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Evidence-based, ethically justified counseling for fetal bilateral renal agenesis

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Abstract

Background—Not much data are available on the natural history of bilateral renal agenesis, as the medical community does not typically offer aggressive obstetric or neonatal care asbilateral renal agenesis has been accepted as a lethal condition.

Aim—To provide an evidence-based, ethically justified approach to counseling pregnant women about the obstetric management of bilateral renal agenesis.

Study design—A systematic literature search was performed using multiple databases. We deploy an ethical analysis of the results of the literature search on the basis of the professional responsibility model of obstetric ethics.

Results—Eighteen articles met the inclusion criteria for review. With the exception of a single case study using serial amnioinfusion, there has been no other case of survival following dialysis and transplantation documented. Liveborn babies die during the neonatal period. Counseling pregnant women about management of pregnancies complicated by bilateral renal agenesis should be guided by beneficence-based judgment informed by evidence about outcomes.

Conclusions—Based on the ethical analysis of the results from this review, without experimental obstetric intervention, neonatal mortality rates will continue to be 100%. Serial

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amnioinfusion therefore should not be offered as treatment, but only as approved innovation or research.

Keywords

Amnioinfusion; beneficence; bilateral renal agenesis; clinical decision making; counseling; ethics; fetal; neonatal; obstetric; perinatal

Introduction

Congenital fetal anomalies of the kidney and urinary tract (CAKUT) are the most common types of anomaly identified through ultrasound 1–3]. The spectrum of congenital fetal anomalies of the kidney and urinary tract is broad, ranging from mild, asymptomatic malformations to severe, life-threatening conditions such as bilateral renal agenesis. Fetal examination of more than 700,000 births studied within a European registry of renal anomalies revealed bilateral renal agenesis has a prevalence of 0.013% 4]. Bilateral renal agenesis, or absence of both kidneys, is commonly referred to as a “lethal” condition. When a fetus is completely lacking both kidneys, oligohy-dramnios develops, which leads to pulmonary hypoplasia and the Potter sequence. Pulmonary hypoplasia is the leading cause of death [5, 6].

A case report of monozygotic twins discordant for bilateral renal agenesis reveals that the twin with bilateral renal agenesis did not suffer from respiratory sequelae likely due to the presence of normal amniotic fluid levels produced by the other twin. The patient with bilateral renal agenesis was able to survive the neonatal period, but ultimately died at 2 months of age from peritoneal dialysis complications [7]. This case study suggests that normal amniotic fluid volumes play an important role in improved pulmonary outcomes, allowing transition to peritoneal dialysis, suggesting serial amnioinfusion may be a potentially therapeutic intervention. A recent publication presents a case study in which an infant was born at 28 weeks' gestation after receiving serial amnioinfusions starting at 23 weeks' gestation after the diagnosis of bilateral renal agenesis at 20 weeks' gestation. This unprecedented intervention allowed the infant to survive through the neonatal period using peritoneal dialysis as a bridge toward renal transplantation at 1 year of age [8]. Prior to this case report, there were no documented survivors with bilateral renal agenesis beyond the neonatal period and the standard of care meant that neither aggressive obstetric nor aggressive neonatal management was offered, because lung development was not compatible with life.

After the reporting of the neonatal outcome of serial amnioinfusion in this single case study and providing information on outcomes with a living survivor, it is unclear if defining bilateral renal agenesis as a lethal condition, defined as 100% mortality even with intervention, remains appropriate [8, 9]. Not much data are available on the natural history of bilateral renal agenesis, as the medical community does not typically offer aggressive obstetric or neonatal care as bilateral renal agenesis has been accepted as a lethal condition. Further complicating interpretation of the data on isolated bilateral renal agenesis is the inclusion of complex bilateral renal agenesis in which the condition is associated with

chromosomal conditions or other structural anomalies. In addition, with the widespread availability of obstetric ultrasound, many pregnancies complicated by bilateral renal agenesis will end in induced abortion. Without data on the natural history of this disease process, counseling pregnant women and families with fetuses affected by this condition is challenging.

Johnson and Luks provide an important discussion on the ethical challenges of innovation in fetal intervention for bilateral renal agenesis and of transitioning from innovation to research and practice in a professionally responsible way [10]. Their paper sets the stage for addressing the ethics of counseling pregnant women whose pregnancies are complicated by life-limiting renal anomalies. Our goal in this paper is to provide an evidence-based ethical analysis and argument, based on a systematic literature review that will provide practical guidance for counseling pregnant women about obstetric management.

Methods

This study was exempt from institutional review board (IRB) approval given that it was a systematic literature review of peer-reviewed articles not using identifiable patient data. The literature review was performed using PubMed, EMBASE, CINAHL, Cochrane Database, and Pediatric Academic Societies' Abstracts Archive databases. Limiting publications to the previous 10 years for natural history outcomes data and articles published in English for both natural history outcomes data and interventions, we used the search terms included (Table 1). We also used the “Similar Articles” function of PubMed and hand-searched the reference lists of articles in this review to identify additional articles.

Our review had goals: to describe the natural history of bilateral renal agenesis and to describe interventions and their outcomes. To describe the natural history of bilateral renal agenesis, our inclusion criterion was any article that included multiple patients diagnosed with bilateral renal agenesis. As a result, while describing the natural history, case series were included and case reports were excluded. Outcomes of interest included number of patients with bilateral renal agenesis who were stillborn, underwent termination of pregnancy (TOP), suffered an intrauterine fetal demise (IUFD) or neonatal demise, or were liveborn, differentiating unilateral from bilateral disease and isolated from complex (associated with other anomalies or syndromes) disease and measuring length of time of survival. Details on natural history outcomes are provided from the studies we analyzed (Tables 2 and 3). To describe interventions for fetal and neonatal benefit and their reported outcomes, we included both case series and case reports, as evidenced in Table 4.

The ethical analysis of outcomes data appeals to the professional responsibility model of obstetric ethics [27]. In obstetric ethics, the physician has ethical obligations to both the pregnant woman and to the fetal patient [28]. The perinatal team has beneficence-based and autonomy-based obligations to the pregnant woman and beneficence-based obligations to the fetal and neonatal patient. These must all be considered in ethical analysis and argument about serial amnioinfusion. A single-minded focus on the fetal patient is not permissible and leads to a clinically incomplete account of serial amnioinfusion, which is an invasive procedure for the pregnant woman [29, 30].

The ethical principle of beneficence obligates physicians to identify and offer clinical management that in deliberative (evidence-based, rigorous, transparent and accountable) clinical judgment is expected to result in net clinical benefit for the patient, i.e. a greater balance of clinical goods (preservation of life and health) over harms (risks of mortality, morbidity, pain, distress, suffering and lost functional status). The strength of the beneficence-based judgment that the proposed clinical management meets this test and should therefore be offered varies with the strength of evidence about outcomes. With stronger evidence, there is an obligation to recommend a specific form of clinical management. When evidence is weak, it is permissible to offer, but not recommend a specific form of clinical management. When evidence is absent, it is not permissible to offer intervention as treatment, but rather only as an experiment.

Results

Our search related to our first goal resulted in 300 articles from PubMed, 18 articles from CINAHL, 28 articles from EMBASE and 173 articles from the Scopus database. The Cochrane Systematic Review database did not reveal any results. The Pediatric Academic Societies' (PAS) Abstracts Archive database revealed seven studies. After removing duplicate studies and examining the titles and abstracts to determine relevance to fetuses and newborns with renal agenesis and the outcomes of isolated anomaly compared to complex disease associated with other anomalies, live-birth rates, stillbirth or termination of pregnancy (TOP) rates, age at death, and interventions reported, 16 articles met our inclusion criteria for review. Our search related to the second goal resulted in two articles. The results related to the first goal are described, followed by results for the second goal.

Outcomes without intervention

The variability in how bilateral renal agenesis is categorized and reported makes data interpretation within and across studies challenging. Renal dysgenesis or abnormal kidney development, manifests in a spectrum and is referred to by many terms that sound similar and can be easily confused with each other. The most severe abnormal kidney development results in bilateral renal agenesis, in which there is complete absence of kidney development. Defining kidneys as dysplastic means kidney tissue is present, but that development is abnormal and incomplete. The extent of dysplasia varies widely and may affect the entire kidney resulting in a small, aplastic remnant kidney or could result in large cystic dysplastic kidneys [31]. Despite different etiologies, various renal anomalies are often grouped together. For example, in the study by Wang et al. [14] and a separate study by Wiesel et al. [4], renal agenesis and renal dysgenesis are categorized together as data were collected using the same ICD-9 code from birth registry data. In another study, Mehler et al. [17] categorize patients with renal dysplasia and renal agenesis together. No definition was provided to delineate renal agenesis and dysplasia as a group from other congenital anomalies of the kidney or urinary tract. Grijseels et al. [19] describe a group of patients affected by dysplasia, encompassing a range of disease from renal agenesis to massive cystic kidneys separate from polycystic disease or hydronephrosis. Slickers et al. [11] defined renal hypoplasia as underdeveloped kidneys with the potential to predispose surviving infants to

developing chronic kidney isease and hypertension and grouped this entity with renal agenesis when referencing outcomes.

Some studies reported on outcomes we identified, but patients with renal agenesis were not presented as a distinct population. The study by Scott [32] reported on outcomes for both bilateral renal agenesis and polycystic disease as a single, but heterogeneous, population because these conditions encompassed the most common renal anomalies. Ulkumen et al. [22] focused on evaluating outcomes in pregnancy with early onset oligohydramnios, noting that five of the 54 pregnancies affected by oligohydramnios or anhydramnios were related to bilateral renal agenesis. Outcomes were reported in total number of pregnancies with oligohydramnios or anhydramnios rather than renal agenesis alone. Nagase et al. [23] analyzed cases affected by oligohydramnios sequence to clarify whether the prognosis was affected by various modes of delivery. Oligohydramnios sequence can be the consequence of either renal agenesis or dysgenesis. Seven cases were given the pathological diagnosis of bilateral renal agenesis at autopsy, but outcomes data were presented for all cases of oligohydramnios sequence. Categorizing the data this way makes it impossible to understand the rate of pregnancy termination, intrauterine death, stillbirth, induced abortion and length of survival for neonatal patients affected by bilateral renal agenesis alone.

It is important to distinguish unilateral cases of renal agenesis from those that are bilateral, because this difference has significant impact on outcomes. Some studies did not define the difference between bilateral and unilateral renal agenesis in terms of outcomes. Kumar et al. [25] analyzed renal anomalies to identify factors associated with poor outcome. Eight patients were noted to have renal agenesis, but it was not specified which were unilateral and which bilateral. Davis et al. [12] investigated maternal diabetes as a link to the etiology of renal agenesis. Of the 89 pregnancies with renal agenesis and maternal diabetes, 22 of them were diagnosed as bilateral, while the other 59 were cases with unilateral renal agenesis. Outcomes data were presented for all pregnancies affected by renal agenesis, but data for patients with unilateral and bilateral disease were grouped together.

Another important factor to consider is whether bilateral renal agenesis is isolated or complex, i.e. associated with other anomalies. Several studies reported data separating isolated from complex disease [4, 17–24]. Induced abortion and intrauterine fetal demise are commonly reported. These data are presented in most of the studies included [11–13, 19–23, 25]. Slickers et al. present data supporting a mean survival time over 10 months (at the time of final interview) for three infants (4% survival), but it is important to note that this study grouped patients with renal agenesis and renal hypoplasia [11]. With the exception of the case studies mentioned earlier [7, 8] there was 100% mortality for all liveborn babies with bilateral renal agenesis during the neonatal period. Of the 16 included articles, only eight highlighted outcomes for both isolated and complex disease along with data on rates of induced abortion or intrauterine fetal demise [4, 18–24].

Outcomes with intervention

Evaluating prenatal interventions and their impact on outcomes and role for improving prognosis is important. Cameron et al. present a case study on a fetus with bilateral renal agenesis in which 10 serial amnioinfusions were utilized between 17 and 33 weeks'

gestation, with the infant delivering at 33 + 6/7 weeks' gestation secondary to chorioamnionitis. The infant did not have significant pulmonary hypoplasia, but ultimately the infant died at 23 days of life secondary to peritoneal dialysis complications [26]. The case study presented by Bienstock et al. also reported on serial amnioinfusion as an intervention for bilateral renal agenesis, presenting information on the only known neonatal patient to have survived bilateral renal agenesis [8].

Discussion

To address both goals, we identified 18 studies in our review that included 2666 infants with renal agenesis. Identifying outcomes for the population of fetuses and newborns with isolated bilateral renal agenesis is challenging. We analyze outcomes without and with intervention.

Outcomes without intervention

For those with documented isolated bilateral renal agenesis without intervention (n = 23), mortality was 100% beyond the neonatal period. The sample size in most studies we reviewed is small. With the exception of these studies that included registry data by Wiesel et al. [4], Wang et al. [14], Garne et al. [24] and studies by Stojanovic et al. [15], the remaining 12 studies present outcomes related to bilateral renal agenesis with groups of less than 75 patients (Table 2). The small sample sizes in these studies likely contribute to the groupings of diagnoses into diagnostically and therefore prognostically heterogeneous categories.

Outcomes with intervention

Case reports presenting serial amnioinfusions are included in Table 4. Spiro et al. [20] include data following prenatal intervention for patients prenatally diagnosed with oligohydramnios of renal origin, including various renal anomalies with a category for data related to renal agenesis. Data were presented on bilateral renal disease, but were not specific to each renal disorder. Interventions included chorionic villus sampling, amniocentesis and serial amnioinfusion. In this retrospective, single-center study, 16 of the 42 renal agenesis patients underwent at least one prenatal intervention, but as this did not clearly identify which interventions were offered to which patients and the outcomes of each intervention, it is not included within Table 4.

While interventions were mentioned in the two included case reports, no conclusions can be drawn about the outcomes of obstetric or postnatal neonatal management because there were no well-designed clinical trials identified. The single case report of intervention should be understood as a report of innovation, i.e. an experiment designed to benefit the patient but incapable of creating generalizable knowledge. This result supports further research to determine if this intervention improves outcomes. The professional responsibility model requires analysis of both outcomes and risks to pregnant, fetal, and neonatal patients. Maternal risks should be comprehensively described. Fetal and neonatal outcomes should include fetal mortality, neonatal mortality, survival to dialysis, survival to transplantation and long-term renal function.

The marked heterogeneity of diagnoses with very different outcomes makes it currently impossible to predict that serial amnioinfusion will have net clinical benefit for pregnant, fetal and neonatal patients. In beneficence-based clinical judgment, net clinical benefit for bilateral renal agenesis is defined as a livebirth followed by peritoneal dialysis, transplant and long-term survival, while posing only reasonable risks to the pregnant woman in this and subsequent pregnancies. In beneficence-based clinical judgment, serial amnioinfusion should be considered an experiment because these outcomes are unknown. When evidence of net clinical benefit for the pregnant, fetal and neonatal patient is unknown, intervention should be offered only as either prospectively approved innovation or prospectively approved research.

Innovation and research are both experiments in which clinical management outcomes cannot be reliably predicted. Innovation is an experiment undertaken in an attempt to benefit an individual patient [33]. Innovation is not designed to produce generalizable results, which are essential for the professionally responsible introduction of serial amnioinfusion for the obstetric management of bilateral renal agenesis. In contrast, research is considered an experiment that is undertaken to create generalizable knowledge. Human subjects research should be conducted only with the review and approval of an institutional review board (IRB).

Because innovation is not research, many IRBs do not consider innovation under their purview. Given the checkered history of innovation in surgery, the Society of University Surgeons has recommended that planned innovation should be undertaken only after prospective review and approval of a Surgical Innovation Committee. Innovative serial amnioinfusion should be undertaken only with such prior prospective review. A similar approach has been recommended for obstetric innovation for maternal or fetal benefit [33, 34]. Well-designed clinical trials of serial amnioinfusion should be undertaken only under IRB-approved protocol. Given the rarity of this condition multi-center research will be required.

Counseling pregnant women about management of pregnancies complicated by bilateral renal agenesis should be guided by deliberative beneficence-based clinical judgment. As part of the informed consent process, the pregnant woman should be informed about the risks of serial amnioinfusion, including infection. In addition, it should be made clear to the pregnant woman that serial amnioinfusion is not treatment, but an experiment. Such words as “treatment” and “therapy” should not be used. The pregnant woman has no beneficence-based obligation to her fetus and future child to enroll in a research study, because fetal and neonatal benefit has not been established. Based upon data currently available in this review suggesting 100% neonatal demise, women who decline enrollment in research for serial amnioinfusion or intervention should be offered a choice between induction of labor for maternal indications only and/or continuation to term with non-aggressive obstetric management followed by non-aggressive neonatal management [12].

Conclusions

The evidence-based ethical analysis and argument we have provided supports an approach in which pregnant women should be informed that without experimental obstetric intervention, neonatal mortality rates from bilateral renal agenesis will continue to be 100%. Serial amnioinfusion may improve outcomes, but should be undertaken only as either innovation (an experiment undertaken to benefit an individual patient) or research (an experiment undertaken with many research subjects to create generalizable knowledge). Serial amnioinfusion should not be offered outside of approved innovation or research. Pregnant women should be informed there is no evidence of fetal or neonatal benefit from such experimental intervention.

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Table 1

Search terms mentioned in methods section.

Search terms for natural history and intervention outcomes				
Bilateral renal agenesis	combined with	Newborn	combined with	Survival
Renal anomalies		Neonate		Outcomes
CAKUT		Neonatal		Mortality

Table 2

Natural history categorical data collected on bilateral renal agenesis patients.

First author (year)	# of pts	Outcomes							Anomalies grouped together
		Stillbirth/TOP	IUFD	Neonatal Demise	Separated unilateral vs. bilateral disease	Separated isolated vs. complex disease	Live-birth	Survival time	
Slickers (2008) [11]	71	✓	✓		✓		✓	n = 3 with 10.6 month mean	Hypoplasia +unilateral and bilateral agenesis
Davis (2010) [12]	22	✓	✓		✓				
Kumar (2013) [13]	12	✓	✓						
Wang (2011) [14]	1946			✓			✓*b*		Renal dysgenesis and agenesis
Wiesel (2005) [4]	95	✓			✓	✓	✓*c*		Renal dysgenesis and agenesis
Stojanovic (201l) [15]	85	✓			✓				
Robbins (2007) [16][a]				✓	✓		*bc*		
Mehler (201l) [17]	2			✓	✓	✓	✓		
Melo (2012) [18]	19	✓		✓	✓	✓	✓*c*		Renal dysplasia and agenesis
Grijseels (201l) [19]	36	✓	✓	✓	✓	✓	✓		Dysplasia as a range of disease
Spiro (2015) [20]	41	✓	✓	✓	✓	✓	✓		
Damen-Elias (2005) 21	33	✓	✓	✓	✓	✓	✓		
Ulkumen (2015) [22]	5	✓	✓		✓	✓			Oligohydramnios sequence and agenesis
Nagase (201l) [23]	32	✓	✓	✓		✓	✓		Oligohydramnios sequence and agenesis
Game (2005) [24]	257	✓			✓	✓			
Kumar (2014) [25]	8	✓	✓						

[a] Reported as hospitalizations (n = 1259) vs. number of patients.

[b] Survival probability reported for 7 days, 1 month, 1 year, 5 year.

[c] Livebirth reported, but subsequent course not reported.

Table 3

Natural history numerical data collected on bilateral renal agenesis patients.

First author (year)	Study characteristics	Isolated vs. multiple	Livebirth	Stillbirth/abortion/TOP	Age at death
Slickers (2008) [11]	To explore potential relations between renal anomaly and maternal BMI, smoking, alcohol, and caffeine exposures Infants with BRA or hypoplasia n = 80 cases; 71 isolated BRA; 5 BRH,4 cases of 1 hypoplastic kidney and one absent kidney; 5 cases excluded for maternal reasons – 75 total	Not reported	n = 49/75 (65%)	n = 26/75 (35%) stillbirth/induced abortion	n = 3 (4%) Survival at interview = 10.6 months mean
Davis (2010) [12]	Investigating maternal diabetes and link to RA n = 89 deliveries n = 22 BRA; 59 unilateral; eight unclear laterality	Not reported	83/89	n = 6 fetal deaths/89	
Kumar (2014) [25]	Identify renal anomalies associated with poor outcome n = 587 total babies noted w anomaly n = 136 with renal anomalies n = ll with absent kidney reported in text n = 8 with renal agenesis (from Table 2 - unspecified unilateral vs. bilateral)	n = 43 with multiple anomalies from total (not delineated for RA)	n = 64 liveborn babies with renal anomalies Of 8 with RA, n = 0 liveborn	Of all renal anomalies: n = 12T0P n = 60 stillborn Of eight infants with RA: n = 5TOP;n = 3IUFD	
Kumar (2013) [13]	To follow antenatal and postnatal course of pregnancies with anomalies to understand prognostication and improve management n = 523 eligible pregnancies with follow up n = 4 bilateral renal agenesis dx< 20 weeks' gestation n = 8 bilateral renal agenesis dx> 20 weeks' gestation	Not reported	n = 0	n = 12	
Nagase (201l) [23]	Analyzed prognosis of OS cases to clarify differences according to delivery method n = 47 cases with OS Excluded pre-viable cases, n = 32 cases of OS Two cases not prenatally diagnosed (emergency transfer cases)	Of 32 cases with OS, n = 19 with associated anomalies	n = 25 liveborn Of these: n = 5 of labor induction n = 17 for natural labor group n = 2 unidentified prenatally	TOP before 22nd week (previa ble) = 15 IUFD c-section n = 2 Induced labor group n = 4 for IUFD Natural labor group n = l IUFD	Labor induced – 5 born alive, alive an average 54 min Natural labor group n = 17 born alive, alive average of 5 h 41 min
Wang (2011) [14]	Conduct 25-year survival analysis of children with defects n = 57,002 children w birth defects from ~6 million live births n = 1946 cases of RA or dysgenesis	Not reported	n = 1946 liveborn		n = 693 deaths 7 days survival P: 71 1 month survival P: 69 1 year survival P: 66 5 year survival P: 64.8
Ulkumen (2015) [22]	To evaluate outcomes in pregnancy with early onset OH n = 54 pregnancies w oligo or anhydramnios Of these, n = 5 bilateral renal agenesis	Thirteen of total 54 weeks/ associated anomalies		n = 39/54TOP	Not reported
Game (2005) [24]	To assess prenatal detection of renal anomalies n = 257 cases of b/l renal agenesis n = 201 with prenatal diagnosis	n = 17 chromosomal associations		n = 201 Prenatal diagnosis n = 158/257 TOP (61%)	
Stojanovic(201l)[15]	To identify prevalence and outcome at 1 year of life for severe renal anomalies n = 985 cases with congenital renal anomaly 1989–2009 Of those, n = 230 with severe renal congenital anomalies n = 85 with BRA		n = 20 liveborn	Two spontaneous abortions 4 still births 59 TOP	Early neonatal death-19 0 survival at 1 year of age

First author (year)	Study characteristics	Isolated vs. multiple	Livebirth	Stillbirth/abortion/TOP	Age at death
Mehler (201l) [17]	Evaluate prenatal/perinatal variables to predict survival and outcomes for the ROH population n = 36 liveborn infants (30 M, 6 F) with ROH 10 weeks renal dysplasia/agenesis (n = 2 b/l agenesis; n = 6 b/l dysplasia; n = 2 unilateral renal agenesis + contralateral multicystic dysplasia)	n = l of BRA with MMC	Total = 36 n = 2 BRA liveborn	Not reported	7/36 died within 48 h – rep failure Of 2 BRA: Died Dl; died D5
Melo (2012) [18]	Studying mortality in 524 newborns with renal and urinary tract anomalies between 1996 and 2006 n = 24 RA/dysplasia; of these five were unilateral (left)	n = 13 multiple malformations n = 3 w/other urinary anomalies n = 2 genetic (Fraser, limb defect)		Thirteen with multiple malformations died in neonatal period (54% mortality)	
Wiesel (2005) [4]	To evaluate prevalence of prenatal ultrasound diagnoses for renal malformations in 20 registries n = 1130 infants with renal malformation diagnosis n = 95 with bilateral renal agenesis or dysgenesis	n = 8 multiple malformations. (5/8 TOP) n = 7 chromosomal syndrome (7/7TOP) n = 7 nonchromal syndrome (5/7 TOP)	n = 12 livebirth	In total: n = 58/95 TOP n = 24/95 stillborn	
Damen-Elias (2005) [21]	To determine long-term prognosis of antenatally detected renal anomalies to improve counseling Congenital renal and urinary anomalies = 402 Structural kidney disease n = 151 n = 33 BRA	n = 10 with additional malformations (six extra-renal)	n = 15 liveborn	n = 33 deaths (27% mortality of 121 deaths) Of the 33 deaths: n = 16TOP n = 2 stillbirths	n = 15 neonatal deaths (< 28 days)
Grijseels (201l) [19]	Evaluate outcomes of fetuses weeks/OH from renal cause n = 71 pregnancies evaluated n = 36 diagnosis renal dysplasia – (agenesis–cystic kidneys) 15 with agenesis; 12 b/l cystic, 4 combo Of 15 with agenesis 10 were bilateral	23/71 total had associated anomalies 12/15 with agenesis had associated anomalies	25/71 total were liveborn n = 6/15 with agenesis were liveborn	n = 29/36 w/dysplasia TOP n = l IUFD n = 5 neonatal death	Postnatal course of liveborn: 3 died 1st day (no resuscitation), 2 died >1 day; 3 infants required MV n = l living patient
Robbins (2007) [16]	Investigating mortality, hospital length of stay and charges related to birth defects Total n = 60,952 infants n = 1259 hospitalizations related to renal agenesis	Not reported	Not reported	n = 344 in hospital death (27.3%)	Not reported
Spiro (2015) [20]	Evaluate outcomes of pts with ROH n = 40,621 pregnancies n = 42 with renal agenesis, 41 BRA n = 16 prenatal intervention (not specified which but chorionic villous sampling, amniocentesis, or amnioinfusion)	21/42 associated with anomalies Of 30 BRA nonsurvivors: 16 with associated anomalies	N=ll/42 livebirth (n = 2 prenatal intervention) (n = l unilateral agenesis)	Of 31 nonsurvivors with BRA: 6 IUFD; 25 abortion 8 neonatal deaths (n = 14 prenatal interventions)	One postnatal follow-up – unilateral renal agenesis

b/l= Bilateral, BRA= bilateral renal agenesis, BRH = bilateral renal hypoplasia, MV= mechanical ventilation, OH = oligohydramnios, OS = oligohydramnios sequence, Pt or Pts = patient or patients, RA = renal agenesis, ROH = renal oligohydramnios.

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Table 4

Intervention numerical data on bilateral renal agenesis patients.

Author (year)	Patient characteristics	Intervention characteristics	Outcomes		
			Delivery (gestational age)	Noted survival?	Cause of death
Cameron et al. (1994) [26]	Bilateral renal agenesis; severe oligohydarmnios noted on ultrasound at 16 weeks' gestation	Serial amnioinfusions: performed between 17 and 33 weeks' gestation (10 total)	Delivered at 33 + 6/7 weeks' gestation secondary to chrorioamnionitis Birth weight: 1965 g	Yes – until 23 days of age	Peritoneal dialysis complications
Bienstock et al. (2014) [8]	Bilateral renal agenesis; severe anhydramnios diagnosed at 20 weeks' gestation	Serial amnioinfusion: performed between 24 and 28 weeks' gestation (5 total)	Delivered at 28 + 5/7 weeks' gestation Birth weight: 1230 g	Yes – underwent renal transplant (donated from father) at 2 years, 7 months	N/A