have allowed earlier and improved imaging of

the fetal urinary tract, thus offering the potential for earlier diagnosis and possibly intervention.<sup>5</sup> Often, these prenatal ultrasonography findings are the sole basis upon which parental counseling is given and other postnatal radiologic studies are performed to determine renal outcome. The degree of renal dilatation, measured by the anteroposterior diameter of the renal pelvis, has been investigated extensively as a predictive tool

of neonatal outcome.<sup>6-8</sup> Yet, no clear consensus has been reached on which threshold (4 mm to 10 mm) is clinically significant as an indicator of kidney damage.<sup>6,9,10</sup>

It is accepted standard of care (although not supported by evidence-based science) to refer infants with CHN to pediatric nephrology, shortly after birth, for further evaluation. The testing will include urinalysis, serum electrolytes and creatinine concentrations, renal and bladder ultrasonography, voiding cystoureterography (VCUG), and for patients with significant hydronephrosis, a diuretic-enhanced renography using technetium Tc 99m diethylene triamine pentaacetic acid (<sup>99m</sup>Tc-DTPA) or technetium Tc 99m mercaptoacetyl triglycine (<sup>99m</sup>Tc-MAG-III) with furosemide administration to estimate absolute and differential kidney function and presence of ureteropelvic junction obstruction (UPJO).<sup>11-13</sup> However, a lack of standardized evaluation limits the development of randomized prospective trials.

Vesicoureteral reflux (VUR) is detected in 20% to 30% of neonates with CHN,<sup>14</sup> and it is thought to increase the risk of kidney damage when children have recurrent urinary tract infections.<sup>15</sup> Currently, many newborn infants who are found to have CHN are also treated with the daily administration of antibiotics to prophylaxis against urinary tract infections and kidney damage. However, there have been no well-designed research studies to show that these practices are necessary in all newborn infants with CHN.<sup>16,17</sup> In addition, literature is unclear regarding the frequency and time interval of follow-up examinations.

The goals of the current study were first to identify clinically significant urinary tract obstruction and VUR that can have negative impact on the developing kidney and second to select which neonates require a full investigation and which do not in order to develop an algorithm for the postnatal evaluation of newborn with CHN.

## MATERIALS AND METHODS

Between April 2002 and January 2010, all neonates born at Rush University Medical Center, Chicago, Illinois, with fetal hydronephrosis were prospectively studied. The study was approved by the Institutional Review Board of the Rush University Medical Center. Maternal written informed consent was obtained prior to the

study. All subjects were assured anonymity in compliance with the Health Insurance Probability and Accountability Act.

Data collected on patient characteristics included delivery data, gender, gestational age, body weight, blood pressure, site of CHN, additional urological anomalies (such as prune belly syndrome or cystic dysplastic kidney), urinalysis, serum creatinine, blood urea nitrogen (BUN), kidney and bladder ultrasonography, VCUG, and <sup>99m</sup>Tc-DTPA or <sup>99m</sup>Tc-MAG-III diuretic renography (furosemide washout test). Exclusion criteria were diagnosis of cystic renal dysplasia with poorly functioning kidney and neurogenic bladder.

All babies with fetal hydronephrosis underwent an ultrasonography examination between 3 and 4 days of life. All ultrasonography examinations were reviewed and analyzed by a single pediatric radiologist to minimize inter-reviewer variability. The degree of hydronephrosis was graded according to the Society for Fetal Urology (SFU) grading classification, according to which grade 1 represents a split pelvis; grade 2, further dilatation of the renal pelvis with a few visualized calyces permissible; grade 3, renal pelvis dilatation with nearly all calyces dilated but intact parenchyma; and grade 4, renal pelvis dilatation with nearly all calyces dilated and parenchyma atrophy or thinning.<sup>10</sup> Patients were classified based on the greatest SFU classification present, and by either unilateral or bilateral involvement. A recent study has classified patients by renal unit where each kidney and ureter is evaluated individually.<sup>18</sup> However, in the present study we felt that patient classification was preferred over the renal unit classification, given the objective of developing an algorithm for the evaluation of newborn CHN with the marked differences in unilateral versus bilateral results.

Voiding cystourethrography was performed and interpreted by staff pediatric radiologists and diuretic renography of either <sup>99m</sup>Tc-DTPA or <sup>99m</sup>Tc-MAG-III performed and interpreted by staff nuclear medicine physicians. The diagnosis of obstructed hydronephrosis was made when there was a differential kidney function of the affected dilated kidney on the renal scan of less than 40% and the clearance half-life of a diuretic renography was greater than 20 minutes. If there was obstruction, a repeat scan was performed at

4 months of age. If significant reflux was present this was followed by a nuclear VCUG annually.<sup>19</sup>

**RESULTS**

The patient characteristics and radiologic data are summarized in the Table. A total of 61 neonates with antenatal diagnosis of hydronephrosis met the inclusion criteria for enrollment. At the initial evaluation, the enrolled patients had a median age of 4 days with a ratio of 47 boys to 14 girls. Of the 61 patients, 4 (7%) had no residual CHN, 23 (38%) had unilateral CHN, and 34 (56%) had bilateral CHN. In unilateral CHN, grade 1 was present in 3 (5%) and grades 2, 3, and 4 were present in 12 (20%), 4(7%), and 4 (7%), respectively. In bilateral CHN, grade 1 was present in 1 (2%), grade 2 in 15 (25%), grade 3 in 7 (11%), and grade 4 in 11 (18%) infants.

Of the 41 newborns who were exposed to diuretic renography, 18 (44%) had UPJO (9 unilateral and 9 bilateral grade 2 or higher SFU classification). Of the 34 neonates who underwent VCUG, 8 (24%) had VUR (7 bilateral grade 2 or higher and 1 unilateral grade 1 SFU grading).

The order of obtaining a diuretic renogram versus a VCUG was also evaluated to determine if the positive results of one could eliminate the need to obtain the other. In unilateral CHN, 6 of 9 patients with UPJO also obtained VCUG, but none was found to have VUR. Similarly, in bilateral CHN, 6 of 9 patients with UPJO also received VCUG and none had VUR.

Of the 23 patients with unilateral CHN, 3 (13%) required surgery (2 for significant UPJO and 1 for high-grade VUR. Of the 34 patients with bilateral CHN, 9 (26%) required surgical intervention; 1 for a significant UPJO, 1 for bilateral duplication with severe upper pole obstruction in both kidneys, and 7 for posterior urethral valves associated with high-grade reflux with additional anomalies (Table). Thirteen newborns with either unilateral (n = 4) or bilateral (n = 9) CHN had additional renal anomalies, including posterior urethral valve (n = 7), ureterocele (n = 2), prune belly syndrome (n = 1), renal VATER malformation (n = 1), duplex kidney (n = 1), and megacoureter (n = 1).

Thirty-five of 57 patients (61%) with CHN underwent repeat ultrasonography evaluations every 4 months and again at 1-year follow-up examination. Twenty-two patients (7%) did not

Summary of Radiologic and Clinical Data of Studied Patients\*

Parameters	Unilateral Hydronephrosis					Bilateral Hydronephrosis				
	All	Grade I	Grade II	Grade III	Grade IV	All	Grade I	Grade II	Grade III	Grade IV
Number of patients	23/61 (38)	3/61 (5)	12/61 (20)	4/61 (7)	4/61 (7)	34/61 (56)	1/61 (2)	15/61 (25)	7/61 (11)	11/61 (18)
Obtained renal scintigraphy	18/23 (78)	3/3 (100)	9/12 (75)	3/4 (75)	3/4 (75)	23/34	1/1 (100)	10/15 (66)	5/7 (71)	7/11 (64)
Obstruction on renal scintigraphy	9/18 (50)	0/3	3/9 (33)	3/3 (100)	3/3 (100)	9/23 (39)	0/1	1/10 (10)	4/5 (80)	4/7 (57)
Obtained VCUG	12/23 (52)	2/3 (67)	4/12 (33)	3/4 (75)	3/4 (75)	22/34 (65)	0/1	10/15 (66)	4/7 (57)	8/11 (73)
Vesicoureteral reflux on VCUG	1/12 (8)	1/2 (50)	0/4	0/3	0/3	7/22 (32)	0/1	2/10 (20)	1/4 (25)	4/8 (50)
Surgical intervention	3/23 (13)	1/3 (33)	0/12	0/4	2/4 (50)	9/34 (26)	0/1	1/15 (7)	2/7 (29)	6/11 (55)
Placed on prophylactic antibiotics	9 (39)	1/3 (33)	5/12 (42)	1/4 (25)	2/4 (50)	13 (38)	0/1	4/15 (27)	2/7 (29)	7/11 (64)
Developed UTI while on antibiotic prophylaxis	2/23 (9)	0/3	1/12 (8)	0/4	0/4	2/34 (6)	0/1	1/15 (7)	0/7	1/11 (14)

\*VCUG indicates voiding cystourethrography and UTI, urinary tract infection.

complete the study and were lost in the follow-up visits. Twenty-eight of 53 patients (80%) demonstrated complete or partial spontaneous remission. Seven of 35 (20%) demonstrated progression of hydronephrosis according to the SFU classification, but 2 later regressed on subsequent scans. The remaining 5 patients underwent surgery because of deterioration of HD associated with impaired kidney function complicated with recurrent urinary tract infections.

## DISCUSSION

This report describes our center's experience on the postnatal evaluation of children with the diagnosis of antenatal hydronephrosis. In our cohort study, males were more frequently affected with CHN than females with a ratio of 47 boys to 14 girls. This gender bias confirms the high prevalence of fetal urinary tract obstruction previously reported in the literature.<sup>20</sup> In clinical practice, there are no clear indications for the initial timing of the postnatal ultrasonography evaluation in neonates with fetal hydronephrosis. It has been shown that ultrasonography assessments performed shortly after birth or during the first 48 hours of life may underestimate the degree of hydronephrosis relative to later follow-up.<sup>21-23</sup> The results of a recent randomized trial suggested that the optimal timing to obtain the initial ultrasonography was after the first 48 hours of life.<sup>21,22</sup> In our study, the initial postnatal ultrasonography examinations were performed within 72 to 96 hours after birth. In this study, of the 31 neonates with grade 1 to 2 unilateral or bilateral hydronephrosis, none required surgical intervention. This finding is consistent with the previous studies that have demonstrated up to 98% of their newborns with grade 1 and 2 isolated hydronephrosis with or without VUR underwent spontaneous remission in follow-up evaluation.<sup>24-27</sup> Thus, we do not recommend obtaining a diuretic renography or VCUG in the routine evaluation of neonates with grade 1 to 2 unilateral hydronephrosis.

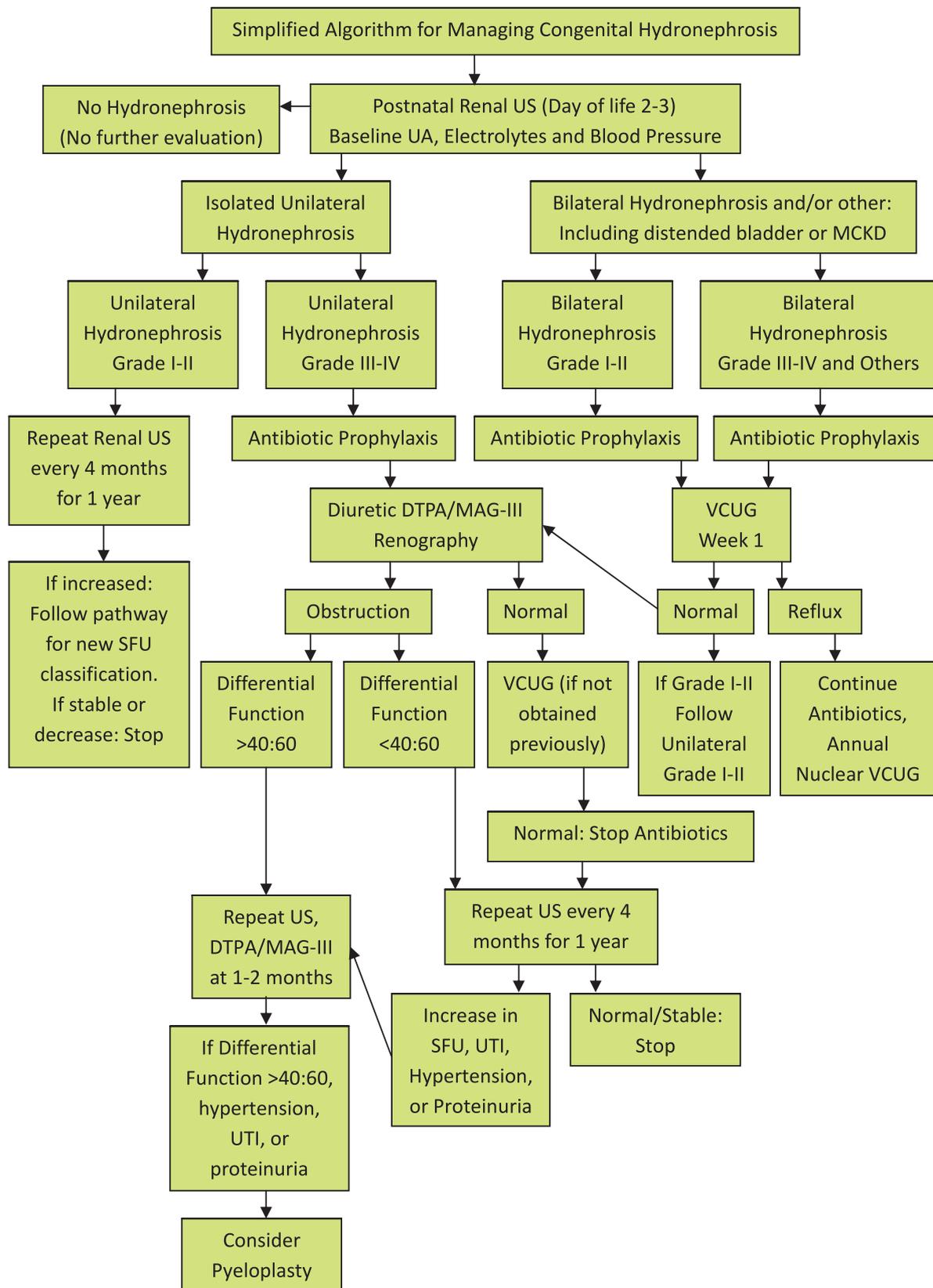
In contrast, the high incidence of surgical interventions for newborns with grade 3 and 4 unilateral (n = 3) or bilateral (n = 7) CHN due to the severe UPJO or high-grade VUR that observed in the present study, warrens the routine use of a diuretic renography in these groups which re-affirm the previously held belief that higher SFU grades of

CHN are associated with a higher rate of surgical intervention, and thus, these patients deserve a more in depth workup. According to the result of our study, despite the high incidence of UPJO, there was no evidence of VUR, suggesting that a VCUG is not indicated in neonates with unilateral CHN regardless of the hydronephrosis grading unless the diuretic renography reveals no evidence of obstruction. However, given the incidence of VUR in the grade 1 to 2 bilateral hydronephrosis (20%) in the present study, we suggest obtaining a VCUG in this group of patients. Furthermore, with the high incidence of VUR associated with PUV in grade 3 to 4 bilateral CHN, we recommend a VCUG should take priority over the diuretic renography in this population (Table).

In patients where there is a distended bladder and the ultrasound findings consistent with posterior urethral valve or impaired kidney function secondary to kidney dysplasia there is a need to assess the patient regardless of the degree of hydronephrosis.<sup>7</sup> Therefore, we recommend grouping these patients with the bilateral hydronephrosis grade 3 to 4 patients for the most stringent evaluation.

Antibiotic prophylaxis for VUR while undergoing VCUG investigation is still the standard of care.<sup>29</sup> Antibiotic prophylaxis is also recommended for severe obstruction.<sup>16</sup> However, we recommend initiation of antibiotic prophylaxis only in patients with moderate to severe (grade 3 or 4) unilateral or bilateral, hydronephrosis until the radiologic investigations (VCUG and renography) are completed. Once reflux or obstructive etiology has been eliminated as etiology for the hydronephrosis antibiotic prophylaxis may be discontinued.

We felt every 4 to 6 months is an adequate interval for follow-up ultrasonography evaluation if the initial ultrasonography reveals significant obstruction. For patients who were determined to have an obstruction on diuretic renography and have differential kidney function greater than 45%, we recommend close follow-up and if this problem persistent a referral for pyeloplasty.<sup>29</sup> In addition, annual follow-up nuclear VCUG is also warranted for patients who are found to have persistent high-grade VUR.<sup>30</sup> Based on these results, we propose the following diagnostic approach on postnatal evaluation of newborns with diagnosis of fetal hydronephrosis (Figure).



Diagnostic algorithm for managing congenital hydronephrosis. UA indicates urinalysis; MCKD, multicystic kidney disease; SFU, Society of Fetal Urology; US, ultrasonography; DTPA, technetium Tc-99m diethylene triamine pentaacetic acid; MAG-III, technetium Tc-99m mercaptoacetyl triglycine; VCUG, voiding cystoureterography; and UTI, urinary tract infection.

The major limitations of this study are the small numbers of patients, selection bias, and loss of follow-up which do not allow us to draw an unequivocal conclusion. Only patients who received a nephrology consultation or referral to pediatric nephrology were recruited for this study. This selects out patients who are more likely to have a pathological etiology of their hydronephrosis as well as higher grades on initial ultrasound. Perhaps, this would be a preferred limitation in an attempt to develop a screening algorithm to catch all pathologic etiologies of hydronephrosis.

### CONCLUSIONS

The result of this study, clearly demonstrates that the SFU grading of CHN determines the extent of radiological evaluations. Our study indicates that mild and moderate unilateral or bilateral CHN rarely coexists with severe UPJO or VUR. Therefore in such patients VCUG and diuretic renography do not seem justified. However, a substantial number of patients with severe CHN are at risk for developing chronic renal disease. Thus, postnatal sonography in combination with renogram scan and VCUG is warranted in the routine examination of neonates presenting with severe unilateral or bilateral CHN.

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This study has been registered by the National Clinical Trial (#01330511).

### CONFLICT OF INTEREST

None declared.

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