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Research Article

Predictors of surgical intervention for antenatally detected Ureteropelvic Junction Obstruction (UPJO): A prospective multivariate analysis

Tarek Ahmed Mahmoud*, Esam El din Salem Morsy, Hany Abd Elraoof Ali Morsy, Abdelmoneim Mohammed Abouzeid, Ahmed Mamdouh Abd Elhamed, Elnisr Rashed Mohamed, Hazem Mohamed Elmoghazy

Department of Medicine, Sohag University, Sohag, Egypt

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ABSTRACT

Objective: We aimed to define the best timing for surgical intervention in infants born with antenatal hydronephrosis due to ureteropelvic junction obstruction to minimize the associated renal damage.

Material and methods: We prospectively followed infants born with antenatally diagnosed UPJO presented at our outpatient clinics for evidence of obstructive injury with a standard protocol with ultrasonography and renal scintigraphy. Indications for surgery included progression of hydronephrosis on serial ultrasonographic follow up, initial Differential Renal Function (DFR) ≤ 35% or >5% loss in subsequent studies, and recurrent Urinary Tract Infections (UTI). Univariate and multivariate analyses were utilized to define the predictors for surgical intervention, while the appropriate cut-off value of the initial APD was determined using the ROC analysis.

Results: Univariate analysis revealed a significant association between surgery, the initial anteroposterior diameter, cortical thickness, society for fetal urology grade, UTD risk group, initial DRF, and recurrent UTI (P-value<0.05). No significant association between surgery and sex or side of the affected kidney (P-value 0.91 and 0.38, respectively). On multivariate analysis, the initial APD, initial DRF, obstructed renographic curve, and recurrent UTI during follow up (P-value<0.05) were the only independent predictors for surgical intervention. An initial APD of 23 mm can predict surgical requirement, with a specificity of 95% and sensitivity of 70%.

Conclusion: For antenatally diagnosed UPJO, the APD value (at the age of 1 week), DFR value (at the age of 6-8 weeks), and occurrence of recurrent UTI during follow-up are significant and independent predictors of the need for surgical intervention. APD, when used with a cut off value of 23 mm, is associated with high specificity and sensitivity for predicting surgical need. Therefore, even bilateral cases can be safely followed using a strict protocol.

Keywords: Antenatal hydronephrosis, Ureteropelvic junction obstruction, Anteroposterior diameter, Differential renal function, Pyeloplast

Abbreviations: ANH: Antenatal Hydronephrosis; APD: Anteroposterior Diameter; DFR: Differential Renal Function; DTPA: Diethylenetriamine Pentaacetate; RIS: Radioisotope Scan; ROC: Receiver operator Curve; SFUG: Society for Fetal Urology Grade; UTD: Urinary Tract Dilation; UTI: Urinary Tract Infection; UPJO: Ureteropelvic Junction Obstruction; VCUG: Voiding Cystourethrography; VUR: Vesicoureteral Reflux

INTRODUCTION

Nowadays, Antenatal Hydronephrosis (ANH) is an increasingly encountered problem due to the widespread use of antenatal ultrasound, it is reported in around 5% of pregnancies. Ureteropelvic Junction Obstruction (UPJO) is the leading cause in most cases and has been managed surgically [1]. However, recently, many series reported an increased rate of spontaneous resolution without any significant renal damage in such cases [2]. So, the management protocol has changed towards initial

*Corresponding author. Tarek Ahmed Mahmoud, E-mail: dr.tarek_ur@yahoo.com.

conservative management with elective surgical intervention in selected cases. However, it is still challenging to identify the candidates for early surgical intervention versus those for watchful waiting. Moreover, another challenge is related to getting the precise cut off values to shift to surgery. Therefore, we aimed to define those factors that can contribute to the proper selection of those patients.

MATERIALS AND METHODS

This is a prospective cohort study that was performed at two tertiary referral centers (Sohag university hospital and Abu El Reesh Japanese children hospital) between January 2018 and June 2021. The study included all cases with ANH due to primary UPJO, detected antenatally and confirmed postnatally at the age of one week without any degree of ureteral dilatation. Parents of included infants were thoroughly informed about the protocol of evaluation and follow up with possible intervention, and the Ethics committee approved the study of Sohag university.

The initial workup included a complete clinical examination with an ultrasonographic assessment to measure the following: renal pelvis's maximum Anteroposterior Diameter (APD), the maximal cortical thickness, and the Society for Fetal Urology Grade (SFUG) of hydronephrosis [3]. Based on this evaluation, the infants were grouped into three groups (P1: low risk, P2: intermediate risk, P^3: high risk) according to the Urinary Tract Dilatation (UTD) classification system. In addition, basic laboratory investigations, including serum creatinine and urine analysis, were done for all patients.

At the age of (6-8 weeks) after birth, the infants were further evaluated with radioisotope scan with Diethylenetriamine Pentaacetate (DTPA) to record the baseline initial DRF and whether the dilated renal unit demonstrated an obstructed curve or not. Obstruction was defined as progressive retention of the radiotracer within the collecting system with continuous upsloping of the Time Activity Curve (TAC) even after the diuretic administration. In addition, the washout curve was considered as it is typically more revealing than the absolute half time values, especially in young children [4,5].

Patients with bilateral hydronephrosis were further evaluated with Voiding Cystourethrography (VCUG) to exclude Vesicoureteral Reflux (VUR). Estimation of urine output using diaper weight. Moreover, at the end of this evaluation, infants who had an initial APD of<10 mm, those with ureteral dilatation, initial serum creatinine >0.7 mg/dl, or urine output< 1.5 ml/kg/hr. [6] and those with neurologic abnormality have been excluded from the study.

Patients were then managed either by conservative or early surgical intervention. Early surgical intervention (within 3 months after birth) was chosen in patients with initial DFR ≤ 35% with an obstructive curve on renogram or progressive increase in the degree of hydronephrosis with parenchymal affection (cortical thickness<5 mm). Otherwise, the patients were managed non-operatively, by performing follow-up ultrasonography (every 3 months), radioisotope scan (every 3 months for those who had progression of hydronephrosis), and urine analysis (every month for high risk patients). Urine culture was performed in case of suspected UTI. Prophylactic antibiotic (amoxicillin) was prescribed for high risk patients (P3) till the age of 1 year or till the time of pyeloplasty if indicated.

The renogram was dismissed for those who had improved the degree of hydronephrosis on two serial examinations. Resolution of hydronephrosis was defined as APD<10 mm documented on two consecutive examinations. While the shift to surgical treatment is indicated in patients demonstrating progressive hydronephrosis, deteriorating renal function (loss of>5% in subsequent radioisotope scan), or repeated UTI (two attacks within 3 months).

In the case of surgical treatment, a standard open dismembered pyeloplasty was performed according to the technique described by Anderson-Hynes, and the patients were then followed with ultrasonography and urine analysis carried out at 3 monthly intervals to ensure improvement. A radioisotope scan was performed after 6 months to assess the residual renal function and ensure patent drainage [7].

Data were analyzed using STATA version 14.2. Data were represented as mean +/- standard deviation, median, and range (for quantitative data) and as number and percentage (for qualitative data). Receiver Operating Curve (ROC) analysis was used to detect the best value of different cut off points. Survival analysis, taking surgery as the endpoint and UTD risk group as a variable, was done using the Kaplan Meier survival and log rank test. Cox proportional hazard analysis was used to perform univariate and multivariate analysis with surgery as the endpoint. P-value was considered significant if less than 0.05.

RESULTS

Between January 2018 till June 2021, 188 neonates presented to our departments with antenatally diagnosed hydronephrosis. After clinical and radiological evaluation, 52 patients were found to have dilated ureter either due to obstructive megaureter, VUR, or Posterior Urethral Valve (PUV). In addition, two patients were diagnosed as having multicystic dysplastic kidneys (Table 1). These cases were excluded from the study to be managed accordingly.

Table 1: Etiology of urinary tract dilation detected on antenatal ultrasound.

Etiology	Number (%)
Obstructive megaureter	4 (2.1%)
Vesicoureteral Reflux (VUR)	39 (20.7%)
Multicystic dysplastic kidney	2 (1%)
Posterior Urethral Valve (PUV)	9 (4.7%)
PUJO data	134 (71.1%)

Total	188 (100%)

The remaining 134 infants were diagnosed as having PUJO (unilateral in 104 infants and bilateral in 30 infants) with a total of 164 renal units. After the initial assessment, 37 renal units were managed with early surgical intervention (Anderson Hynes pyeloplasty), and the rest (127 renal units) were managed conservatively according to the scheduled protocol. During the period of follow up, 17 cases (17 renal units) were missed, and these cases were excluded from our study. So finally, we had 117 patients (92 males and 25 females) with a total of 147 renal units. Improvement was reported in 78 renal units (53.06%), complete in 67 units, and partial in 11 units with residual non-progressive hydronephrosis. The mean time of follow up was 23.2 ± 7.6 months, while the mean time to resolution was 9.0 ± 5.3 months. Patient demographics of the conservative group are demonstrated in (Table 2).

Table 2: Baseline characteristics of the conservative group (n= 78).

Variable	**Summary statistics**
Baseline creatinine	
Mean ± SD	0.46 ± 0.12
Side	
Left	51 (65.38 %)
Right	27 (34.62 %)
Initial postnatal APD (mm)	
Mean ± SD	16.55 ± 4.74
Initial postnatal cortical thickness (mm)	
Mean ± SD	6.12 ± 1.22
Initial postnatal SFU grading system	
SFU1	12 (15.38%)
SFU2	38 (48.72%)
SFU3	25 (32.05%)
SFU4	3 (3.85%)
Initial postnatal UTD system	
P1	25 (32.05%)
P2	50 (64.10%)
P3	3 (3.85%)
Initial postnatal DRF (%)	
Mean ± SD	52.20 ± 13.24
Initial postnatal renogram curve	
Patent drainage	50 (64.10%)
Poor (Obstructed) drainage	28 (35.90%)

Surgery was needed in 69 renal units (37 after the initial evaluation and 32 after a conservation period). The mean time to surgery was 5.2 ± 3.8 months. Indications for termination of conservative management were>5% loss of renal function in 10 renal units, progression of hydronephrosis in 9 renal units, and recurrent UTI in 13 renal units. Patient demographics of the intervention group are demonstrated in (Table 3).

Table 3: Baseline characteristics of the intervention group (n= 69).

Variable	**Summary statistics**
Baseline creatinine	
Mean ± SD	0.46 ± 0.16
Side	
Left	31 (44.93%)
Right	38 (55.07%)
Initial postnatal APD (mm)	
Mean ± SD	31.99 ± 13.97

Initial postnatal cortical thickness (mm)	
Mean ± SD	5.10 ± 1.73
Initial postnatal SFU grading system	
SFU1	0
SFU2	6 (8.70%)
SFU3	29 (42.03%)
SFU4	34 (49.28%)
Initial postnatal UTD system	
P1	5 (7.25%)
P2	30 (43.48%)
P3	34 (49.28%)
Initial postnatal DRF (%)	
Mean ± SD	38.64 ± 15.49
Initial postnatal Renogram Curve	
Patent drainage	3 (4.35%)
Poor (Obstructed) drainage	66 (95.65%)

With the statistical analysis of the surgically managed patients, univariate analysis revealed no significant association between surgery and gender or side of UPJO (P-value 0.91 and 0.38, respectively). Furthermore, surgical intervention was linked to the initial grade of hydronephrosis, APD, cortical thickness, initial DRF, and occurrence of recurrent UTI (P-value<0.05) (Table 4). Survival analysis taking the UTD risk group as a variable and surgery as an endpoint revealed that the UTD risk group P3 (high risk) is significantly associated with the need for surgery (Figure 1).

Table 4: Univariate Cox proportional hazard analysis for prediction of surgery.

Variable	Hazards ratio (95% confidence interval)	P value
Female *vs.* Male gender	1.04 (0.57:1.89)	0.91
Baseline creatinine	0.79 (0.11:5.60)	0.81
Right *vs.* left side	1.66 (1.03:2.67)	0.38
Initial postnatal APD (mm)	1.09 (1.07:1.11)	<0.0001
Initial postnatal cortical thickness (mm)	0.67 (0.56:00.80)	<0.0001
Initial postnatal SFU grade 4	19.60 (8.11:47.36)	<0.0001
Initial postnatal UTD system (P3)	12.03 (4.65:31.14)	<0.0001
Initial postnatal DRF (%)	0.95 (0.94:0.97)	<0.0001
Obstructed drainage curve in initial postnatal Renogram	19.31 (6.05:61.60)	<0.0001
Presence of recurrent UTI	2.95 (1.65:5.26)	<0.0001

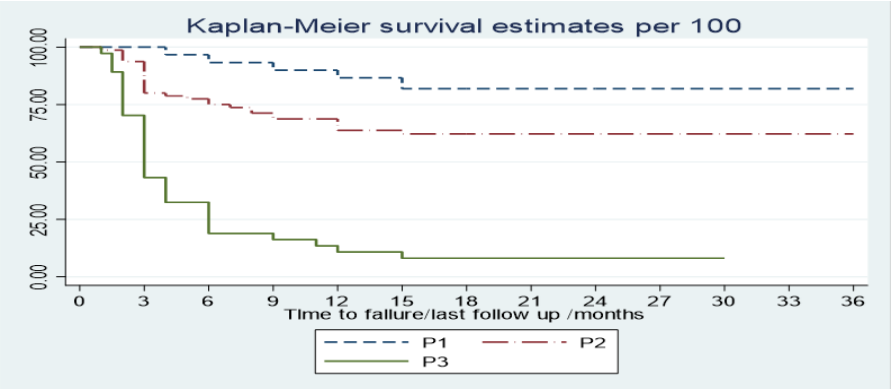

Figure 1: Kaplan-Meier survival analysis showing the association between initial postnatal UTD system and surgery.

However, on studying our data with the multivariate analysis, the initial APD (P-value<0.0001), initial DRF (P-value<0.002), presence of obstructive curve on renogram (P-value<0.0001), and occurrence of recurrent UTI during follow up (P-

value<0.0001) were the only significant and independent predictors for surgery (Table 5). Using ROC analysis to determine the sensitivity and specificity of different cut off values of the initial APD (Figure 2). An initial APD of 23 mm can predict surgical requirement, with a specificity of 94.9% and a sensitivity of 69.6% (Table 6).

Table 5: Multivariate Cox proportional hazard analysis for prediction of surgery (include significant variable in univariate analysis).

Variable	Hazards ratio (95% confidence interval)	P value
Initial postnatal APD (mm)	1.08 (1.05:1.12)	<0.0001
Initial postnatal cortical thickness (mm)	0.99 (0.81:1.20)	0.94
Initial postnatal SFU grade 4	2.33 (0.21:25.86)	0.49
Initial postnatal UTD system (P3)	0.62 (0.18:2.14)	0.45
Initial postnatal DRF (%)	0.98 (0.96:0.99)	0.002
Obstructed drainage curve in initial postnatal renogram	8.88 (2.67:29.58)	<0.0001
Presence of recurrent UTI	2.88 (1.56:5.32)	0.001

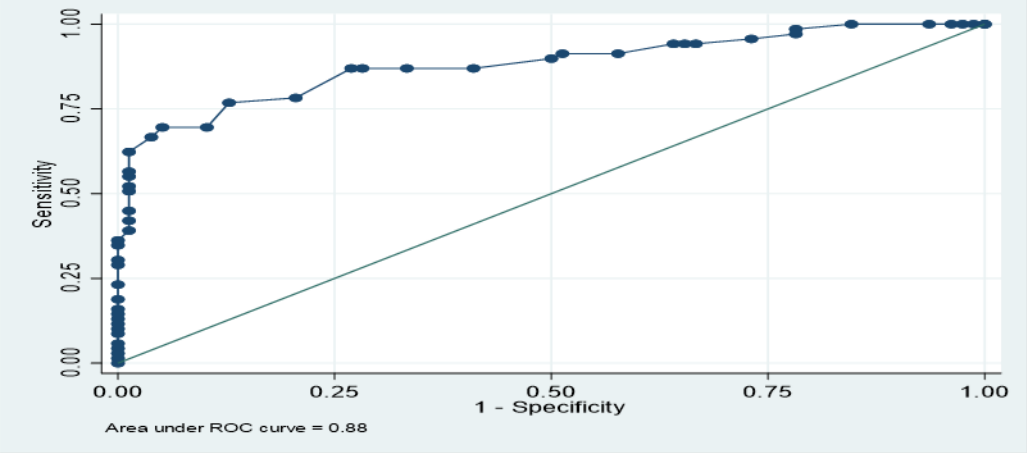

Figure 2: Receiver operating curve for anteroposterior diameter.

Table 6: ROC analysis was made to determine the Sensitivity and specificity of various cut off values of AP diameter of renal pelvis.

Cut off point	Sensitivity	Specificity
>15 mm	91.3	42.3
>20 mm	78.3	79.5
>23 mm (best cut off point)	69.6	94.9
>24 mm	66.7	96.2
> 32 mm	39.13	98.72

DISCUSSION

The therapeutic approach for antenatal hydronephrosis caused by UPJO has shifted from primary surgical intervention to initial conservative management with elective surgery in selected cases. Although there is general agreement that progressive hydronephrosis, significant DFR impairment, and the presence of symptoms (UTI, pain) are reasonable indications for pyeloplasty, precise cut offs for the previous factors are still debated.

Many authors recommend expectant management for antenatally diagnosed UPJO, which has become standard practice at many centers [8-11]. The main goal is to avoid unnecessary surgeries while preserving renal function. The argument for that is the high liability for spontaneous resolution, mainly in the first year of life [12]. In this series, we report the resolution of hydronephrosis in 78 renal units (53.06%), including complete in 67 renal units and a partial one in 11 renal units. Many cases had initial criteria that indicate surgical intervention, such as initial high-grade hydronephrosis. However, those patients had improved hydronephrosis during the follow up. In addition, 28 renal units had an initial obstructed drainage pattern that showed improvement in subsequent studies. Therefore, based on these initial data, those patients successfully managed and avoided unnecessary intervention.

Furthermore, the decisive problem with conservative management is to identify infants in whom renal function will be preserved and those in whom it will deteriorate. In our series, patients were meticulously monitored for anatomical and functional changes. We offered early surgical intervention (within 3 months after birth) for 37 renal units. And for those

who were on conservative management, 32 renal units were shifted to surgical intervention due to progressive hydronephrosis, decreased DRF>5%, or recurrent UTI. The mean time to conservative management failure (time to surgery) was 5.2 months, which was comparable to 5.6 months as reported by Onen, et al., and less than other reports of 9-11 [13-15].

While the indications for surgery in our cohort are comparable to the published literature our exciting finding was about the thirty patients with bilateral PUJO. Bilateral PUJO does not seem to be a contraindication for an initial trial of conservative management, supposing that the infant has normal chemistry and urine output [16]. Onen, et al. have reported a trial of initial conservative management for 19 newborns diagnosed with bilateral PUJO with a high resolution rate. In our series, we have dealt with each renal unit separately and resolution was reported bilaterally in 9 patients and unilaterally in 16 patients. Regarding DTPA results in those patients, the absolute number of DFR was not our primary concern but the pattern of drainage (either obstructive or not), in addition to cortical thickness loss on serial ultrasonographic examinations.

The surgical intervention rate varied widely among several published studies ranging from 12% to 52% [17,18]. In our series, the rate of surgical intervention was 47%, which is considered relatively high. The explanation for this finding is that we work as tertiary referral centers. Most of our patients have higher grades of hydronephrosis as denoted on initial examinations, where 91 renal units (62%) had SFU grades 3-4. A published study by Onen that presents low rate surgical intervention at 12% shows only 15% of patients with grade 3-4 hydronephrosis [19]. In addition to the relatively smaller sample size, we think that the prospective nature of our study and the frequency of follow up influenced our surgical intervention rate.

In this cohort, we found that the initial APD, initial DRF with an obstructive curve on renogram, and recurrent UTI were predictors of the need for surgical intervention. While, cortical thickness, SFU grade 4 hydronephrosis, and UTD P3 (high risk) were not [20]. These results are similar to reports published by other centers.

Survival analysis taking the UTD risk group as a variable and surgery as an endpoint revealed a significant link between the high-risk group and the need for surgical intervention; however, on the multivariate analysis, this link was found to be insignificant (P-value>0.05). To the best of our [21] knowledge, this prospective analysis is the first one to address the relation between the UTD system and the need for surgery in antenatally diagnosed UPJO.

Many studies have proposed urinary tract infection as an indication for surgical intervention. In our series, despite the antibiotic prophylaxis given to high risk patients (UTD P3), 21.7% of the operated renal units were associated with recurrent UTIs [22]. Two of our patients were admitted to the intensive care unit for neonatal sepsis. Using ROC analysis, our data revealed that an APD of 23 mm (best cut off) can portend surgical need, with a specificity of 95% and sensitivity of 70%. With this cut off value, only 5% of the operated patients might not have undergone surgery if put on conservative management. Some authors reported different cut off values ranging from 16 mm to 24.3 mm. Based on our data, using a lower APD, e.g., 15 mm, can result in unnecessary surgical intervention in up to 5 8% of the operated cases.

Limitations of our study come from the small number of cases and the relatively short follow up period. Therefore, a longer period of follow-up is required to assure persistent improvement for both intervention and conservative groups of the study.

CONCLUSION

In conclusion, for antenatally diagnosed UPJO, the APD value (at the age of 1 week), DFR value (at the age of 6-8 weeks), and occurrence of recurrent UTI during follow up are significant and independent predictors of the need for surgical intervention. APD, when used with a cut off value of 23 mm, is associated with high specificity and sensitivity for predicting surgical need. Therefore, even bilateral cases can be safely followed using a strict protocol.

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