Unilateral Renal Agenesis Diagnosed on Early Prenatal Transvaginal Scans

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ABSTRACT: **Background:** Unilateral renal agenesis is a rare finding. There are no large-scale studies reporting this finding in early pregnancy.

Objectives: To evaluate the incidence of unilateral renal agenesis (URA) and of associated anomalies diagnosed by early prenatal transvaginal sonography.

Methods: We performed a retrospective chart review of all 59,382 transvaginal scans performed at 14–16 weeks gestation by a single operator at different clinics during the period 1994–2013.

Results: The incidence of URA was 1:1212 (49/59382 cases). Associated anomalies were diagnosed in 22 cases (45%). Renal anomalies were diagnosed in 22.4%. Extra-renal anomalies (with exclusion of a single umbilical artery or nuchal edema as isolated findings) were diagnosed in 24.5%. Ambiguous genitalia were diagnosed in 8.2%.

Conclusions: URA is a rare finding in early transvaginal sonography. Associated anomalies are common and should be sought.

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KEY WORDS: unilateral renal agenesis (URA), early prenatal scans, incidence, associated anomalies

Unilateral renal agenesis (URA) is a rare finding. Its incidence has been estimated to be 1 in ~2000 when combining data from both prenatal and postnatal studies [1]. Previous research reported prenatal diagnosis of a solitary kidney later in pregnancy [2-4]. To date, there are no large-scale prenatal studies reporting this finding in early pregnancy, excluding cases of regressed abnormal kidneys (multi-cystic dysplastic kidney or other dysplastic kidneys). In the present study we aimed to evaluate the incidence of URA and its associated anomalies in a large population scanned in early pregnancy via transvaginal sonography.

PATIENTS AND METHODS

We conducted a retrospective chart review of all early prenatal anatomical surveys performed by a single physician (M.B.) between 1994 and 2013. All surveys were performed transvaginally at 14–16 weeks gestation. Prior to 2004, an Elscint 300 device with an annular 7.5 MHZ transducer was used. Since 2004 we have been using an iU22 device (Philips Healthcare, Bothell, WA, USA) with a 3 to 9 MHz vaginal transducer. The kidneys were examined on both coronal and sagittal sections. In these sections the kidney is normally visualized as an echogenic structure in the renal fossa, easily distinguishable from the surrounding structures, with a hypoechogenic pelvis [Figure 1].

Color Doppler should confirm the presence of the renal vessels. In cases of URA the above findings were missing, and the lumbar fossa was empty with the adrenal gland appearing elongated ("lying down adrenal sign") [1]. To exclude an ectopic kidney, it was sought in other possible ectopic locations, including following an ipsilateral renal artery from its origin. In cases where unilateral renal agenesis was diagnosed, charts were further reviewed for gender (based on diagnostic criteria by Bronshtein et al. [5]) and associated anomalies. All pregnancies with the diagnosis of fetal URA were followed to birth/abortion/termination of pregnancy for confirmation of the diagnosis of URA and associated anomalies. The study was approved by the institutional Helsinki Committee.

RESULTS

During 1994–2015, 59,382 early anatomical scans were performed and unilateral renal agenesis was diagnosed in 49 cases (0.083% or 1:1212). The right kidney was missing in 21 fetuses and the left kidney in 23. Side documentation was not available in five cases. Most of the fetuses were males (37, 75.5%). There were 8 females (16.3%), and 4 fetuses had ambiguous genitalia (8.2%). All gender determinations remained unchanged at follow-up after birth, spontaneous abortion, or termination of pregnancy.

Associated anomalies were diagnosed in 22 cases (45%) [Table 1]. Excluding four cases of nuchal edema and single umbilical artery (SUA) as solitary findings, the number of cases with associated anomalies was 18 (36.7%). Renal anomalies were diagnosed in 11 cases (22.4%) and included pelvic kidney (5 cases), multi-cystic dysplastic kidney (2 cases), hydronephrosis (2 cases), and 1 case each of a hyperechogenic kidney and double collecting system. Of the 11 cases in which renal anomalies were diagnosed, 6 cases had only renal anomalies,

while in 5 cases extra-renal anomalies were diagnosed as well. Extra-renal anomalies were diagnosed in a total of 16 cases. With exclusion of the four isolated nuchal edema/SUA cases the prevalence of extra-renal anomalies was 12/49 (24.5%). These anomalies included skeletal anomalies (4 cases: radial agenesis in 2, hemivertebra in 1, syndactyly in 1), cardiac anomalies (2 cases: hypoplastic left heart syndrome in 1, coarctation of aorta in 1), central nervous system anomalies (2 cases: hydrocephalus in 1, ventriculomegaly in 1), cystic hygroma (n=1), flat nose (n=1), and echogenic bowel (n=1). In most cases where associated anomalies were diagnosed, renal agenesis was diagnosed on the left and in males. Among fetuses with ambiguous genitalia, additional associated anomalies were diagnosed in three of four cases.

Among all pregnancies with the diagnosis of fetal URA, termination of pregnancy was performed in 11 cases (22.4%). All had associated anomalies. The cases in which associated anomalies were diagnosed but in which termination of pregnancy was not performed were those with isolated SUA, isolated nuchal edema, hydronephrosis, pelvic kidneys, and a case with both nuchal edema and hyperechogenic kidney. There was one case of a spontaneous abortion among all cases with URA. This fetus had ambiguous genitalia without any other associated anomalies. All other pregnancies were carried to term. All diagnoses of URA and of associated anomalies remained unchanged upon birth, termination of pregnancy, or spontaneous abortion.

Figure 1. Transvaginal coronal view of a 16-week fetus. The aorta (arrow) is demonstrated in the midline. A kidney with a double collecting system (arrows 1 and 2) is demonstrated on one side, with an empty renal fossa on the contralateral side

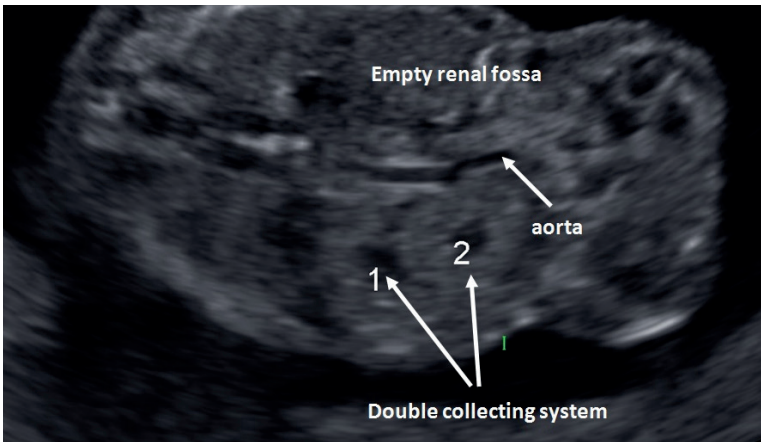

Table 1. URA-associated anomalies and termination of pregnancy

Patient no.	Extra-renal anomalies	Renal anomalies	TOP
Males			
1	Ectrodactyly		Yes
2	SUA		No
3	Syndactyly	MCDK	Yes
4	Coarctation	DCS	Yes
5	SUA	Hyperechogenic kidney	No
6		Hydronephrosis (5 mm, 15 wk)	No
7	NE		No
8		Pelvic kidney	No
9	NE		No
10	Hydrocephalus		Yes
11		MCDK	Yes
12		Pelvic kidney	No
13	SUA	Pelvic kidney	No
14	SUA		No
15		Hydronephrosis (5 mm, 16 w)	No
16		Pelvic kidney	No
Females			
17	SUA, hemivertebra		Yes
18	Cystic hygroma, limb, SUA, HLHS		Yes
19	Echogenic bowel, NE	Pelvic kidney	Yes
Ambiguous genitalia			
20	Flat nose		Yes
21	Multiple		Yes
22	Cloaca, ventriculomegaly		Yes

TOP = termination of pregnancy, SUA = single umbilical artery, NE = nuchal edema, HLHS = hypoplastic left heart syndrome, MCDK = multi-cystic dysplastic kidney, DCS = double collecting system

DISCUSSION

In this study, we present a large series of early prenatal diagnosis of URA from a total number of 59,382 early anatomical scans. We found an incidence of 1 per ~1200 for unilateral renal agenesis. The male to female ratio was 4.6:1, with 8% of cases diagnosed with ambiguous genitalia. Associated anomalies were diagnosed in 45% of fetuses. Termination of pregnancy was performed in 22.4% of all cases in which URA was diagnosed.

The incidence of URA found in our series is higher than that reported by previous prenatal studies (1 in ~8000) [2]. It is closer to the incidence reported in a meta-analysis of both prenatal and postnatal studies combined, which was 1 in ~2000 [2]. The higher incidence found in our study might be even more striking since the previously reported studies, which included later scans and postnatal findings, are biased as some cases diagnosed as URA later might actually represent regressed dysplastic kidneys. The higher incidence found in our study might be attributed to the transvaginal approach employed in our group of patients and to the earlier timing of scanning in our series. The resolution advantage of early transvaginal sonography in general, especially in obese woman, has been shown before [3,4]. Also, later in pregnancy, as the kidneys become more hypoechogenic it is sometimes difficult to differentiate kidneys from a large adrenal. Thus, an empty renal fossa could easily be missed due to a large adrenal gland [5]. Another possible contributing factor to the lower rate of detection in previous studies might be the inclu-

sion of multiple operators, sometimes from several countries [6]. It is well known that prenatal sonography is significantly operator-dependent [7-9]. In our series, a single operator performed a very high volume of scans, implying good scanning capabilities.

The rate of URA-associated anomalies in our study is in the same range as reported by Westland et al. [2]. However, in their systematic review [2] no mention was made as to whether prenatal studies were included in the analysis of associated anomalies. One can assume that continued postnatal follow-up of the URA patients in our group would have likely increased the rate of associated anomalies. For example, the most common renal anomaly in Westland's review was vesico-ureteral reflux, which can develop after birth and is not readily diagnosed prenatally [10]. Moreover, an important category of associated anomalies found in our group is female genital tract anomalies. These are very difficult to diagnose prenatally and were diagnosed postnatally in 11% of female patients with URA in Westland's review [2]. Nevertheless, the rate of ambiguous genitalia in our series was as high as 8.2%. The association between disorders of sex development and renal anomalies has been shown before [11]. However, a specific association between URA and ambiguous genitalia has not been reported previously. A careful inspection for possible ambiguous genitalia should therefore be performed in fetuses with URA.

Several studies have examined the prognosis of URA with and without concomitant anomalies. Westland and co-authors found that renal injury, defined as the presence of hypertension and/or albuminuria and/or the use of renoprotective medication, was present in 32% of all children with a single functioning kidney (SFK) at a mean age of 9.5 years. Children with concomitant ipsilateral congenital anomalies of the kidneys and urinary tract (CAKUT) had higher proportions of renal injury (48.3 vs. 24.6%, $P < 0.05$) [12]. Follow-up has shown that ~40% of patients with a solitary functioning kidney were in renal failure at the age of 30 years [13]. In contradistinction, a recent study that followed 32 children with prenatally diagnosed congenital SFK (20 of whom had URA) demonstrated that it was associated with little or no renal damage in infancy or childhood. However, no associated CAKUT were found in this series [14]. CAKUT accounts for 34–59% of pediatric and 7% of adult end-stage renal disease [15-17]. Based on the high prevalence of CAKUT with URA, some recommend that patients with URA be monitored throughout life [12].

Since contralateral compensatory kidney enlargement is considered a good prognostic sign in URA [14,18], Nagar at al. [19] suggested using the fetal renal-to-abdominal (RTA) ratio as a prognostic measurement in URA, with a large RTA indicating that compensatory nephrogenic mechanisms are intact [19].

CONCLUSIONS

Unilateral renal agenesis is a rare disorder with an incidence of 1 in ~1200 in early transvaginal prenatal scans. When it is diagnosed, fetuses should be carefully evaluated for associated renal and extra-renal anomalies as well as for ambiguous genitalia, both prenatally and postnatally, as these may affect prognosis.

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