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One-Year Follow-Up Results of Patients With Prenatally Diagnosed Hydronephrosis and Evaluation of Renal Functions

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Abstract

Hydronephrosis is the most common urologic anomaly detected in the fetus. Obstructive uropathy can cause long-term mortality and morbidity by leading to renal damage and decreasing renal functions. We aimed to determine the etiological reasons and frequency of prenatal determined hydronephrosis, also to evaluate the association between some (clinical and laboratory) parameters and renal functions during study. 48 patients with antenatally detected hydronephrosis were followed prospectively. The ultrasonography scan and renal functioning tests were performed on day 3rd-7th of life and repeated on week 4th-6th, months 3rd, 6th and 12nd. The degree of hydronephrosis at the end of study was decreased significantly when compared to antenatal hydronephrosis severity ($p<0.05$). Transient hydronephrosis was diagnosed in 22 (28.9%) of 76 renal unit with prenatal hydronephrosis. Ureteropelvic junction obstruction was the most common cause of antenatal hydronephrosis. Positive correlations between the end study glomerular filtration rate (GFR) and tubular reabsorption of phosphate, blood urea nitrogen and creatinine levels were found at the end of the study. Some significant negative correlations between the end study GFR and fractional excretions of K^+ and Mg^{++} were found at several periods of the study. Transient hydronephrosis is one of the most important reasons of prenatally detected hydronephrosis. The patients with antenatal hydronephrosis must be followed-up closely. Tubular functioning test may be impaired in early stages. The episodic evaluation of tubular functions may predict renal damage before the development of renal failure.

Keywords: Prenatal hydronephosis, renal functions, renal ultrasonography

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Introduction

As a result of the increased use of ultrasonography in routine prenatal practice, most anomalies can be detected in the fetus. The presentation of urologic problems of the neonate has changed in this way. The most common organ system anomalies detected by maternal sonography are the genitourinary anomalies.[1] When these anomalies are detected by the prenatal ultrasound (US) and managed, pyelonephritis, hypertension, or even end-stage renal failure associated with these urologic abnormalities could be prevented.[2] Hydronephrosis is the most common detected urologic anomaly of the fetus. However, there is no specific guideline to evaluate these infants; how frequently and which to image or whether specific intervention is necessary. So that the postnatal approach to fetal renal pelvis dilatation remains controversial.[3]

In this prospective study we aimed to determine the etiological reasons and frequency of prenatal determined hydronephrosis, to evaluate the association between some (clinical and laboratory) parameters and renal functions during one year follow-up period.

Highlight

- Hydronephrosis is the most common detected urologic anomaly of the fetus.
- Patients with antenatal hydronephrosis should be evaluated in postnatal period.
- We suggest that a careful follow-up should include the evaluation of renal and tubular functioning tests in addition to other screening methods.

Materials and Methods

Informed consent information was obtained from all patients in the study and the research protocols were approved by the Ethics Committee at Erciyes University (Approval date: 2005, Approval number: 2005/304).

Fourty eight patients born during one year with antenatally detected hydronephrosis were followed prospectively in Erciyes University, Medical Faculty Pediatric Nephrology department. Hydronephrosis was classified into three degrees (mild, moderate, severe) according to antenatally sonographic measurement of fetal renal pelvic diameter and gestational age.[4]

Postnatally, all infants with prenatal hydronephrosis were given prophylactic amoxicilin- (10 mg/kg/day). If both two US findings and voiding cystouretrography (VCUG) were normal antibiotic prophylaxis was discontinued. All children were investigated according to a systematic procedure illustrated in **Figure 1**.

The US scan, renal functioning tests (BUN, creatinine, electrolytes), glomerular filtration rate (GFR) according to Schwartz formula and tubular functioning tests (TRP, FENa, FEK, FEMg, urine Ca/Cr, urine protein/cr) were performed on day 3-7 of life and repeated on weeks 4th-6th, months 3rd, 6th and 12nd. On admission and on every routine visit blood pressure, body weights and lengths were measured, urinalysis and urine culture tests were performed. Urinary tract infection were defined by the presence of 10^5 CFU/mL bacteria in bagged specimens. Infants with proven urinary tract infection were treated with suitable antibiotics.

A voiding cystourethogram was performed for infants whose renal US scan showed greater than 5 mm AP pelvic diameter on day 3rd-7th of life or week 4th-6th. If the VCUG showed the presence of vesicoureteral reflux (VUR), it was classified according to the report of the International Reflux Study Committee.[5]

Surgery was performed in cases with evidence of obstructive injury, which was defined as a reduction in differential renal function below 40%, ultrasonographic progression of hydronephrosis with renal cortical atrophy, and with posterior urethral valve (PUV).

Statistical analysis was performed in SPSS 11.0 programme. Chi-square and Pearson tests were used. A p value of less than 0.05 was considered to be significant.

Results

Demographic data and antenatal findings of patients are given in **Table 1**.

Degree of hydronephrosis at postnatal period and causes of hydronephrosis:

Of the 96 kidney units of 48 patients, 76 units were antenatally detected to be pathological. The degree of hydronephrosis in right units was more commonly severe. The ratio of the patients with severe hydronephrosis was decreased from 43.4% (33 of 76) to 7.8% (6 of 76) at the end of the study. The difference of severe hydronephrosis ratios between beginning and at the end of the study was significant ($p<0.05$).

Postnatal outcome of antenatally hydronephrotic kidney units in each of three degrees are seen on **Table 2**.

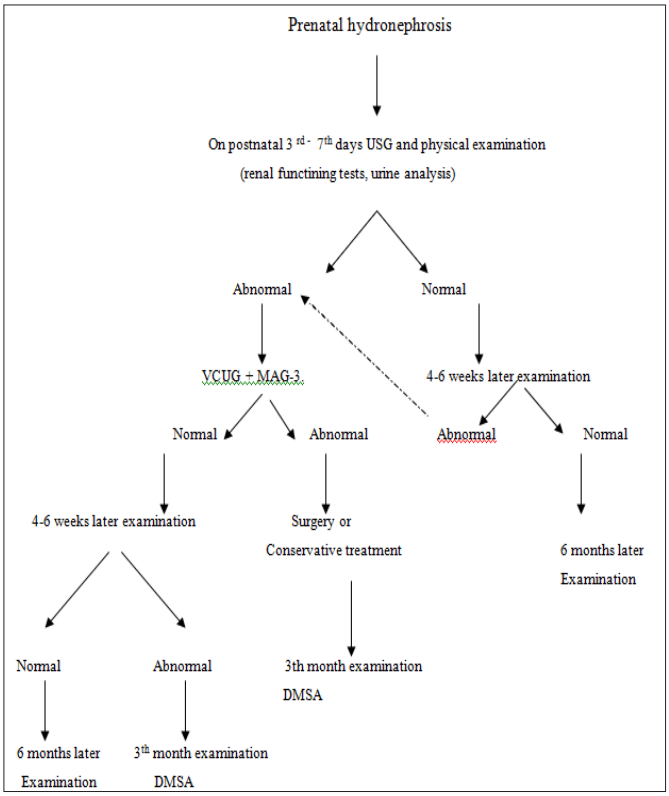

Figure 1. Investigation procedure

Table 1
Demographic data and antenatal findings

Patient number (N)	48
Follow up period (months) Mean ± SD	17.1±5.6
Female/Male	15/33
Antenatal detection time (weeks)	29.6±6.8
<24 weeks	15
≥25 weeks	33
Age of mother (Years)	27.0±5.0
Gestationel age (weeks)	38.6±2.2
The number of renal unit with antenatal detected hydronephrosis	
Right	10
Left	10
Bilateral	28
All	76
The degree of antenatal detected hydronephrosis (number of renal unit)	
Mild	25
Moderate	18
Severe	33

Table 2
Postnatal outcome of antenatally hydronephrotic kidney units

Degree of antenatal hydronephrosis	Postnatal evaluation				
	Not hydronephrosis at any postnatal period (Transient)	Hydronephrosis at the end of the study			
		No	Mild	Moderate	Severe
Mild (n=25)	14	5	6	-	-
Moderate (n=18)	3	7	2	4	2
Severe (n=33)	5	10	4	10	4
Total (n=76)	22	22	12	14	6

Transient hydronephrosis was diagnosed in 22 (28.9%) of 76 renal unit with antenatal hydronephrosis. Antenatal degree of patients with transient hydronephrosis was mild in 14 (63%) of 22, whereas moderate in 3 (14%) and severe in 5 (23%) of 22.

Transient hydronephrosis ratios were 56% (14 of 25) in mild group, 16% (3 of 18) in moderate group and 15% (5 of 33) in severe hydronephrotic kidney units.

Ureteropelvic junction obstruction (UPJO) was the most common cause of antenatal hydronephrosis. In children with UPJO (n=30) the degree of antenatal hydronephrosis was severe in 17 (56.7%), moderate in 9 (30%) and mild in 4 (13.3%). In children with VUR (n=10) the degree of antenatal hydronephrosis was severe in 4 (40%), moderate in 1(10%) and mild in 5 (50%). In children with UPJO the degree of antenatal hydronephrosis was more severe, but in children with VUR it was seemed to be variable.

Ureterovesical junction obstruction (n=5), PUV+VUR (n=9) were the other etiologic causes of antenatal hydronephrosis. Surgery was performed in 23 renal units.

Urinary tract infection:

Fourty eight urinary tract infection attacks were seen in 48 patients during study. In 16 patients there was no urinary tract infection. The most common underlying pathology in patients with urinary tract infection was PUV. Escherichia coli was the most common cause of urinary tract infection.

Evaluation of the association between some parameters and renal functions:

There was a negative correlation between end study GFR and fractional K^+ excretion at the 3rd month and 1st year ($p<0.05$).

There was a negative correlation between end study GFR and fractional Mg^{++} excretion at the 3rd and 6th months ($p<0.05$).

There was positive correlation between end study GFR and tubular reabsorption of phosphate at 1st year and negative correlation between end study GFR and serum BUN levels of 1st year.

Otherwise a negative correlation tendency between end study GFR and fractional Na^+ excretion of 1st year was determined ($p=0.056$).

Correlation results are seen on **Table 3**.

Table 3
Relationship with GFR and some parameters

Parameters	GFR at the end of the study (end study GFR)							
	4th-6th weeks		3rd month		6th month		First year	
	r	p	r	p	r	p	r	p
Weight	0.18		0.11		0.06		0.006	
Blood Pressure	0.05		-0.17		-0.12		-0.05	
BUN	-0.18		-0.03		-0.09		-0.49	0.001
FENa	-0.02		-0.19		-0.07		-0.30	0,056
TRP	0.36	0.02	0.30		-0.03		0.38	0.01
Ca/Cr	-0.26		-0.05		-0.16		0.13	
Protein/Cr	-0.06		0.29		-0.11		0.09	
FEK	-0.28		-0.34	0.02	-0.10		-0.44	0.003
FEMg	-0.26		-0.40	0.01	-0.29	0.04	0.03	

Significant p values are cited in the table, r: correlation coefficient FE: Fractional excretion

There were no correlations between end study GFR and other parameters (weight, height, blood pressure, Fe Na, Protein/creatinine and Calcium/creatinine ratios).

Discussion

The present research investigated the follow-up results of patients with antenatally detected hydronephrosis and evaluated the association between some clinical-laboratory parameters of these patients and renal functions during study.

The relationship between the antenatal degree of hydronephrosis and its' clinical outcome have been evaluated in several prospective and retrospective studies. Otherwise still there is no consensus on both timing and necessity of surgery, using invasive technique and conservative follow-up.[3,4,6-9] Unknowns about

hydronephrosis and increasing frequency of admission to hospitals led us to perform this study and to investigate if there are any probable prognostic factors.

Of the patients with antenatal hydronephrosis, 35-50% will have normal postnatal scans and are diagnosed as transient hydronephrosis.[10] Meeta Mallik et al[9] reported 38% transient hydronephrosis, Nejat Aksu et al[7] reported 24.8%. In the present study we found the ratio as 29.3% and it was smilar to previous data.

Ureteropelvic junction obstruction was the most common etiologic reason as reported in literature. In our study VUR ratio seems to be higher than others. VCUG was performed for all infants with pelvic dilation at first and-or second postnatal US examination. Therefore we were able to diagnose patients even with low degree of VUR.

The third trimester sonogram is important having the highest positive predictive value (PPV) to predict further urologic abnormality. The PPV for an AP diameter >7mm in the third trimester is 69%.[11] In our study five patients, with severe antenatal hydronephrosis degree, were diagnosed as transient hydronephrosis. Furthermore three patients' postnatal US findings were pathological whereas antenatal US were normal. These findings confirm that antenatal degree of hydronephrosis does not always correlate with postnatal outcome. However in our study the ratio of transient hydronephrosis was highest in antenatally mild graded group than moderate and severe ones. The degree of antenatal hydronephrosis in children diagnosed as UPJO tended to be more severe compared with other patients. On the other hand the degree of antenatal hydronephrosis in the patients with VUR was variable. According to these findings of our study it may be thought that the antenatal US findings always may not consist with postnatal US findings.

There is a consensus about timing of the first postnatal ultrasound. It must be done at least 48-72 hours later to avoid the false negative results. Because at first hours the baby is relatively oliguric.[6,7,9,11-13] In addition a second scan at 6th weeks is suggested because initial scans might be normal and postnatal hydronephrosis cannot be recognised.[10] Poor correlation between prenatal and postnatal US findings and the presence of VUR has been documented previously and so in our study. Antenatal degree of hydronephrosis and postnatal US findings of renal units with reflux were variable. Jawson et al. suggests postnatal investigation when anteroposterior pelvic diameter (APPD) is above 5 mm.[3] Ismaili et al[14] suggests that when APPD is above 7 mm. Because intermittent renal pelvic dilation can be seen in VUR, even in the presence of normal US finding the work up for prenatal hydronephrosis should go on. Keeping in mind the future results of missing VUR, we continued further evaluation when there was a APPD > 5 mm.

Many different retrospective and prospective studies have been performed to evaluate clinical characteristics and postnatal outcome of fetal hydronephrosis. Despite much investigation much controversy still exists.[15] Renal functions are deteriorated in some children. Possible prognostic factors have been investigated to avoid unnecessary investigation and missing the diagnosis for underlying etiology. Therefore we evaluated renal functions, tubular functions and GFR at every period in our study. Only one patient diagnosed as PUV, was on chronic renal insufficiency period. In the past few decades, the mortality rates associated with PUV has declined from 50% than 5%. Despite all the advances, 24-33% of patients with PUV still have end-stage renal failure in childhood period. A common predictor of future renal function is the lowest creatinine concentration in the first year of life. Salam M.[16] suggests the lowest creatinine concentration in the first year of life as a highly predictive and appropriate outcome measure to evaluate the effects of antenatal intervention on renal function when compared with the most recent creatinine concentration. Long-term renal function is variable in patients with obstructive uropathy. The creatinine level at one year of age has been best correlated with long-term outcomes; there are better outcomes when the serum creatinine is <0.8 mg/dl by one year of age.[17] Smilarly, a negative correlation was determined between end study GFR and serum BUN levels of 1st year in our study. Also recently significantly increased risk for end stage renal disease was reported in those children who have structural abnormality in childhood, even if renal function was normal.[18]

More efficient predictors of the clinical course apart from serum creatinine and renal scans are required. Some urinary biomarkers like neutrophil gelatinase-associated lipocalin (NGAL) or kidney injury molecule-1 are investigated in patients with hydronephrosis recently.[19] Those are both associated with kidney injury and originated from the renal tubular system. Several abnormalities in tubular function may occur in obstructive nephropathy.[20] Electrolyte and fluid balance abnormalities are expected in infants with severe obstructive uropathy.[17] The value of tubular functions in predicting the future renal damage in patients with hydronephrosis has been evaluated. In the prospective study of Miklovicova et al. 62 pediatric patients who underwent surgery for obstructive uropathy were examined. Selected biochemical markers of glomerular and tubular function, proteinuria, and ultrasound findings were evaluated. With respect to tubular function, 26% of patients had decreased concentration ability.

Proteinuria was detected in 4.8% of patients. On US, 66.7% of kidneys after surgery had residual dilatation of the renal pelvis. In our study, a negative correlation between end study GFR and fractional K^+ excretion at the 3th month and 1st year was determined. Similarly a negative correlation between end study GFR and fractional Mg^{++} excretion at the 3th and 6th months was found. There was a positive correlation between end study GFR and tubular reabsorption of phosphate at 1st year. Otherwise a negative correlation tendency between GFR of at the end of study and fractional Na^+ excretion of 1st year was determined (p=0.056). These results reflect not only patients with obstructive uropathy but also all prenatal hydronephrosis patients.

These significant relationships shown in the study suggests that a careful follow-up should include the evaluation of renal and tubular functioning tests in addition to other screening methods. Abnormalities found in these tests may predict the degree of renal

damage and probable decrease in GFR in the future. However our study group was small and future studies are warranted to investigate prognostic factors for renal damage in prenatally detected hydronephrosis.

Ethics Committee Approval: The Ethical Committeeof Erciyes University, Faculty of Medicine, approved this study (date: 2005, number: 2005/304).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

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Conflict of Interest: The authors have no conflict of interest to declare.

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