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Empty fetal renal fossa results of a tertiary center

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Abstract

Objective: Our aim is to present the anomalies included empty renal fossa (ERF) in the ultrasonographic examination performed in the perinatology outpatient clinic of our hospital in 2020.

Methods: Ultrasonography requests were made in Kayseri City Hospital Perinatology Outpatient Clinic between January 1 and December 31, 2020, and 2405 ultrasonographic examinations were performed on 1961 pregnant women. The reports of the patients were analyzed retrospectively after the ethics committee approval of our hospital was obtained. All ultrasonographic examinations were performed by an experienced perinatologist using Samsung HS70A (Hampshire, UK), probe CA 1-7A. The fetuses diagnosed with empty renal fossa were screened in terms of accompanying anomalies and the detected anomalies were noted.

Results: Pregnant women were between 13 and 34 (mean 23.9) years old and their gestational ages were between 17 and 34 weeks. The incidence of empty renal fossa was found to be 0.75% for all pregnant women. An empty renal fossa finding was observed in a total of 15 fetuses. Horseshoe kidneys were present in four fetuses (0.20%), bilateral renal agenesis was present in five fetuses (0.25%), left renal agenesis was present in two fetuses (0.10%), pelvic kidneys (one on the right and two on the left) were present in three fetuses (0.15%), and crossed fused ectopic kidney was present in one fetus (0.05%).

Conclusion: The cause of ERF seen with anhydramnios is bilateral renal agenesis. In the presence of normal amniotic fluid, it should be considered that ERF may be due to various reasons and since the prognosis may change according to the accompanying anomalies, we must increase the accuracy of prenatal diagnosis.

Keywords: Empty renal fossa, renal agenesis, renal ectopia, horseshoe kidney, lying down adrenal sign.

Özet: Üçüncü basamak bir merkezin boş fetal renal fossa sonuçları

Amaç: Amacımız, 2020 yılında hastanemizin perinatoloji polikliniğinde gerçekleştirilen ultrason muayenelerinde boş renal fossanın (BRF) yer aldığı anomalileri sunmaktır.

Yöntem: Kayseri Şehir Hastanesi Perinatoloji Polikliniğinde 1 Ocak – 31 Aralık 2020 tarihleri arasında yapılan ultrason muayenesi talepleri sonucunda 1961 gebede 2405 ultrason muayenesi gerçekleştirildi. Hastanemizden alınan etik kurul onayı sonrasında hastaların raporları retrospektif olarak analiz edildi. Tüm ultrason muayeneleri, Samsung HS70A (Hampshire, Birleşik Krallık), prob CA 1-7A kullanan deneyimli bir perinatolog tarafından gerçekleştirildi. Boş renal fossa tanısı alan fetüsler eşlik eden anomaliler için tarandı ve tespit edilen anomaliler kaydedildi.

Bulgular: Gebeler 13 ile 34 (ortalama 23.9) yaş arasındaydı ve gebelik haftaları 17 ile 34 hafta arasındaydı. Boş renal fossa insidansı tüm gebeler için %0.75 olarak bulundu. Boş renal fossa bulgusu toplam 15 fetüste gözlemlendi. Dört fetüste (%0.20) at nalı böbrek anomalisi, beş fetüste (%0.25) bilateral renal agenezi, iki fetüste (%0.10) sol renal agenezi, üç fetüste (%0.15) pelvik böbrek (sağda bir ve solda iki tane) ve bir fetüste (%0.05) çapraz kaynaşmış ektopik böbrek anomalisi mevcuttu.

Sonuç: Anhidramniyoz ile birlikte görülen BRF'nin nedeni bilateral renal agenezidir. Normal amniyotik sıvı varlığında çeşitli nedenlerden dolayı BRF düşünülmelidir ve prognoz eşlik eden anomalilere göre değişebildiğinden, prenatal tanı doğruluğunu artırmamız gerekmektedir.

Anahtar sözcükler: Boş renal fossa, renal agenezi, renal ektopi, at nalı böbrek, düzleşmiş adrenal bez belirtisi.

Introduction

Urinary system anomalies including the morphological and functional pathologies of the fetal kidney, ureter, bladder, and urethra constitute 15–20% of all anomalies in the prenatal period.[1] The fetal urinary system can be evaluated ultrasonographically after 11th week of pregnancy. Most of the renal anomalies can be detected in the second trimester. Standard anatomical examination of fetal kidneys includes evaluation of bilateral renal fossa,

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kidney size, the morphology of cortex, and collecting system. The fetal kidneys are located paravertebrally, just below the fetal stomach level, and their pelvis faces the midline. In the third trimester, cortex-medulla distinction can be made. There are adrenal glands on top of both kidneys.[2] Renal blood flow is evaluated with Doppler examination. When the renal anomaly is unilateral, the amount of amniotic fluid is generally normal. Therefore, it should not be allowed to miss the diagnosis in cases of possible unilateral renal agenesis or renal ectopia. It should be careful with the examination of the bilateral renal fossa and pelvic region.[3] When fetal kidneys are not observed in their normal anatomical localization in the ultrasonographic examination, this situation is called "empty renal fossa" (ERF). The frequency of ERF in fetuses has been reported as 0.29% in pregnancies with normal amniotic fluid, and the most common cause is renal ectopia or unilateral renal agenesis.[3] Empty renal fossa pathologies include renal agenesis, pelvic kidney, horseshoe kidney, and crossed fused ectopic kidney. The "lying down adrenal sign" defined by Hoffman et al. in 1992 is observed in ultrasonography.[4] Defected migration during early embryological development causes renal ectopia, and failure in the onset of pronephros-mesonephros causes the absence of kidneys and ureters.[3] If ERF is present, careful evaluation of the fetal anatomy is required to assess for associated complex anomalies including chromosomal disorders and syndromes such as VACTERL syndrome.[5]

Our aim is to present the anomalies included empty renal fossa (ERF) in the ultrasonographic examination performed in the perinatology outpatient clinic of our hospital in 2020.

Methods

Obstetric anomaly screening, obstetric ultrasonography, and obstetric Doppler ultrasonography requests were made in Kayseri City Hospital Perinatology Outpatient Clinic between January 1 and December 31, 2020, and 2405 ultrasonographic examinations were performed on 1961 pregnant women, 34 of whom were twin pregnancy and the reports of the patients were analyzed retrospectively after the ethics committee approval of our hospital was obtained (decision number: 314, 18.02.2021). All ultrasonographic examinations were performed by an experienced perinatologist (E.T.) using Samsung HS70A (Hampshire, UK), probe CA 1-7A. For fetal biometry, the biparietal diameter (BPD), head circumference (HC), abdominal circumference (AC), and femur length (FL) of the fetuses were measured. Biometry, amniotic fluid and fetal anatomy were evaluated according to the International Obstetrics and Gynecology Ultrasound Association (ISUOG).[6] After the "lying down adrenal sign" is detected in at least one renal fossa, the whole abdomen and thorax were scanned axially, coronally, and sagittally in terms of the ectopic kidney. If the kidney is found at the pelvic region, near the bladder, the diagnosis is "pelvic kidney". When both kidneys are fused at any point (upper or lower pole) we diagnosed a "horseshoe kidney". "Crossed fused ectopic kidney" was diagnosed when both kidneys were fused end-to-end. "Renal agenesis" was diagnosed when renal artery could not be visualized in Doppler ultrasonography and kidney could not be observed in other possible regions. Fetuses diagnosed with ERF were also screened in terms of accompanying anomalies and the detected anomalies were noted. Diagnostic weeks and gender of fetuses were specified.

Karyotype analysis was not recommended for cases with a diagnosis of a pelvic kidney with ERF and crossed fused ectopic kidney because it would not affect the fetal prognosis. Karyotype analysis was recommended for all other cases.

Prenatal diagnoses were confirmed by the radiologist (S.T.) in pregnancies with delivery by postnatal ultrasonographic evaluation (**Fig. 1**).

Results

Ultrasonographic examination was performed on 1961 pregnant women who were referred to the perinatology outpatient clinic with consultation or the suspicion of anomaly in 2020. Racial origin of 170 pregnant women were Asian immigrants. Of the total pregnancies, 34 were twin pregnancies. Empty renal fossa findings were observed in a total of 15 fetuses. Pregnant women were between 13 and 34 (mean 23.9) years old and their gestational ages were between 17 and 34 weeks. Twelve pregnancies were diagnosed at the second trimester (between 17 and 23 weeks of gestation) and three pregnancies were diagnosed at the third trimester (between 27 and 36 weeks of gestation). Of the 15 fetuses, 10 were female and 5 were male. The incidence of ERF was found to be 0.75% for all pregnant women, 0.60% for Caucasian, and 1.76% for Asian immigrants. Horseshoe kidneys was found in four fetuses (0.20%), bilateral renal agenesis in five (0.25%), left renal agenesis in two

(0.10%), pelvic kidneys in three (one on the right and two on the left) (0.15%), and crossed fused ectopic kidney (0.05%) in one.

The number of unilateral ERF cases was 6 (two left renal agenesis, three pelvic kidneys, one crossed fused ectopic kidney) and it was observed at a rate of 40%. Bilateral renal agenesis was observed in nine cases (60%) with five bilateral renal agenesis, four horseshoe kidneys.

One of four fetuses with horseshoe kidneys was found no additional anomaly and was male. One of other fetuses with horseshoe kidneys had anencephaly, the other two had coexistence of neural tube defects and hydrocephalus (Chiari 2); Also, two of them had additional lower extremity anomaly and one had major cardiac anomaly; all of these fetuses were female. In a fetus with a neural tube defect, kidneys were fused from the lower pole. Fusion was observed in the upper pole of the remaining three fetuses with horseshoe kidneys (**Fig. 2**). In fetus number four mentioned in **Table 1**, lower pole fusion was observed, and upper pole fusion was observed in fetuses number one, two and three. There were complex anomalies in fetuses number one, two and four. While only the number one fetus with anencephaly was evacuated, other fetuses were delivered. The diagnosis week of fourth fetus was realized at 36th week due to the pregnancy without follow-up. Also, in our horseshoe kidney cases, only the number three fetus was male, the others were female.

One of the fetuses with bilateral renal agenesis had dextrocardia, one had occipital encephalocele, and the other had scoliosis and an echogenic focus in the heart. No additional anomaly was observed in the other two fetuses. All fetuses with bilateral renal agenesis had anhydramnios. The amniotic fluid amount was sufficient in other fetuses. Four fetuses were female, only one was male. In our cases, the number of bilateral renal agenesis was five, and it was observed at a frequency of 33.3%. In **Table 1**, dextrocardia in fetus number 8, scoliosis and echogenic focus in the heart in fetus number 9, and occipital encephalocele in fetus number ten were detected. No additional anomalies were found in the others. Four were females and one was male. Fetus number seven, male, was not evacuated by family decision, Cesarean delivery occurred when he was 35 weeks old according to the last menstrual period. Fetus number 10 was an intrauterine exitus around four weeks after diagnosis and delivery was immediately performed. Fetus numbers eight and nine

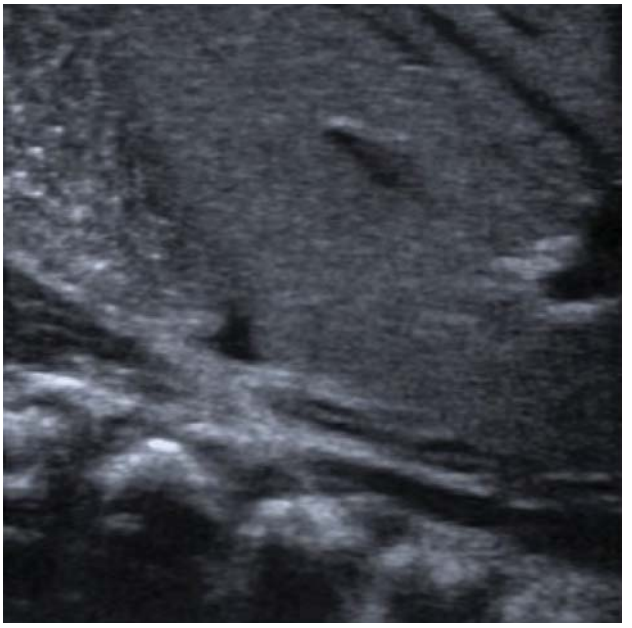

Fig. 1. In sonographic image, "lying down adrenal sign" of a newborn with a pelvic kidney is seen.

were evacuated with perinatologist recommendation and family decision. The number of cases with unilateral renal agenesis was two and none had a left kidney. They were both males. A persistent right umbilical vein was detected in fetus number five and mild hydronephrosis in the right kidney in fetus number six. Both fetuses were born healthy.

There was no left kidney in all fetuses with unilateral renal agenesis, hydronephrosis in the other kidney in one and persistent right umbilical vein in another

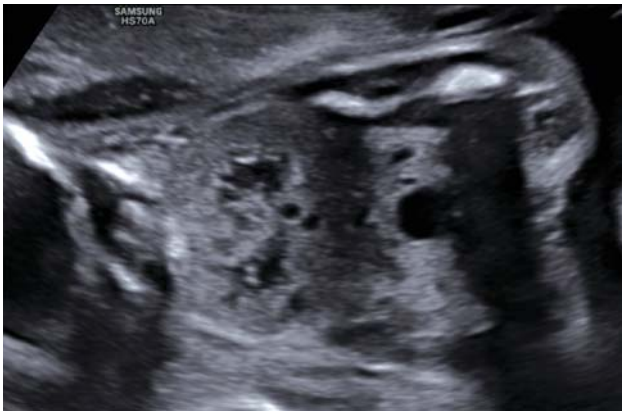

Fig. 2. The horseshoe kidney fused from the upper pole is seen.

Table 1. General characteristics of fetuses with empty renal fossa (ERF).

Fetus no	Maternal age	Diagnosis (Week)	ERF reason	Accompanying anomaly	Result	Gender
1 (FN)	27	19	Horseshoe kidney (upper pole fusion)	Anencephaly	Evacuation	F
2 (FN)	13	22	Horseshoe kidney (upper pole fusion)	Hydrocephalus, NTD, hypoplastic right ventricle, VSD, tricuspid valve dysplasia, right foot talipes	Delivery (33 weeks C/S)	F
3	24	21	Horseshoe kidney (upper pole fusion)	None	Delivery	M
4	23	36	Horseshoe kidney (lower pole fusion)	NTD, hydrocephalus, food talipes	Delivery	F
5 (FN)	31	34	Left renal agenesis	Persistent right umbilical vein	Delivery (C/S)	M
6	21	21	Left renal agenesis	Right hydronephrosis	Delivery	M
7	22	23	Bilateral renal agenesis	None	Evacuation not accepted; delivery with C/S at 35 weeks according to the last menstrual period	M
8	31	22	Bilateral renal agenesis	Dextrocardia	Evacuation	F
9	20	18	Bilateral renal agenesis	Scoliosis, echogenic focus	Evacuation	F
10	17	17	Bilateral renal agenesis	Occipital encephalocele	Evacuation after intrauterine exitus	F
11	21	20	Bilateral renal agenesis	None	Evacuation	F
12	29	21	Left pelvic kidney	Echogenic focus in the left ventricle	Delivery	M
13	34	27	Left pelvic kidney	None	Delivery	F
14	26	23	Right pelvic kidney	None	Delivery	F
15	20	21	Crossed fused ectopic kidney	None	Delivery (C/S)	F

C/S: cesarean section; **ERF:** empty renal fossa; **F:** female; **FN:** foreign national; **M:** male; **NTD:** neural tube defect; **VSD:** ventricular septal defect.

fetus were accompanying, renal artery outflows were not observed on the side of agenesis in Doppler.

There were three pelvic kidneys in our cases, and they were observed in the left lateral in fetuses number twelve and thirteen shown in **Table 1**, and in the right lateral pelvic in fetus number 14. Fetus number 12 was male and also echogenic focus was observed in the left ventricle of the heart. The fetuses number 13 and 14 were female and no additional anomalies were found in both.

Among our cases, fetus number fifteen in **Table 1** had a crossed fused ectopic kidney and it was a twin, no extrarenal anomaly detected. The left renal fossa was observed empty (**Fig. 3**). It was a female and was delivered healthily. No anomaly was found in the other twin.

Horseshoe kidney anomaly with anencephaly and Chiari 2 anomaly was found in two of the Asian immigrants and left renal agenesis with persistent right umbilical vein was detected in the third pregnant.

Among the 15 fetuses with ERF, five fetuses with bilateral renal agenesis were diagnosed in the second trimester during the investigation of the cause of anhydramnios, seven in the second-trimester screening, and the remaining three in the sonographic examinations at

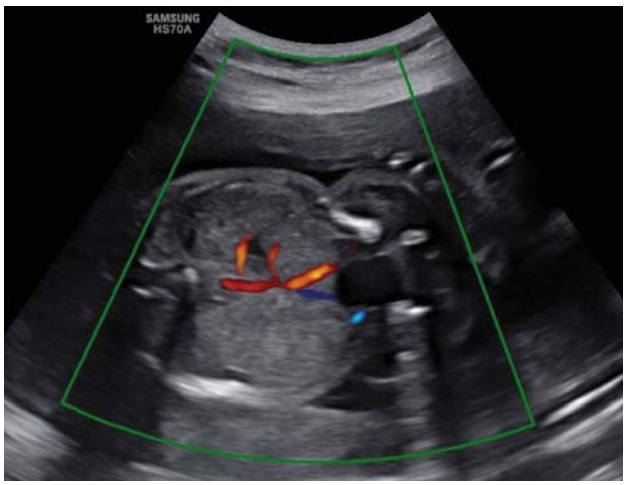

Fig. 3. In the case of cross-fused ectopic kidney on Doppler ultrasonography, both renal arteries are observed on the same side.

27, 34, and 36 weeks of gestation. A total of five fetuses were evacuated. Four of them were fetuses with bilateral renal agenesis and the other with anencephaly with horseshoe kidney.

Fetal karyotyping was offered in 11 cases and only was performed in one. Fetal karyotype of fetus number three with isolated horseshoe was normal. Genetic analysis could not be done in other cases as their families did not want fetal karyotype.

Fetuses number one, two, and five of our 15 cases with ERF belonged to Asian immigrants. a foreign family. The first two had horseshoe kidneys and other accompanying system anomalies were present. Fetus number five had left renal agenesis and persistent right umbilical vein. While fetus number one was evacuated, other fetuses were delivered.

General characteristics of fetuses with ERF are summarized in **Table 1**.

Discussion

An ideal method for evaluating the presence and growth of the fetal kidneys is prenatal sonography. Kidneys can be seen at 12 weeks of gestation. They are located on either side of the spine in the posterior abdomen. When no kidney is visualized in its normal paravertebral location, the diagnosis of an empty renal fossa is made on prenatal ultrasonography, adrenal gland is oriented longitudinally in the renal fossa.

The most common renal fusion anomaly of the kidney is the horseshoe kidney occurring in 1 in 400 births, with twice as many in males.[7,8] Although it is common in the postnatal period, prenatal diagnosis is made less frequently.[9] Kidneys are fused on both sides of the midline to contain equal amounts of renal tissue. Kidneys frequently undergo horseshoe fusion from the lower poles. The kidneys appear medially or anteriorly rotated. The horseshoe kidney shape can be traced in the coronal plane. Upper pole, both upper and lower pole, or alternative fusions are less common.[8] Although the horseshoe kidney clinic is silent in the adult population and there is no increase in the risk of tumors or urinary system stones, the risk of anomalies is three times higher in these fetuses and is also associated with chromosomal syndromes such as Turner or trisomy 18.[5] Boatman et al.[10] reported that complex anomalies (mainly skeletal, cardiovascular, central nervous system, and anorectal malformations) were observed in almost one third of the patients with horseshoe kidneys in their study. In addition, the gender of the patients with accompanying anomalies were 17 male and 15 female.[10] The four horseshoe kidneys detected in our study were found with a rate of 26.6% among all ERF cases. Central nervous system, cardiac and skeletal system anomalies were seen together in 75% of our horseshoe kidney cases. Since the prenatal diagnosis of isolated horseshoe kidney is more difficult, we think that we encountered horseshoe kidney more frequently in fetuses with complex anomalies in our cases. We hypothesize that it is due to the fact that most of the pregnant women were sent to our clinic with suspected anomaly. Contrary to the literature, horseshoe kidney anomaly was observed three times more frequently in female fetuses. This might be due to the small sample size.

Renal agenesis is characterized by a congenital absence of the kidney. Bilateral renal agenesis is incompatible with life. Unilateral renal agenesis is 3–4 times more common than bilateral renal agenesis and is three times more common in males.[11] Unilateral renal agenesis can be diagnosed after ectopic kidney and renal hypoplasia have been ruled out. Cho et al.[12] measured and compared the anteroposterior and transverse diameter ratios of unilateral renal agenesis, ectopic multicystic dysplastic kidney, pelvic kidney and healthy fetus kidneys in the second and third trimesters. Unilateral renal agenesis and ectopic multicystic dysplastic kidney were observed with compensatory hypertrophy in the third trimester compared to normal kidneys, while compensatory hypertrophy was not observed in the pelvic kidneys. In bilateral renal agenesis, anhydramnios accompanies after the 16th gestational week, the fetus bladder cannot be visualized even if the examination is repeated. Since adrenal glands extend towards the renal fossa in cases of agenesis, it should not be considered as a kidney by mistake. The normal sonographic appearance of the adrenals is observed as a small inverted “Y” or “V”, they have a central hyperechogenic medulla and peripheral hypoechoic cortex, and they do not have a pelvis.[13] The renal artery cannot be visualized in color Doppler examination in agenesis. Since the adrenal gland artery is significantly smaller than the renal artery, it can be distinguished by careful examination.[5] Retroperitoneal colon segment filled with hypoechoic content filling ERF in the third trimester may also be mistaken for a kidney. Careful examination reveals that the corticomedullary separation is not noticed and the renal

artery is not observed in the Doppler.[5] Since the rate of occurrence with chromosomal anomalies and genetic syndromes in bilateral or unilateral renal agenesis can reach up to 30%, the fetus should be examined separately in terms of accompanying anomalies.[11] In a study by Tutuş it was reported that Blake pouch's cyst and also corpus callosum agenesis were observed in a patient with bilateral renal agenesis.[14] Unlike the literature, the number of bilateral renal agenesis was higher in our cases than unilateral agenesis. We think that it is due to the fact that most of the pregnant women were referred with the suspicion of anomaly. The fact that both fetuses with unilateral renal agenesis were male was consistent with the literature.[11]

Unilateral ERF is caused by the pelvic kidney at a rate of approximately 42%[15] and its frequency is 1 in 500 to 3000 live births.[16,17] It occurs when the upward migration of the kidney towards the lumbar area is impaired between the sixth and the tenth gestational weeks.[18] A pelvic kidney can mimic renal agenesis in prenatal ultrasonography. When an empty renal fossa and lying down adrenal sign are detected, possible renal locations should be screened before the diagnosis of renal agenesis is made. Also, in unilateral renal agenesis, hypertrophy can be observed in the contralateral kidney even in the intrauterine 22nd week, while the contralateral kidney size in the pelvic kidney is within normal limits.[12] Most ectopic kidneys are located within the bony pelvis. Hill et al.[19] defined the pelvic kidney as ipsilateral or midline, but Meizner et al.[20] found that postnatally opposite the sacrum and below the aortic bifurcation. In the study conducted by Yüksel and Batukan, 24 of 40 ERF cases with at least one ERF and normal amniotic fluid amount were found to have pelvic kidney and 13 had unilateral renal agenesis.[3] In the cases in our study, our rate of a pelvic kidney was 20% among all ERFs and its incidence among unilateral ERFs was 50% and it was consistent with the literature.[3,15]

A crossed fused ectopic kidney is defined as the fusion of one kidney with its ureter crossing the midline to the other kidney. Its frequency is reported as 7.5 per 10,000 newborns.[21] There are several subtypes of the crossed fused ectopic kidney. It can be seen as sigmoid or "S" shaped, lump shaped, "L" shaped discoid.[22] A crossed fused ectopic kidney can be isolated, or it can be seen especially with uterine anomalies, imperforate anus, or skeletal anomalies.[5] Jazicek et al.[23] retrospectively analyzed 185 fetuses with ERF between 2005 and 2015 and when they examined 10 fetuses with crossed fused ectopic kidneys, they found a double collecting system in two cases, bilateral hydronephrosis in one, a single umbilical artery in four, ventricular septal defect in one, and persistent left superior vena cava in one.

Chow et al.[15] retrospectively examined unilateral ERF cases between 1989 and 2003 and identified 93 ERF cases. The most common cases were renal agenesis (47%), ectopic kidney (42%), normal localization (11%), but no dysplastic kidney cases. They pointed out that 42% of the cases were accompanied by multisystemic anomalies. Markov et al.[24] prospectively investigated ERF cases between 2007 and 2010 other than bilateral renal agenesis. They identified 9 cases of ectopic kidney (seven of them pelvic kidney, one iliac settlement and one crossed fused ectopic kidney) and 8 cases of unilateral renal agenesis. While 16 of the 17 cases were isolated anomalies, they pointed out that there was tetralogy of Fallot and a single umbilical artery association in only one case that resulted in evacuation. They noted that a case with unilateral renal agenesis was diagnosed after birth. The number of unilateral ERF cases in our study was 6 and the number of bilateral ERF cases was 9, and complex multisystem anomalies were observed in bilateral ERF cases. However, due to the small number of cases, it may not be very accurate to compare.

As it is known, the frequency of congenital anomalies may differ depending on race, socioeconomic level, geographical regions, and environmental factors, so the rate of ERF in Asian immigrants in our study was approximately three times higher than Caucasians. However, this excess should not be generalized due to the small number of our cases.

The low number of cases and the families not wanting fetal karyotype are the limitations of our study. Diversity with a higher number of cases and association with the genetic study will shed more light on the subject we touched upon.

Conclusion

The cause of ERF seen with anhydramnios is bilateral renal agenesis. In the presence of normal amniotic fluid, it should be considered that ERF may be due to various reasons and since the prognosis may change according to the accompanying anomalies, we must increase the accuracy of prenatal diagnosis. In our cases, the incidence of ERF was higher according to the total number of pregnant women examined. This was attributed to the spe-

cial-problematic cases being sent to the perinatology outpatient clinic.

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Compliance with Ethical Standards: The authors stated that the standards regarding research and publication ethics, the Personal Data Protection Law and the copyright regulations applicable to intellectual and artistic works are complied with and there is no conflict of interest.

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