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Ureteropelvic junction obstruction in the first three months of life: is sex a prognostic factor?

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Abstract. – OBJECTIVE: Ureteropelvic junction obstruction (UPJO) is a blockage that occurs at the point where the renal pelvis (the part of the kidney where urine collects) meets the ureter (the tube that carries urine from the kidney to the bladder). This study compared outcomes between male and female patients with UPJO.

PATIENTS AND METHODS: 402 UPJO patients diagnosed and treated before the age of three months were divided into two groups: males and females. The following information was extracted: age at diagnosis, age at surgery, the parenchymal thickness of the UPJ and contralateral sides (preoperatively and at 1 and 3 years postoperatively), pelvic diameter, and kidney function.

RESULTS: There were 287 male and 115 female patients (a ratio of 2.5:1). The parenchymal thickness (PTs) at diagnosis and surgery were 5(4) mm and 5(3) mm in males, respectively. In females, these values were 5(3) mm and 6(5) mm, respectively. There was a significant decrease in male PT at the time of surgery compared to diagnosis ($p<0.05$). After the first postoperative year, PTs were 8(4) mm and 9(4) mm in males and females, respectively, and after the third postoperative year, PTs were 9(4) mm and 10(4.75) mm in males and females, respectively.

CONCLUSIONS: Among patients diagnosed with UPJO during the first three months of life, males had a more severe disease course than females. Additionally, females experienced better clinical improvement during the long-term postoperative period.

Key Words:
Ureteropelvic junction obstruction (UPJO), Prognosis, Sex.

Introduction

Antenatal hydronephrosis (HN) is seen in 1-5% of all pregnancies[1]. The most common cause of HN is ureteropelvic junction obstruction (UPJO; 10-30% of cases), which reduces urine flow from the renal pelvis to the ureters[2]. UPJO is mainly a congenital condition that can be detected by antenatal US during the second trimester[3]. Recent studies have focused on the effect of the Urinary Tract Dilation ultrasound classification system, both prenatally and postnatally, to stratify the risk of infants with prenatally diagnosed hydronephrosis developing renal impairment or undergoing surgery. A strong correlation has been shown between the grade of hydronephrosis and the chance of spontaneous resolution. The Society for Fetal Urology suggested a grading system for hydronephrosis in four grades, according to which grade I resolves in approximately 50% of patients, and grades II, III, and IV resolve in 36%, 16%, and 3% of cases, respectively[4]. Surgery is required in 20% of patients due to severe symptomatic obstruction[5]. If surgery is needed and untreated on time, UPJO can cause chronic infection, urolithiasis, and progressive deterioration of kidney function[6].

The natural history and pathophysiology of asymptomatic and symptomatic UPJO have been evaluated, and management guidelines that consider their pathophysiology, epidemiology, diagnosis, and classification have been proposed[4]. However, the guidelines do not mention sex-dependent differences in the follow-up period. In particular, they do not focus on the early stages, which are the most critical periods for kidney damage. Thus, in this retrospective clinical study, we compared outcomes between male and female UPJO patients in the first three months of life to determine if there were sex-dependent differences preoperatively and postoperatively in the follow-up period in this critical age group[7].

Patients and Methods

Study Type

Cross-sectional observational study

The clinical data of 402 UPJO patients who underwent Anderson-Hynes dismembered py-

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eloplasty at our clinic between 1980 and 2018 were retrospectively reviewed.

The first ultrasonography of all patients was performed in the first postnatal month, mostly in 3 days to 1 week. Since there was no change in the kidney parenchyma in the first month (8), this ultrasound (US) values were expected as basic US. Changes in the first 3 months were compared with the US performed in this period.

Indications for surgical operation were defined as follows: symptomatic disease state (including hematuria, pain, etc.), gradual enlargement of the anteroposterior (AP) diameter of the renal pelvis with parenchymal loss, and/or gradual loss of renal functional uptake (>10%) on nuclear scan, and infection due to stasis in the obstructed urinary tract. The medical records of the patients were retrospectively reviewed, and the following information was extracted: age at diagnosis, age at surgery, the parenchymal thickness of the UPJ and contralateral sides (preoperatively and at 1 and 3 years postoperatively), pelvic diameter, and kidney function. The patients were divided into males and females based on whether the UPJO was diagnosed and treated before three months of age. Patients with bilateral UPJO were excluded from the study.

Ethical Approval

Approval for this study was obtained from the local ethics committee of Kanuni Sultan Suleyman Training and Research Hospital KAEK/2020.07.132.

Statistical Analysis

Descriptive statistics were used to define continuous variables (Mean with standard deviation). The conformity of the data to the normal distribution was examined with the Shapiro-Wilks test. Examining the relationship between two continuous variables not conforming to normal distribution was performed with the Mann-Whitney U test. Categorical variables were expressed as counts and percentages, and variables that did not conform to a normal distribution were expressed as median and interquartile range (IQR). The variation between two dependent continuous variables that did not conform to the normal distribution was examined using the Wilcoxon Signed-Rank test. The variation between more than two independent continuous variables that did not conform to the normal distribution was examined using the Friedman test. For meaningful results, post hoc pairwise comparisons were made with the Wilcoxon Signed-Rank test. The statistical significance level was determined as $p<0.05$. A comparative analysis for qualitative data was done using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium).

Results

Of the patients with surgically treated UPJO, 402 patients without bilateral obstruction were included in the study, comprising 287 males (71%) and 115 females (29%), with a ratio of 2.5:1. The obstruction involved the left side in 236 patients (59%) and the right side in 166 patients (41%).

In the first 3-month period, parenchymal thickness (PT) at the time of diagnosis and at the time of surgery was 5 (4) mm ($p<0.001$) and 5 (3) mm ($p<0.001$), respectively, in males, with a significant decrease at the time of surgery ($p=0.023$). In females, these values were 5 (3) mm ($p=0.008$) and 6 (5) mm ($p<0.001$), respectively ($p=0.51$). There was no significant difference in females, but there was a considerable decrease in males.

At the time of surgery, median kidney function was 42 (17) mm ($p=0.330$) and 44 (16.5) mm ($p=0.066$) for males and females, respectively ($p=0.560$) (Table I).

After the first and third postoperative years, the PT in males was 8 (4) mm ($p<0.001$) and 9 (4) mm ($p=0.007$), respectively, whereas the corresponding values were 9 (4) mm ($p=0.058$) and 10 (4.75) ($p=0.374$), respectively, in females. A significant difference in parenchymal improvement was found in both groups over the years ($p<0.001$). Although there was a recovery in both males and females, females tended to recover better (Table I).

The pelvic diameters of the UPJO at the time of surgery, after the first postoperative year, and after the third postoperative year were 28 (14) mm ($p<0.001$), 8.6 (6) mm ($p<0.001$), and 8 (7.38) mm ($p\leq0.001$), respectively, in males, and 27 (12) mm ($p<0.001$), 9.15 (8) mm ($p\leq0.001$), and 8.5 (5.9) mm ($p=0.01$), respectively, in females. There were no differences in pelvic diameter between the genders ($p=0.794$) and there were significant improvements during the follow-up period ($p<0.001$) (Table I).

Table I. Comparison of male and female ureteropelvic junction obstruction (UPJO) groups in the first three months.

	Male UPJO	Female UPJO	*p*-value
Total cases*	287 (71%)	115 (29%)	
Sex (male:female)*	2.5:1		
Side (Right- Left) (n)*	R:117 L: 168	R: 48; L: 69	
Parenchymal thickness at diagnosis**(mm)	5 (4)	5 (3)	0.045[m]
Parenchymal thickness at surgery** (mm)	5 (3)	6 (5)	0.39[m]
Kidney function at surgery (%)**	42 (17)	44 (16.5)	0.560[m]
p-value (kidney function at diagnosis-kidney function at surgery)**	$p = 0.023$[w]	$p = 0.51$[w]	
Parenchymal thickness postoperative 1-year follow-up**	8 (4)	9 (4)	0.058[m]
Parenchymal Thickness postoperative 3-year follow-up**	9 (4)	10 (4.75)	0.0374[m]
p-value (Parenchymal thickness at diagnosis - Parenchymal thickness at surgery)	$p = 0.023$[w]	$p = 0.51$[w]	
p-value (Parenchymal thickness at surgery - Parenchymal thickness at postoperative 1- and 3-year)	$p < 0.001$[w]	$p < 0.001$[w]	
Pelvic diameter at Surgery (mm)**	28 (14)	27 (12)	0.794[m]
Pelvic diameter at postoperative 1-year**	8.6 (6)	9.15 (8)	0.593[m]
Pelvic diameter at postoperative 3-year**	8 (7.38)	8.5 (5.9)	0.693[m]
p-value (Pelvic diameter at Surgery (mm) - Pelvic diameter at postoperative 3-year)	$p < 0.001$[f]	$p < 0.001$[f]	

[m]Mann-Whitney U test; [f]Friedman test; [w]Wilcoxon signed-rank test; n = Number of cases. *Descriptive statistics. **Median and interquartile range (IQR). UPJO: Ureteropelvic junction obstruction.

Discussion

UPJO affects one out of every 2,000 children[8,9] by decreasing urine flow from the renal pelvis into the ureters[7]. In most patients, neonatal ureteropelvic junction obstruction (UPJO) and hydronephrosis gradually resolve without any surgical intervention. However, a strong correlation has been shown between the grade of hydronephrosis and the chance of spontaneous resolution. If HN continues to progress, the prognosis concerning renal function is poor, and impaired renal function has been reported in up to 28% of patients[10]. Since renal function loss deteriorates without treatment, surgical corrective operation is found to be the fundamental approach for UPJO. Therefore, surgical intervention is the treatment of choice for this group of patients[11-13].

In neonates who were found to have mild to moderate hydronephrosis on an antenatal scan, a follow-up scan should be done after 48 hours to avoid a transient neonatal dehydration period; however, in severe cases, a scan should be performed within the first 48 hours as it might need urgent intervention[4]. The first ultrasonography of all patients was performed in the first postnatal month, mostly in the first week if antenatally diagnosed. In the literature, a study[8] has shown that renal dimensions, parenchymal thickness, and left kidney PT were related to the body mass index (BMI) and weight of the infant. The size of the kidneys and the medullary parenchymal thickness showed no association with age in the first 30 days of life.

These initial ultrasounds formed the basis of follow-up data, and the Fetal Urology Society (SFU) values on these ultrasounds determined our follow-up intervals. According to established guidelines, the management strategy depends on the results of a detailed assessment focusing on the degree of HN, parenchymal thickness, and AP diameter of the renal pelvis. A nuclear scan to determine urine drainage and renal function should also be performed, but these guidelines do not distinguish between male and female UPJO patients[14]. This study suggests sex-dependent differences in the clinical course of UPJO in the first three months of age. Specifically, males are more frequently diagnosed in the prenatal and neonatal stages, with the condition developing more aggressively in the first three months and causing a decrease in kidney function by the time surgery is performed; thus, the male sex seems to be a poor prognostic factor for UPJO. The prognosis of newborn male babies is worse in general. As compared with females, males had more postnatal complications, including lower Apgar scores, a greater need for

supplemental oxygen, higher rates of respiratory distress syndrome, more pulmonary interstitial emphysema, and higher overall perinatal mortality rates. These are some clues as to why males fare worse than females in UPJO anomalies. The disease is known to be more common in the male gender, and additionally, we consider that it may also show a more insidious and aggressive course. In this way, we sought to determine if the observed later effects of male sex in UPJO in the first three months could be attributed to poorer neonatal profile or whether there was evidence for an intrinsic male effect. If the pathway is simply mediated through the neonatal course, there is separate male vulnerability; then alternative causal pathways need to be assessed. Further research is needed to fully understand this important issue[8,10].

During the postoperative period, the focus of UPJO treatment is to diminish symptoms and preserve or heal kidney function. However, there is a lack of exact evaluation of the success of treatment due to the label course of kidney function following surgery[15,16]. Stabilization of renal function is known to occur within 5 years after surgery, and it is preserved for the long term. The most important finding of our study was that in the first 3-month period from surgery to the postoperative third year time, although parenchymal improvement was significant in both males and females, females had better improvement in this age group (p<0.001). In these males, it can be thought that the reasons for the poor course between diagnosis and surgery affect recovery even years later.

The prevalence of vesicoureteral reflux (VUR) associated with UPJO on the affected side due to a malformed renal tract ranges from 7.3% to 11.3%[17-19]. UPJO is seen in approximately 20% of patients with horseshoe kidneys and 8-15% of those with multicystic dysplastic kidney (MCDK) at the contralateral side[20-22]. The role of voiding cystourethrogram (VCUG) in asymptomatic unilateral isolated prenatally diagnosed UPJO is questionable, and several authors have not favored performing a VCUG to identify concomitant VUR, reserving it only for children presenting with urinary tract infection. However, in children with antenatally diagnosed bilateral hydronephrosis, a VCUG becomes mandatory to exclude bladder outlet obstruction in the form of a posterior urethral valve[4]. VUR was detected in 7-8% of our patients, with similar frequencies in both males and females.

The advantage of this study is that it included UPJO patients in the first three months with one of the largest series in the literature; however, they were all from a single center. More accurate, generalizable, and detailed data could be obtained by conducting a larger multicenter series as part of a multidisciplinary study.

Conclusions

In conclusion, although male and female UPJO patients diagnosed in the first three months of life may initially have the same level of renal function, further decline in function is likelier in males, which necessitates more frequent preoperative and even postoperative follow-up. If necessary, tailored surgical management is recommended.

Conflict of Interest
The authors declare that they have no conflict of interests.

Ethics Approval
All the investigators ensure that the study has been conducted according to the Declaration of Helsinki Guidelines. Approval for this study was obtained from the local ethics committee of Kanuni Sultan Suleyman Training and Research Hospital KAEK/2020.07.132.

Availability of Data and Materials
The study data are available at our University Hospital archive.

Informed Consent
Informed consent is not applicable due to the retrospective design of the study.

Authors' Contribution
Conceptualization, methodology and writing-original draft preparation (Ö.K.), data collection (Ö.K., S.Ç.), writing-review and editing and supervision (S.Ç.). All authors have read and agreed to the published version of the manuscript.

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