Congenital Urinary System Anomalies: Prenatal Diagnosis/ Postnatal Outcome

✉ Miraç Özalp¹, ✉ Hatice Sonay Yalçın Cömert², ✉ Ömer Demir³, ✉ Hidayet Şal³, ✉ Turhan Aran¹,
✉ Mehmet Armağan Osmanağaoğlu¹

¹Karadeniz Technical University Faculty of Medicine, Department of Obstetrics and Gynecology, Division of Perinatology, Trabzon, Turkey

²Karadeniz Technical University Faculty of Medicine, Department of Pediatric Surgery, Trabzon, Turkey

³Karadeniz Technical University Faculty of Medicine, Department of Obstetrics and Gynecology, Trabzon, Turkey

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ABSTRACT

Objective: To evaluate the relationship of fetal urinary system anomalies with aneuploidy and additional structural malformations, to compare the preliminary diagnoses made in the prenatal period with the results of the postnatal period.

Methods: Two hundred eighty-two cases diagnosed as fetal urinary system anomaly in our clinic between 2016-2019 were evaluated within the scope of the study. Age, gestational week, gravida, parity, fetal gender, type of anomaly, presence of additional anomaly, prenatal diagnosis method, fetal karyotype result, termination status and postnatal results were recorded.

Results: Hydronephrosis (HN) was in the first place among fetal urinary system anomalies. When congenital malformations accompanying urinary system anomalies were examined, central nervous system anomalies were the most common group with 26.4%. Urinary system anomalies, which are most frequently associated with additional anomalies; bilateral renal agenesis (50%), bilateral multicystic dysplastic kidney (50%) and extrofia vesica (50%). Considering the karyotype results, trisomy was observed in 26% of the cases, PKHD1 in 4% and triploidy in 2%. According to the karyotype result, when the group with normal karyotype and trisomy group was compared, the difference between the presence of additional anomalies ($p=0.004$), bilateral HN ($p=0.012$) and termination results ($p=0.002$) was found statistically significant. The rate of cases followed in pediatric surgery clinic/outpatient clinic in the postnatal period is 26% and 38.2% of these cases have undergone surgical intervention.

Conclusion: Appropriate diagnosis, follow-up and treatment of urinary system anomalies that have a broad clinical spectrum, with a multidisciplinary approach, are of great importance in both the prenatal period and the postnatal period.

Keywords: Hydronephrosis, karyotype, polycystic kidney, prenatal diagnosis, trisomy

INTRODUCTION

Congenital urinary system abnormalities include structural and functional malformations of the kidney, urethra, bladder and urethra. With the advanced technology ultrasonography devices

used today, it has become possible to detect many of these anomalies in the prenatal period (1). Congenital abnormalities of the kidney and urinary system (CAKUT) account for about 20-30% of all abnormalities detected in the prenatal period (2). The total

ORCID IDs of the authors: M.Ö. 0000-0002-2255-1642; H.S.Y.C. 0000-0002-5281-4933; Ö.D. 0000-0003-4376-8733; H.Ş. 0000-0002-3586-6125; T.A. 0000-0001-9488-9776; M.A.O. 0000-0001-5115-5262.

Corresponding Author: Miraç Özalp,

E-mail: ozalpmirac@gmail.com

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rate of CAKUT in live or stillborn infants is about 0.3 to 1.6 per 1,000 births (3).

The fetal kidney develops from the mesoderm layer, and the process that begins on the 26th day of embryogenesis goes through the stages of pronephrosis, mesonephrosis, and metanephrosis. Metanephrosis is the last stage of kidney development. It consists of metanephric mesenchyme and ureter bud, and begins to function between 6th-10th weeks. Fetal urine production starts in the 9th week of embryogenesis. Metanephrosis migrates from its initial caudal position and settles in the pelvis opposite the sacral somites, reaching its permanent location in the lumbar region in the 8th week of embryogenesis. The bladder and urethra develop from the urogenital sinus (4). Fetal urinary system abnormalities can be caused by defects in genes encoding signaling and transcription factors or monogenic abnormalities (5,6). Although some malformations are seen together with syndromes accompanied by multiorgan anomalies, most of the cases are non-syndromic. In addition, environmental factors such as exposure to teratogens during prenatal period may cause CAKUT by disrupting kidney morphogenesis (7,8).

Urinary system anomalies not only affect the existing system, but may also affect other fetal functions. Some of these abnormalities can cause oligohydramnios and, as a result, fetal pulmonary hypoplasia, facial deformities, and limb contractures. Most urinary system abnormalities are progressive. Functional recycling is possible with intrauterine or postnatal treatment methods (9,10). For this reason, prenatal diagnosis of urinary system anomalies; it plays an important role in determining the timing, place and mode of birth.

In our study, our aim was to determine the frequency of fetal urinary system anomalies, to determine their relationship with aneuploidy and additional structural malformations, and to compare prenatal diagnoses with postnatal period results.

METHODS

In this study, 282 cases of fetal urinary tract anomaly detected during fetal anomaly screening or routine obstetric ultrasound examination in Karadeniz Technical University Faculty of Medicine, Clinic of Perinatology between January 1, 2016 and June 31, 2019 were retrospectively evaluated. Age, week of pregnancy, gravida, parity, fetal sex, type of anomaly, presence of additional anomaly, prenatal diagnosis method, fetal karyotype result, termination status and postnatal results were recorded for all pregnant women with fetal urinary system anomaly. Urinary system anomalies were divided into subgroups such as renal agenesis, hydronephrosis (HN), multicystic dysplastic kidney (MCDK), polycystic kidney (PCK), ectopic kidney, duplication of collector system, megacystis and posterior urethral valve (PUV). The most widely accepted renal pelvic diameter (RPD) scoring system was used to define and grade fetal HN. Accordingly, the limit value for the anteroposterior diameter measurement of the renal pelvis in the transverse plane was determined as 4 mm until the 32nd gestational week, and 7 mm at 33 and more gestational weeks. Cases of HN that

underwent spontaneous resolution were excluded from the study during their follow-up in the prenatal period. For the purpose of prenatal diagnosis, each family that will be karyotyped was given genetic counseling prior to the procedure. Chorionic villus sampling (CVS), amniocentesis (AC) or cordocentesis (CC) were applied to the cases for genetic diagnosis. Written and verbal information was given to the families about the method of karyotyping and possible complications, informed consents were obtained. Interventions were performed with ultrasonography. Fetuses with aneuploidy or structural malformation incompatible with life were evaluated in the council consisting of perinatology, pediatric surgery and medical genetics doctors, and families were offered the option of termination of pregnancy. Evaluation of the newborn in the postnatal period was performed by pediatric surgery doctors within the first 7 days after birth.

For the study, the necessary ethics committee permission was obtained with the decision of the Ethics Committee of Karadeniz Technical University Faculty of Medicine (decision number: 2019/28).

Statistical Analysis

In the study, SPSS 24 Version was used for recording and calculating statistical data. (IBM Corp., SPSS Statistics for Windows, Version 24.0. Armonk, NY.) The suitability of numerical variables for normal distribution was tested by the Kolmogorov-Smirnov test. Categorical variables were determined using frequency and percentage; numerical variables were determined using mean and standard deviation or median and minimum-maximum values. The relationship between two categorical variables was investigated by chi-square test. The arguments were compared with the Mann-Whitney U test. The study was conducted in a 95% confidence interval and $p < 0.05$ value was considered statistically significant.

RESULTS

The study group consisted of 282 pregnant women with fetal urinary system anomaly. The mean age of the pregnant women included in the study was 30, and the mean week of gestation diagnosed with fetal urinary system anomaly was 23 weeks. Fetal sex was found to be 158 male (56%), 117 female (41.4%) and 7 unspecified (2.5%). Table 1 shows the demographic characteristics of the cases.

Among the abnormalities of the fetal urinary system, HN was the first. In 198 pregnant women (70.2%), fetal HN was observed, of

Table 1. Demographic data

Age	30±5.4
Gravida	3±0.6
Parity	1±0.3
Diagnosed pregnancy week	23.2±5.6
Fetal sex, F/M/U*, n (%)	117/158/7 (41.4%, 56%, 2.5%)
*F: female, M: male, U: undefined	

which 112 (39.7%) were unilateral and 86 (30.5%) were bilateral. In other pregnant women, unilateral MCDK in 15 (5.3%), bilateral MCDK in 2 (0.7%), unilateral renal agenesis in 8 (2.8%), bilateral renal agenesis in 4 (1.4%), PCK in 5 (1.8%), ectopic kidney in 16 (5.7%), collecting system duplication in 14 (5%), megacystis in 15 (5.3%), extrophia vesica in 2 (0.7%) and 3 of them (1.1%) had PUV (Table 2). An ultrasound image of the fetus diagnosed with a PUV was presented in Figure 1. Central nervous system abnormalities in 14 (26.4%) cases, fetal cardiovascular system abnormalities in 13 (24.5%) cases, and gastrointestinal system abnormalities in 7 (13.2%) were the most common groups in the study of other abnormalities accompanying urinary system abnormalities (Table 2). In addition, urinary system abnormalities that were most commonly associated with additional abnormalities were bilateral renal agenesis (50%), bilateral MCDK (50%), and extrophia vesica (50%) (Table 2). In addition to other organ abnormalities, anhydramnios developed in 7 cases (13.2%).

A total of 50 cases (45.9%) of karyotyping were performed, including AC for 37 cases, chorionic villi biopsy for 8 cases and CC for 5 cases. Fifty-nine patients (54.1%) refused to undergo karyotyping, although it was recommended. Karyotype results were observed to be normal in 34 (68%) patients. In one case, triploidy (69XXX) and in two cases, the *PKHD1* gene was positive, making all the remaining aneuploidy trisomies, and trisomy was

present in 13 (26%) patients (Table 3). An ultrasound image of the fetus with PKHD1 was shown in Video 1.

When the normal and trisomy groups were compared according to karyotype results, a statistically significant difference was found between the groups in terms of termination and bilateral HN ($p=0.002$, $p=0.012$) (Table 4). As a result of the karyotype, additional anomalies were observed, mainly 46.2% CNS anomaly and 23.1% CVS anomaly in trisomy patients. Two (15.4%) of cases

Figure 1. Ultrasound image of the fetus diagnosed with posterior urethral valve

Table 2. Distribution of fetal urinary system anomalies and accompanying anomalies

Urinary system anomalies	n	%	Additional anomaly (n)	Additional anomaly (%)
Unilateral hydronephrosis	112	39.7	23	20.5
Bilateral hydronephrosis	86	30.5	17	19.8
Unilateral MCDK	15	5.3	3	20
Bilateral MCDK	2	0.7	1	50
Unilateral renal agenesis	8	2.8	3	37.5
Bilateral renal agenesis	4	1.4	2	50
PKD	5	1.8	1	20
Ectopic kidney	16	5.7	-	-
Duplication of collector system	14	5	-	-
Megacystis	15	5.3	2	13.3
Extrophia vesica	2	0.7	1	50
Posterior urethral valve	3	1.1	-	-
	282	100	53	-
Accompanying anomalies	n	%		
CNS	14	26.4		
CVS	13	24.5		
GIS	7	13.2		
Face	5	9.5		
Skeletal dysplasia	5	9.5		
Single umbilical artery	9	16.9		
	53	100		

MCDK: multicystic dysplastic kidney, PKD: polycystic kidney disease, CNS: central nervous system, CVS: cardiovascular system, GIS: gastrointestinal system

with trisomy karyotype had isolated urinary system abnormalities, while the other 11 (82.4%) patients had additional abnormalities. Considering the presence of additional anomalies in patients with normal or trisomy as a result of karyotype, the difference was statistically significant ($p=0.004$) (Table 4).

Of fetuses with urinary system anomalies; Due to the fact that the result of karyotyping procedure performed in 10 of them was aneuploidy, due to the fact that 4 had bilateral renal agenesis, and 5 had normal karyotype results but other system anomalies accompanying it, a total of 19 cases (6.7%) were terminated by the decision of the perinatology council (Table 5). In 4 cases with aneuploidy as a result of karyotype, pregnancies continued with the decision of families.

The number of patients who can be followed up in the pediatric

surgery clinic/outpatient clinic in the postnatal period is 82, and when the cases that go to termination are excluded, the rate is 34.6%. During follow-up, 21 cases with HN regressed spontaneously, 19 cases were diagnosed with VUR, 9 of them operated, 14 cases underwent surgery due to ureteropelvic junction stenosis, 2 cases of PUV and 1 case of ureterovesical obstruction, and 11 cases are still being followed. Eight of the patients who were diagnosed with unilateral MCDK in the prenatal period came for follow-up in the postnatal period and the diagnosis was confirmed in these cases. Six of the cases with prenatal unilateral renal agenesis were controlled in the postnatal period and the diagnosis was confirmed in all of them. Ectopic kidney in 6 cases, duplication of the collecting system in 2 cases, and PUV diagnosis in 1 case were confirmed. The case with PUV diagnosis was operated.

Table 3. Karyotyping technique and results

Karyotyping technique	n	%
AC	37	74
CVS	8	16
CS	5	10
	50	100
Karyotype result	n	%
Normal	34	68
Trisomy 21	8	16
Trisomy 18	2	4
Trisomy 13	2	4
Trisomy 16	1	2
Triploidy (69XXX)	1	2
Other (PKHD1)	2	4
	50	100

AC: amniocentesis, CVS: chorionic villus sampling, CS: cordocentesis

Table 5. Karyotype analysis of termination cases

Karyotype technique	n	%
AC	11	57.9
CVS	4	21
None	4	21
	19	100
Karyotype result	n	%
Normal karyotype	5 (1*)	33.3
Tr-21	5	33.3
Tr-18	2	13.3
Tr-13	1	6.7
Tr-16	1	6.7
Triploidy (69XXX)	1	6.7
	15	100

*PKHD1 (+) case, AC: amniocentesis, CVS: cardiovascular system

Table 4. Comparison of normal and trisomy group according to karyotype result

	Normal karyotype group (n=34)	Trisomy group	p*
Age	(n=13)	p*	0.667
Gestational week	19±3	21±6	0.165
Termination	5	9	0.002
Presence of additional anomaly	1	5	0.004
Anomaly	-	-	-
Unilateral hydronephrosis	10	4	0.109
Bilateral hydronephrosis	13	3	0.012
Megasistis	5	5	1
Unilateral MCDK	2	-	-
Bilateral MCDK	1	-	-
Bilateral renal agenesis	1	-	-
Ectopic kidney	1	-	-
Duplication of collector system	1	-	-
Extrophia vesica	-	1	-

*P<0.05, MCDK: multicystic dysplastic kidney

DISCUSSION

Fetal HN is a common finding in antenatal ultrasonography observed in 0.6-4.5% of pregnancies and 20-40% of the cases are bilateral (11). The rate of cases with bilateral HN in our study was 43%, which is consistent with the literature. Most cases of fetal HN are clinically benign and temporary. Temporary HN occurs in 41-88% of cases, is associated with temporary stenosis in the ureteropelvic junction at an early stage and improves as the fetus matures (12). No criteria have been defined that can identify all newborns with significant pathology, and exclude infants with transient/physiological HN. Although a low threshold value (RPD >4 mm) in the second trimester has more sensitivity in detecting babies with CAKUT, it will include a large number of cases that are subjected to unnecessary tests and without kidney disease. In addition, RPD can be affected by gestational week, fetal bladder distension, and maternal hydration. In a study involving 74 cases with fetal HN in 2005 (13), spontaneous resolution was observed in the postnatal period in 74% of cases, which was found to be 56.5% for cases of unilateral HN and 46.2% for cases of bilateral HN in our study. In HN cases; the severity of HN, its being unilateral or bilateral, the presence of associated renal and extrarenal anomalies, gestational age and assessment of amniotic fluid status can give more insight into the postnatal process.

When the causes of chronic renal failure (CRF) in childhood are examined, it is seen that urinary system malformations have an important place. In order to reduce the incidence of CRF, it is very important to recognize these malformations in the early period, to make appropriate follow-up and treatment. The detection rate of bilateral renal agenesis in the prenatal period is 84-91%. In these cases, the fetal kidneys, ureters and bladder are not ultrasonographically monitored and the cases are accompanied by oligo-anhydramnios (14,15). In our study, 4 cases of bilateral renal agenesis diagnosed in the prenatal period were terminated by the decision of families and in 3 cases the diagnosis was confirmed after termination, and in 1 case, ventricular septal defects and micrognathia were additionally detected. In cases of bilateral renal agenesis, oligo-anhydramnios is the most difficult condition to detect additional anomalies in the prenatal period. The diagnosis of unilateral renal agenesis is more likely to be skipped during the prenatal period due to normal amnion fluid and bladder volume. The diagnosis depends on the correct exclusion of the presence of a second kidney in the renal fossa or ectopic region. Prenatal detection rate for unilateral renal agenesis is 59-80% (14). In our study, 6 of the 8 cases diagnosed with unilateral renal agenesis in the prenatal period were evaluated in the postnatal period and the diagnosis was confirmed. MCDK occurs with a frequency of 1/3,600-4,300. Although the disease can involve both kidneys, most cases are unilateral, and the left kidney is more frequently affected (16). In our study, 15 cases were diagnosed with unilateral MCDK in the prenatal period, and 8 cases were confirmed in the postnatal period. In 5 of these 8 patients who continued their follow-ups, involution occurred in the multicystic kidney, and a compensatory hypertrophy developed in the contralateral kidney.

In addition, VUR developed in the contralateral kidney in 1 case. VUR is the most common renal abnormality in the contralateral kidneys of patients with MCDK and this rate is 21% (17).

Studies that identified HN in the second trimester as RPD >4 mm showed that HN (18%) was higher in fetuses with Down syndrome compared to normal control group fetuses (0.5-3%) (18,19). For this reason, it is used as a marker in fetal aneuploidy screening, but there is no indication of chromosome analysis alone. However, it should be known that it increases the risk of age-related chromosome anomaly 1.5 times and prenatal counseling service to be given to pregnant women should be planned accordingly. In a study involving 375 cases with isolated HN, the incidence of Down syndrome was found to be 0.53% (20). Another study involving 682 fetuses with renal defects found that the incidence of chromosomal abnormalities was 13% (21). The incidence of aneuploidy in isolated bilateral renal agenesis was 5%, and the incidence of aneuploidy in the presence of additional abnormalities in patients with unilateral and bilateral renal agenesis was 33% and 40%, respectively. In addition, the most common chromosomal abnormalities in renal agenesis and MCDK cases are Tr-13 and Tr-18 (21). In our study, the proportion of fetuses with chromosomal abnormalities was 6.2% when cases where karyotyping was recommended but refused to perform were excluded. The most common group in which we recommend karyotyping is the group with a combination of unilateral HN and additional abnormalities, while the most common chromosomal anomaly in this group is Down syndrome. While being a reference center for prenatal diagnosis made it easier for us to catch fetuses with chromosomal abnormalities, anxiety about possible complications of karyotyping and, as a result, rejection of the procedure was our main limitation.

When urinary system anomalies are detected in the ultrasonography performed during prenatal period, other systems should also be carefully scanned. Because urinary system anomalies are mostly found together with other system anomalies. In addition, in cases with urinary system anomalies, in the presence of additional anomalies, the risk of chromosomal anomaly is increased. In the study of Hürçan et al. (22), the rate of fetuses with other congenital malformations accompanying urinary system anomalies was found to be 61.7%, and 23.6% in the study of Batukan et al. (23). In our study, the presence of other accompanying congenital anomalies was found to be 18.8%. Both in the study of Hürçan et al. (22) and in our study, the most common accompanying anomalies were central nervous system anomalies. The high proportion of accompanying anomalies in our study group was consistent with the literature.

In cases where severe uteroplacental insufficiency and early membrane rupture are excluded, if the bladder cannot be monitored with oligo-anhydramnios on ultrasound, it is considered that there is no functional kidney tissue. In this case, the first things that should come to mind for diagnosis are bilateral renal agenesis, bilateral MCDK disease or infantile PCK disease. Distinguishing these diseases from each other is possible only with detailed ultrasonographic examination. Long-term absence

of amniotic fluid in these cases causes pulmonary hypoplasia, which leads to severe respiratory failure at birth. In the study of Balsak et al. (24), the termination rate in cases with urinary system anomalies was found to be 14%, and fetuses with PCD disease were the first. In our study, 6.7% of the cases were terminated and bilateral renal agenesis, aneuploidy and PCK disease were the main causes. The fact that the number of fetuses with urinary system abnormalities was higher in our study was evaluated as the main cause of the difference.

In fetuses with sonographic findings compatible with lower urinary tract obstruction, there is no clear evidence that prenatal vesicoamniotic shunt administration improves renal function and long-term patient survival in prospective and retrospective studies. In addition, it was observed that the complication rate associated with the procedure was 45% (10,25). For these reasons, vesicoamniotic shunt is not performed in our clinic during the prenatal period. In addition, since chromosomal abnormalities are detected in about 25% of cases with urethral obstruction, karyotype analysis is required before treating cases (21). Intrauterine treatment is not recommended as more complex urethral anomalies are seen in female fetuses and the chance of success is lower. If intervention is to be made during antenatal period; the parents should be informed in detail about the risks and benefits of the procedure, neonatal survival and kidney results, and the procedures should be performed by experts.

In postnatal evaluations, the proportion of cases with spontaneous resolution HN was 30.8%, the most common causes of transient HN are VUR and obstruction in the ureteropelvic junction. In a study of Barbosa et al. (26) involving 1,034 cases of fetal HN, the rate of spontaneous resolution in the postnatal period was reported as 25%. The proportion of our patients who underwent surgery in the Postnatal period is 38.2%. Surgical indications were determined as recurrent febrile urinary tract infections and decreased relative kidney function in serial kidney scans. A study published in 2016 found that fetuses diagnosed with HN had a surgical intervention rate of 47% in the postnatal period (27). Both spontaneous resolution and surgical intervention rates of fetuses with HN in the postnatal period were found to be consistent with the literature.

CONCLUSION

Abnormalities of the urinary system can be detected mostly by ultrasonography in the prenatal period, and can be associated with chromosomal abnormalities and other structural malformations. Appropriate diagnosis, follow-up and treatment of these anomalies with a wide clinical spectrum, both in the prenatal period and in the postnatal period with a multidisciplinary approach, is of great importance.

Ethics Committee Approval: Ethics Committee of Karadeniz Technical University Faculty of Medicine, (decision number: 2019/28).

Informed Consent: Written and verbal information was given to the families about the method of karyotyping and possible complications, informed consents were obtained.

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REFERENCES

1. Policiano C, Djokovic D, Carvalho R, Monteiro C, Melo MA, Graça LM. Ultrasound antenatal detection of urinary tract anomalies in the last decade: outcome and prognosis. *J Matern Fetal Neonatal Med* 2015; 28: 959-63.
2. Queisser-Luft A, Stolz G, Wiesel A, Schlaefer K, Spranger J. Malformations in newborn: results based on 30,940 infants and fetuses from the Mainz congenital birth defect monitoring system (1990-1998). *Arch Gynecol Obstet* 2002; 266: 163-7.
3. Andrés-Jensen L, Jørgensen FS, Thorup J, Flachs J, Madsen JL, Maroun LL, et al. The outcome of antenatal ultrasound diagnosed anomalies of the kidney and urinary tract in a large Danish birth cohort. *Arch Dis Child* 2016; 101: 819-24.
4. Glassberg KI. Normal and abnormal development of the kidney: a clinician's interpretation of current knowledge. *J Urol* 2002; 167: 2339-51.
5. Boualia SK, Gaitan Y, Tremblay M, Sharma R, Cardin J, Kania A, et al. A core transcriptional network composed of Pax2/8, Gata3 and Lim1 regulates key players of pro/mesonephros morphogenesis. *Dev Biol* 2013; 382: 555-66.
6. Sanna-Cherchi S, Sampogna RV, Papeta N, Burgess KE, Nees SN, Perry BJ, et al. Mutations in DSTYK and dominant urinary tract malformations. *N Engl J Med* 2013; 369: 621-9.
7. Saisawat P, Kohl S, Hilger AC, Hwang DY, Yung Gee H, Dworschak GC, et al. Whole-exome resequencing reveals recessive mutations in TRAP1 in individuals with CAKUT and VACTERL association. *Kidney Int* 2014; 85: 1310-7.
8. Vivante A, Hwang DY, Kohl S, Chen J, Shril S, Schulz J, et al. Exome sequencing discerns syndromes in patients from consanguineous families with congenital anomalies of the kidneys and urinary tract. *J Am Soc Nephrol* 2017; 28: 69-75.
9. Zanetta VC, Rosman BM, Bromley B, Shipp TD, Chow JS, Campbell JB, et al. Variations in management of mild prenatal hydronephrosis among maternal-fetal medicine obstetricians, and pediatric urologists and radiologists. *J Urol* 2012; 188: 1935-9.
10. Ruano R, Sananes N, Wilson C, Au J, Koh CJ, Gargollo P, et al. Fetal lower urinary tract obstruction: proposal for standardized multidisciplinary prenatal management based on disease severity. *Ultrasound Obstet Gynecol* 2016; 48: 476-82.
11. González R, Schimke CM. Ureteropelvic junction obstruction in infants and children. *Pediatr Clin North Am* 2001; 48: 1505-18.
12. Nguyen HT, Herndon CD, Cooper C, Gatti J, Kirsch A, Kokorowski P, et al. The Society for Fetal Urology consensus statement on the evaluation and management of antenatal hydronephrosis. *J Pediatr Urol* 2010; 6: 212-31.
13. Ahmad G, Green P. Outcome of fetal pyelectasis diagnosed antenatally. *J Obstet Gynaecol* 2005; 25: 119-22.
14. Wiesel A, Queisser-Luft A, Clementi M, Bianca S, Stoll C. Prenatal detection of congenital renal malformations by fetal ultrasonographic examination: an analysis of 709,030 births in European countries. *Eur J Med Genet* 2005; 48: 131-44.
15. Stoll C, Tenconi R, Clementi M. Detection of congenital anomalies by fetal ultrasonographic examination across Europe. *Community Genet* 2001; 4: 225-32.
16. Schreuder MF. Unilateral anomalies of kidney development: why is left not right? *Kidney Int* 2011; 80: 740-5.
17. Kara A, Gurgoze MK, Aydin M, Koc ZP. Clinical features of children with multicystic dysplastic kidney. *Pediatr Int* 2018; 60: 750-4.
18. Coco C, Jeanty P. Isolated fetal pyelectasis and chromosomal abnormalities. *Am J Obstet Gynecol* 2005; 193: 732-8.

19. Corteville JE, Dicke JM, Crane JP. Fetal pyelectasis and Down syndrome: is genetic amniocentesis warranted? *Obstet Gynecol* 1992; 79: 770-2.
20. Signorelli M, Cerri V, Taddei F, Groli C, Bianchi UA. Prenatal diagnosis and management of mild fetal pyelectasis: implications for neonatal outcome and follow-up. *Eur J Obstet Gynecol Reprod Biol* 2005; 118: 154-9.
21. Nicolaides KH, Cheng HH, Abbas A, Snijders RJ, Gosden C. Fetal renal defects: associated malformations and chromosomal defects. *Fetal Diagn Ther* 1992; 7: 1-11.
22. Hürçan E, Biler A, Ekin A, Tosun G, Taner EC. Fetal üriner sistem anomalilerinin prenatal tanısı. *Perinatoloji Derg* 2018; 26: 1-6.
23. Batukan C, Holzgreve W, Danzer E, Rudin C, Ermiş H, Tercanlı S. Fetal üriner sistem anomalilerinin prenatal tans ve doğum öncesi yaklaşım: 173 olgunun analizi. *J Turk Ger Gynecol Assoc* 2002; 3: 23-32.
24. Balsak D, Başoğlu N, Toğrul C, Başoğlu Ö, Seçkin KD, Karaaltı MO, et al. Üriner sistem anomalisi saptanan fetüslara yaklaşım. *Jinekoloji - Obstetrik Neonatol Tıp Derg* 2015; 12: 135-9.
25. Morris RK, Middleton LJ, Malin GL, Quinlan-Jones E, Daniels J, Khan KS, et al. Outcome in fetal lower urinary tract obstruction: a prospective registry study. *Ultrasound Obstet Gynecol* 2015; 46: 424-31.
26. Barbosa JA, Chow JS, Benson CB, Yorioka MA, Bull AS, Retik AB, et al. Postnatal longitudinal evaluation of children diagnosed with prenatal hydronephrosis: insights in natural history and referral pattern. *Prenat Diagn* 2012; 32: 1242-9.
27. Scalabre A, Demède D, Gaillard S, Pracros JP, Mouriquand P, Mure PY. Prognostic value of ultrasound grading systems in prenatally diagnose unilateral urinary tract dilatation. *J Urol* 2017; 197: 1144-9.