PEDIATRIC UROLOGY
Original Article

Effective predictors for surgical decision in antenatal hydronephrosis: a prospective multiparameter analysis

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Cite this article as: Kıllı İ, Avlan D, Taşkınlar H, Kara PP, Apaydın FD, Delibaş A, et al. Predictors effective for surgical decision in antenatal hydronephrosis: prospective multiparameter analysis. Turk J Urol 2017; 43: 361-5

ABSTRACT

Objective: The majority of antenatal hydronephrosis disappears spontaneously. In our study, we have investigated the effective predictors for surgical decision in antenatal hydronephrosis.

Material and methods: Forty-four patients found to have renal pelvic anteroposterior (AP) diameter more than 10-mm on antenatal ultrasonograpy were followed after birth. The study groups were divided into two groups: follow-up and surgery group. On follow-up, longitudinal diameter of the kidney, parenchymal thickness of the kidney, AP diameter of renal pelvis, AP diameter of middle calyces on ultrasonograpy, and differential renal function, 20th minute clearance, half-life of radionuclide tracer (T1/2), Tmax, Tmax-T1/2, normalised residual activity (NORA) on diuretic renography were evaluated. Ultrasonograpy and diuretic renography measurements were compared in patients whose hydronephrosis resolve or proceeded to surgery.

Results: Forty-four patients were diagnosed as antenatal hydronephrosis, spontaneous resolution occurred in 23 (52%), and surgery was performed in 21 patients (48%). Mean age at operation was 8.5±6.5 months (3-24 months). Mean AP diameter of renal pelvis was 29.5±14.2 mm for surgery group, 13.6±4.2 mm for follow-up group ($p<0.001$). Univariate analyses showed significance for all ultrasonographic measurements and only the differential renal function by diuretic renography. Multivariate logistic regression analysis showed significance for AP diameter of renal pelvis (odds ratio 1.37; 95% Cl 1.13-1.66), and differential renal function (odds ratio 1.14; 95% Cl 1.01-1.29).

Conclusion: AP diameter of renal pelvis and differential renal function were the most effective parameters for surgical decision. These parameters can be used for appropriate management of antenatal hydronephrosis.

Keywords: Antenatal; hydronephrosis; renography; ultrasonography.

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Submitted: 28.03.2017

Accepted: 10.05.2017

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Available online at www.turkishjournalofurology.com

Introduction

Antenatal hydronephrosis (ANH) is enlargement of the collecting system of fetal kidney which is seen in 1-5% of antenatal ultrasonograms. Among etiologies of hydronephrosis, transient dilation of collecting systems, ureteropelvic junction obstruction (UPJO), ureterovesical junction (UVJ) obstruction, and vesicoureteral reflux (VUR) can be enumerated. Knowing the responsible etiopathologic factor is important in the determination of treatment alternatives. Since many cases are benign, and have a tendency to resolve spontaneously, postnatal conservative follow-up gains momentum. The selection of patients with candidates for surgery is still a debatable issue.[1,2]

In cases with hydronephrosis, consensus has not been arrived on whether any urinary tract obstruction coexists and the patient who will probably benefit from treatment. Timing of surgery is important to refrain from permanent renal damage. For the follow-up of these patients ultrasound (US), and diuretic renography (DRG) have been widely used.[1,2] In our study, all parametres routinely used in US, and DRG for the monitorization of the patients with ANH were evaluated, and their benefits, and effectiveness on decision –making process for surgery were investigated.

Turk J Urol 2017; 43(3): 361-5
DOI:10.5152/tud.2017.81568

Material and Methods

The patients whose AP diameters of renal pelvis were greater than 10 mm as detected on antenatal ultrasonograms obtained between March 2013, and August 2014 were included in the study. Approval of the study was retrieved from Local Ethics Committee of Mersin University (Date: 02.21.2013; No: 2013/67). The patients were prospectively evaluated. The first ultrasonographic examinations of the patients were performed at 1. postnatal week. The first ultrasonograms were obtained within the first 1-2 days after birth in cases with bilateral hydronephrosis presumably secondary to the presence of posterior urethral valve (PUV). In cases with unilateral or bilateral hydronephrosis associated with ureteral dilatation, voiding cystouretrography (VCUG) was performed between 4., and 6. weeks after birth so as not to overlook VUR. In cases with bilateral hydronephrosis suggesting the presence of bladder outlet obstruction, VCUG was performed at 1. postnatal week. One month after the second US, the first DRG was realized at postnatal 6., and 7. weeks. In patients with suspect obstruction as detected on US and DRG, US was repeated at 3. postnatal month, and the patients whose hydronephrosis aggravated or persisted were monitored as for the presence of obstruction. Patients with increase in AP diameter of renal pelvis, and decrease in parenchymal thickness with obstructive pattern on DRG curve and/or differential renal function detected on repeat US were operated. Control US, and DRG examinations were performed in cases with low degree of suspicion for obstruction. Patients with low degree of suspicion and persistent hydronephrosis were followed up at 6 month-intervals. Patients whose hydronephrosis did not aggravate as detected on control US, and whose signs of obstruction disappeared completely on 2. DRG were followed up at 12 month-intervals. As prophylaxis, the patients received amoxycillin (15 mg/kg/day) for the first three months, then they were prescribed trimethoprim-sulphametaxole (2 mg/kg/day). US, and DRG measurements were performed by the same experienced physician.

During ultrasonographic examinations, thickness of renal parenchyma, AP diameters of both renal pelvis, and middle calyx were examined. Differential renal function on DRG, renal clearance at 20. minute, T max (time elapsed to reach the peak height of the renogram curve), and $T_{1/2}$ (time to reach thehalf-life of the radionuclide substance), measurements of NORA (normalized residual activity) were calculated. NORA is defined as residual radionuclide substance in the kidney within a certain time period. It is obtained by dividing total renal activity by renal activity at 1., and 2. minutes. $NORA_{20}$, and $NORA_{30}$ are values obtained at 20., and 30. minutes after administration of diuretics. $NORA_{20}$ <1.0 demonstrates a satisfactory renal drainage. For test Tc- 99m MAG-3 scanning was used.

Statistical analysis

For statistical analysis of data IBM SPSS (IBM Statistical Package for the Social Sciences; Armonk, NY, USA) 18.0 package program was used. Categorical measurements were summarized as numbers, and percentages, and numerical variables as mean and standard deviation (median or min. and max). For intergroup comparisons of categorical measurements chi-square test was used. Fitness of numerical variables to normal distribution pattern was evaluated using Kolmogrov-Smirnov test. For intergroup comparison of numerical variables independent groups t-test was used. To investigate the interactions among numerical variables Pearson correlation coefficient, and related p value were calculated. Logistic regression analysis was used to determine measurements effective on the decision to operate. ROC analysis was made to determine the appropriate cut-off value of AP diameter of renal pelvis. In all tests p=0.05 was considered as the level of statistical significance.

Table 1. Demographic characteristics of the patients

		Group		
Patient characteristics		**Surgery (n=21)**	**Follow-up (n=23)**	**p**
Gender	Male	15 (71%)	21 (91%)	0.12
	Female	6 (29%)	2 (9%)	
Laterality	Left	13 (62%)	14 (61%)	0.76
	Right	7 (33%)	9 (39%)	
	Bilateral	1 (5%)	-	
Diagnosis	UPJO	14 (67%)	22 (96%)	0.001
	Others*	7 (33%)	1 (4%)	
	Age at the time of surgery (month)	8.5±6.5 (3-24)	-	-

*Other diagnoses; ureterovesical junction obstruction (n=1), ureterocele (n=2), posterior urethral valve (n=1), ureteropelvic junction obstruction + ureterovesical junction obstruction (n=1), duplicated collecting system (n=2), hydroureteronephrosis (n=1).

Table 2. Comparison of ultrasonographic measurements (Mean±SD) in the groups of surgery, and follow-up

Ultrasonographic measurements (mm)	Surgery	Follow-up	p
Longitudinal axis of the kidney	74.0±21.3	59.3±11.3	0.006
Parenchymal thickness	5.5±2.9	7.1±2.1	0.04
AP diameter of renal pelvis	29.5±14.2	13.6±4.2	0.001
AP diameter of middle calyx	14.5±6.9	6.5±2.9	0.01
	UPJO	**Other pathologies**	
Longitudinal axis of the kidney	78±2.5	64.1±6.9	0.14
Parenchymal thickness	5.5±3.5un	5.4±1.3	0.92
AP diameter of renal pelvis	34.3±14.7	17.5±5.3	0.01
AP diameter of middle calyx	16±5.8	4±0.0	0.002

UPJO:Ureteropelvic Junction Obstruction; SS: standard deviation; AP: anteroposterior, Odds Ratio: 1.37; 95% CI 1.13-1.66

Table 3. Comparison of renographic measurements (Mean±SD) in the groups of surgery, and follow-up

Renographic measurements	Surgery	Follow-up	P
Renal clearance at 20.minute	0.6±0.2	0.6±0.2	0.82
Tmax	18.6±11.4	15.2±7.9	0.25
$T_{1/2}$	17.4±19.4	23.3±6.6	0.58
Tmax-$T_{1/2}$	6.2±7.2	11.0±5.4	0.15
$NORA_{20}$	1.3±0.4	1.6±0.7	0.13
$NORA_{30}$	1.2±0.4	1.4±1.6	0.52
Differential renal Function	41.4±12	48.7±4.5	0.01
	UPJO	**Other**	
Renal clearance at 20. minute	0.6±0.3	0.8±0.1	0.23
Tmax	18.6±12.8	18.2±8.5	0.93
$T_{1/2}$	0.7±0.0	29±9.4	0.02
Tmax-$T_{1/2}$	0.0±0.0	9.5±5	0.08
$NORA_{20}$	1.4±0.5	1.3±0.3	0.69
$NORA_{30}$	1.2±0.4	1.1±0.3	0.33
DifferentialRenal Function	40.1±12.0	44.6±11.4	0.41

UPJO: Ureteropelvic Junction Obstruction; Odds ratio for differential function 1.14; 95% CI; 1.01-1.29

Results

A total of 44 newborns with the diagnosis of ANH were followed up after the birth. Table 1 is showing patient characteristics. Twenty three (52%) patients were followed up, and 21 (48%) patients were operated. Mean age at surgery was 8.5±6.5 months (3-24 months). US measurements are given in Table 2. Based on the multivariate regression analysis, AP diameter of renal pelvis was found to be the most effective US measurement effective on the decision to operate. Each 1 mm increase in AP diameter of renal pelvis was found to increase the risk of surgery for 1.37-fold (odds ratio) (95% CI 1.13-1.66). DRG measurements are given in Table 3. Based on multivariate logistic regression analysis, the most effective DRG measurement on the decision to operate appeared to be differential renal function. Each one unit drop in the measurement increased the risk of being operated for 1.14 –fold (odds ratio). (95% CI 1.01-1.29). When all parametres studied on US, and DRG were evaluated in combination, AP diameter of renal pelvis was the most effective measurement on the decision to operate in multivariate logistic regression analysis (odds ratio 1.36; 95% CI 1.12-1.65). Sensitivity, and specificities of AP diameter of renal pelvis on the decision to operate was evaluated based on their cut-off values according to ROC analysis (Table 4).

Table 4. Sensitivity, and specificity of anteroposterior diameter of renal pelvis in the decision-making process for surgery as demonstrated in ROC analysis

Measurement	APDRP >14.2 mm	APDRP >15.5 mm	APDRP >20 mm
AUC	0.923	0.923	0.923
p	<0.001	<0.001	<0.001
Sensitivity	94.7%	84.2%	84.2%
Specificity	65.2%	69.6%	95.7%

AUC: Area under curve; APDRP: Anteroposterior diameter of renal pelvis

Discussion

In this study, in the follow-up of the patients diagnosed as ANH, AP diameter of renal pelvis, and differential renal function were found to be the most effective measurements on the decision to operate. In addition, longitudinal axis of the kidney, thickness of renal parenchyma, and AP diameter of middle calyx were also effective measurements on the decision for surgery.

Symptoms of ANH can herald many congenital urinary system diseases and they may regress spontaneously after birth together with development of urinary system. This fetal US finding is unique in that it harbours disease, and physiology dilemma within itself, and it takes the place in the common field of management shared by perinatology, pediatric urology, and pediatric nephrology. Physicians providing health services in this field should identify cases with hydronephrosis which regress spontaneously. On the other hand, they should continue to follow hydronephrotic patients, determine urinary system diseases without deteriorating renal functions, and take care not to delay their surgery. In their meta-analysis Lee et al.[3] analyzed the grade of ANH, and incidence of coexisting urinary system disease, and reported incidence of urinary system disease in patients with mild, moderate,

Turk J Urol 2017; 43(3): 361-5
DOI:10.5152/tud.2017.81568

and severe hydronephrosis as 11.9, 45.1, and 88.3 percent. Within this perspective a consensus on generally acceptable systematic follow-up scheme of ANH management is not available.[1]

Hydronephrosis in 52% of the ANH patients followed up in our study regressed spontaneously, and surgical treatment was required in 48% of them. UPJ obstruction was found in ANH patients who underwent surgery, and 33% of them were operated for other obstructive lesions. Other obstructive lesions consisted of UVJ obstruction, PUV, UPJ obstruction + UVJ obstruction. These findings were consistent with the literature. In other investigations transient hydronephrosis (41-88%), UPJ obstruction (10-30), VUR (10-20%), UVJ obstruction (5-10%), multicystic dysplastic kidney (4-6%), duplicated collecting system (2-7%), and PUV (1-2%) have been reported in respective number of ANH patients.[1] Dudley et al.[4] investigated 100 patients with ANH, and indicated that ANHs resolved during prenatal period (n=8) or at 6. postnatal weeks (n=36). Stone formation was reported during long-term follow-up of their patients.[5] In our study we detected UPJ obstruction in 32% of AHNs. In the literature in 4.9-54.3% of the patients with ANH, UPJ obstruction has been reported.[3]

In our study, the markers which directed treatment in ANHs were investigated. In evaluations performed, measurement of AP diameter of renal pelvis was found to be the most effective predictive factor on the decision to operate. As AP diameter of renal pelvis increases, the likelihood of regression of the hydronephrosis decreases, while indication of surgery increases. Each 1 mm increase in ultrasonographic measurement, increased the surgical risk 1.36-fold. Mean AP diameters of renal pelvis were calculated as 29.5±14.2 mm in patients who had undergone surgery, while it was 13.6±4.2 mm in patients whose hydronephrosis regressed (p<0,001). Longpre et al.[6] demonstrated that ANH (SFU-The Society for Fetal Urology grade-4) patients with longer AP diameter of renal pelvis, and calyceal dilation had a lower probability of spontaneous recovery, and initial AP diameter of renal pelvis was an important determinant effective on the decision to operate. The authors measured AP diameter of renal pelvis as 29 mm in patients in whom they performed surgery, and it was estimated as 9.4 mm in patients whose hydronephrosis regressed (p<0.05). Based on ROC analysis, they predicted that hydronephrosis could regress in cases with AP diameter of renal pelvis less than 19.3 mm in 83% of the cases. Ransley et al.[7] reported that grade of ANH rarely increase in SFU grade-1 patients with renal dysfunction and AP diameter of renal pelvis was <10 mm without any calyceal dilation. They indicated that AP diameter of renal pelvis was >12 mm in patients who required surgery, and added that this cut-off value had a low predictive value. In our study a significant intergroup difference was found when longitudinal axis of kidney, thickness of renal parenchyma, and AP diameter of middle calyx were compared. Passerotti et al.[8] reported that in 1441 patients with ANH decrease in parenchymal thickness detected in the first postnatal US was correlated with UPJ obstruction, and VUR in univariate, and VUR in multivariate analysis. Koff et al.[9] recommended serial US examinations so as to determine the site of obstruction, and to demonstrate the disease progression. They evaluated longitudinal axis of the kidney with US, and detected atrophy of the ipsilateral kidney, and compensatory atrophy of the contralateral kidney. DRG is also used for the monitorization of ANHs. Although in the algorithm, the importance of differential renal function has been emphasized, different measurements have been also evaluated in DRG. In our study, we found that decrease in only differential renal function was an important factor effective on the decision for surgery. However it has only limited practical benefit, because decision to operate should be taken before development of renal function.

In conclusion, even though algorithms recommended for the follow-up of ANHs were widerly adopted, and used, a consensus has not been reached about interpretation of the measurements employed for the determination of the patient who will benefit from surgical treatment, and the type of surgery, and it is left to the "experience, and preference" of the clinician. Generally surgical indications include, split renal function less than 40% or more than 10% decrease during follow-up, AP diameter of renal pelvis more than 10 mm or more than 5 mm increase during follow-up, Grade III, and IV dilatation according to The Society for Fetal Urology criteria.[1] However lots of measurements are performed during US, and DRG which have uncertain impact on the decision of surgery. This study has supported the viewpoint which asserts that AP diameter of renal pelvis, and differential renal function are effective predictors. Besides we have evaluated other markers, and demonstrated that longitudinal axis of the kidney, thickness of renal parenchyma, and AP diameter of middle calyx are significant predictors. These measurements are significant in the formulation of treatment strategies.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Mersin University Clinical Investigations Local Ethics Committee.

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

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - İ.K., D.A.; Design - İ.K., D.A.; Supervision - İ.K., D.A., A.N.; Resources - İ.K.; Materials - İ.K.; Data Collection and/or Processing - İ.K.; Analysis and/or Interpretation - İ.K., D.A., A.N.; Literature Search - İ.K.; Writing Manuscript - A.N.; Critical Review - İ.K., D.A., A.N., H.T., D.A.; Other - İ.K., D.A., H.T., P.K., D.A., A.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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