

Outcome after prenatal diagnosis of congenital anomalies of the kidney and urinary tract

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Abstract Congenital anomalies of the kidney and urinary tract are common findings on fetal ultrasound. The aim of this prospective observational study was to describe outcome and risk factors in 115 patients born 1995–2001. All prenatally diagnosed children were stratified into low- and high-risk group and followed postnatally clinically and by imaging at defined endpoints. Risk factors were evaluated using odds ratios. Neonatal diagnosis included pelvi-ureteric junction obstruction ($n=33$), vesicoureteral reflux ($n=27$), solitary mild pelvic dilatation (postnatal anteroposterior diameter 5–10 mm; $n=25$), and further diagnosis as

primary obstructive megaureter, unilateral multicystic dysplastic kidney, renal dysplasia and posterior urethral valves. In 38 children with prenatal isolated hydronephrosis, ultrasound normalized at median age of 1.2 years (range 0.1–9). Surgery was performed in 34 children at median age of 0.4 years (0.1–10.8). Persistent renal anomalies without surgery were present in 43 children and followed in 36 for median time of 16 years (12.2–18). Oligohydramnios and postnatal bilateral anomalies were significantly associated with surgery and impaired renal function.

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Conclusion: The majority of children had a favourable postnatal outcome, in particular children with prenatally low risk, i.e. isolated uni- or bilateral hydronephrosis. Oligohydramnios and postnatal bilateral anomalies were risk factors for non-favourable outcome.

What is Known:

- *In congenital anomalies of the kidney and urinary tract significantly poorer outcome is known in patients with bilateral renal hypoplasia or solitary kidney associated with posterior urethral valves.*
- *Other factors as proteinuria and vesicoureteral reflux were associated with a higher risk of progression to chronic renal failure in these patients.*

What is New:

- *Unlike other studies giving us above-mentioned information, we included all patients with any kind of prenatally diagnosed congenital anomalies of the kidney and urinary tract. Our study shows long-term follow up (median 16 years, range 12.2–18 years), especially in patients not needing surgery, but with persistent anomalies.*
- *During postnatal long-term follow up (median 2.2 years, range 0.1–18 years) one third each showed normalization, need of surgery or persistence of anomalies without need of surgery. Our study revealed a good prognosis in the majority of these children, in particular with prenatally low risk, i.e. isolated uni- or bilateral hydronephrosis, and revealed oligohydramnios and postnatal bilateral anomalies as risk factors for a non-favourable outcome, defined as need of surgery, persistent anomalies with impaired renal function, end stage renal failure or death.*

Keywords Congenital anomalies of the kidney and urinary tract (CAKUT) · Prenatal · Postnatal · Outcome · Risk factors

Abbreviations

ADPKD	Autosomal dominant polycystic kidney disease
APD	Anteroposterior diameter
CAKUT	Congenital anomalies of the kidney and urinary tract
CRP	C-reactive protein
DMSA	Dimercaptosuccinic acid scintigraphy
ESRF	End-stage renal failure
GFR	Glomerular filtration rate
IVU	Intravenous urography
MAG-3	Mercaptoacetyltriglycine-3 scintigraphy
MCDK	Multicystic dysplastic kidney
POM	Primary obstructive megaureter
PUV	Posterior urethral valves
PUJO	Pelvi-ureteric junction obstruction
US	Ultrasound
UTI	Urinary tract infections
VCUG	Voiding cystourethrography
VUR	Vesicoureteral reflux

Introduction

Congenital anomalies of the kidney and urinary tract (CAKUT) are the most frequent findings on fetal ultrasound (US) with a prevalence of 0.1–2.3 % [6, 8, 10, 16, 24, 27]. The predictive value of these prenatal findings is often difficult to assess. Parents are concerned about apparently abnormal findings on fetal US and strongly interested in prognosis including need of surgery as many parents are afraid of surgery and associated risks, especially in very young children. Oligohydramnios, renal cysts, bladder outlet obstruction, extra renal malformations, low birth weight and prematurity appear to be negative prognostic factors for postnatal outcome [7, 8]. Which specific prognostic factors promote termination of pregnancy is still a matter of debate [11]. Some studies suggested that the prognostic value of prenatal pelvic dilatation correlated with the postnatal need for active treatment [14, 31]. In CAKUT, significantly poorer outcome was observed in patients with bilateral renal hypoplasia or solitary kidney associated with posterior urethral valves (PUV) [25]. In addition, elevated plasma creatinine at diagnosis, proteinuria and vesicoureteral reflux (VUR) were associated with a risk of progression to chronic renal failure [25].

The primary aim of this study was to describe the course of patients prenatally diagnosed with CAKUT with postnatal follow-up by an interdisciplinary schedule. The secondary aim was to analyse potential risk factors for non-favourable outcome, defined as need of surgery, persistent anomalies with impaired renal function, end-stage renal failure (ESRF) or death.

Patients and methods

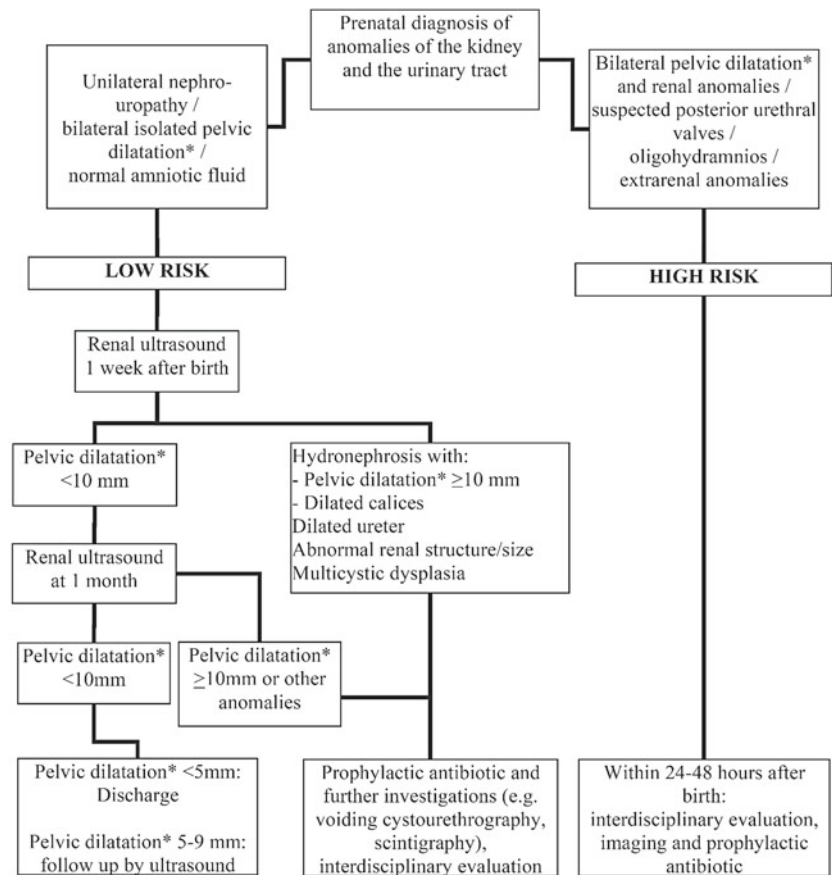
Patients

This single centre prospective observational study included a sample of 115 children, prenatally diagnosed with CAKUT between 1995 and 2001, with the aim of enrolling a minimum of 100 patients. Inclusion criteria were both any kind of assumed CAKUT on prenatal US and postnatal follow-up in our hospital based on local guidelines (Fig. 1). Prenatally diagnosed patients were stratified into low- and high-risk group (Fig. 1) and prospectively followed clinically and by imaging from 1995 to 2012. We describe the follow-up prenatally, postnatally and at the most recent clinical assessment.

Five study endpoints were defined: normalization of US findings, surgery (decision taken by an interdisciplinary team of paediatric nephrologists, urologists and radiologists), and persistent anomalies not requiring surgery with or without impaired renal function, ESRF and death.

Written informed consent had been obtained from all parents or guardians.

Fig. 1 Risk stratification and follow-up of children with prenatal US diagnosis of congenital anomalies of the kidney and the urinary tract



* Pelvic dilatation measured as anteroposterior diameter

Prenatal evaluation

Ultrasound was performed by obstetricians of the obstetric unit of the University Hospital Zurich ($n=44$), obstetricians of other hospitals in the greater area of Zurich ($n=58$) or private obstetricians ($n=13$).

The following clinical data were evaluated: diagnosis of CAKUT (some patients had more than one diagnosis), date (weeks of pregnancy) of first diagnosis, prevalence of oligohydramnios (not further defined), extra renal fetal malformations, fetal interventions, duration and complications of pregnancy. Prenatal hydronephrosis was defined as pelvic dilatation with anteroposterior diameter (APD) >7 mm in the third trimester [31].

Postnatal evaluation

Children were divided into two groups according to our local guidelines (Fig. 1): low-risk group patients underwent the first renal US 1 week after birth whereas high-risk group patients had their first imaging within

24–48 h. All children were examined by a paediatrician at least once within the first week after birth.

Ultrasound (US): Postnatal hydronephrosis was defined as pelvic dilatation measured as APD and graduated in mild (5–9 mm), moderate (≥ 10 –14 mm) or severe (≥ 15 mm). Size and structure of the kidney, dilatation of calices or ureters, and bladder morphology were also reported.

Voiding cystourethrography (VCUG) VUR was graded I–V (mild: I–II; severe: III–V) according to the international reflux study [15], except in those children with VUR associated with obstruction of the upper urinary tract, where VUR was not graded.

Functional imaging: Intravenous urography (IVU) was performed until 1999 ($n=27$) and was replaced by *Mercaptoacetyl triglycine-3 (MAG-3) scintigraphy* ($n=38$) in 2000. *Dimercaptosuccinic acid (DMSA) scintigraphy* was performed during the whole study period ($n=19$) to detect focal parenchymal defects.

Clinical follow-up and final examination

All patients were followed including measurement of growth [22], blood pressure using age-related charts [1, 7], and US of the kidneys and urinary tract. Renal function was classified according to the KDIGO guidelines stage 1–5 [2] and proteinuria was evaluated in patients with persistent anomalies. Glomerular filtration rate was estimated by the Schwartz formula [26] with a K-factor of 40 based on local comparison with Cr-EDTA clearance measurements [4]. In patients with either normalization of US or surgery, the last examination was defined as the date of normalization and surgery, respectively. Decision for surgical intervention was taken by an interdisciplinary team of paediatric nephrologists, urologists and radiologists. Vesicoureteral reflux in patients on antibiotic prophylaxis was surgically treated if a first break-through urinary tract infection (UTI) occurred. Patients with pelvoureteric junction obstruction (PUJO) underwent surgery if ipsilateral renal function on scintigraphy was $\leq 40\%$, function declined during follow-up $\geq 10\%$ or the patient suffered complications (e.g. urolithiasis). All patients with PUV underwent surgery in the neonatal period. Nephrectomy or heminephrectomy were performed in case of non-

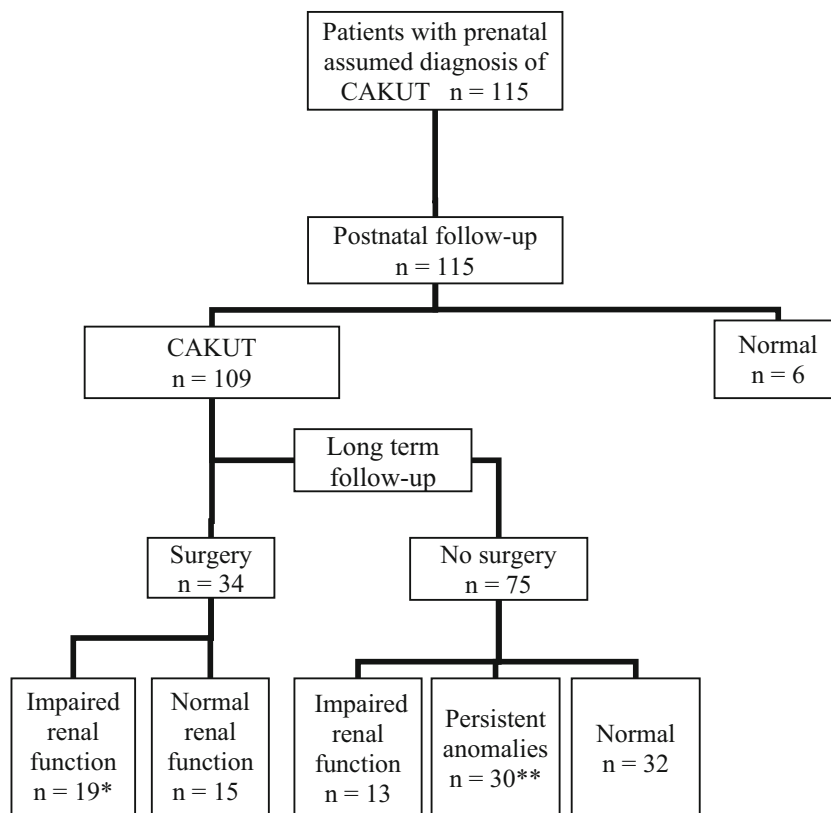
functioning kidneys combined with a risk constellation for UTI (e.g. ipsilateral VUR or ureterocele).

Definitions

Urinary tract infections (UTI): Pyelonephritis was defined as fever $>38.0\text{ }^{\circ}\text{C}$, elevated C-reactive protein (CRP), leucocyturia and bacteriuria ($\geq 10^5$ CFU/ml; urine collected by catheter). Cystitis was defined as UTI with neither fever nor elevated CRP.

UTI-prophylaxis: Oral antibiotic prophylaxis during the first 2 months of life consisted of amoxicillin (12.5 mg per kg body weight twice daily) and was given to all children in the high-risk group and to those children in the low-risk group with suspected primary obstructive megaureter (POM), unilateral multicystic dysplastic kidney (MCDK) and/or pelvic dilatation ≥ 10 mm until VUR was excluded by VCUG. If prophylaxis was continued beyond 2 months of age, medication was changed to cotrimoxazole (9 mg per kg twice daily) and continued up to 2–3 years of age.

Fig. 2 Flow-sheet of the study.
 *One patient with PUV died in the neonatal period due to severe extrarenal anomalies; two patients developed ESRF. **Lost on follow-up $n = 7$



* One patient with PUV died in the neonatal period due to severe extrarenal anomalies; two patients developed ESRF.
 ** Lost on follow-up $n = 7$

Renal function: Impaired renal function was defined as GFR <90 ml/min per 1.73 m² (>1 year) according to the KDIGO guidelines stage 2–5. ESRF was defined as patients undergoing renal replacement therapy.

Outcome: Normalization of US was defined as normal structure and size of both kidneys, absence of pelvic or ureteral dilatation (APD of renal pelvis not detectable or <5 mm) and normal configuration of the bladder. Non-favourable outcome was defined as need of surgery, persistent anomalies with impaired renal function, ESRF or death.

Statistical analysis

Statistical analysis was performed with SPSS for Windows version 18.0 (IBM Corporation, New York, USA). Differences between subgroups were calculated using the Fisher's exact test for categorical variables. Bivariate correlation analysis was performed by using the Spearman correlation coefficient (*r*). To assess risk factors, odds ratios and 95 % confidence interval were calculated. Kaplan-Meier curves were used to analyse timing of events of study endpoint. A *p* value of <0.05 was considered statistically significant.

Results

A total of 115 children with prenatally assumed diagnosis of CAKUT and postnatal follow-up fulfilled the study criteria (Fig. 2). Patients' characteristics are given in Table 1.

Prenatal evaluation

Prenatal diagnoses are summarized in Table 2. The prenatal extent of pelvic dilatation was not consistently reported and therefore not included in our data. Oligohydramnios had been diagnosed in 10 pregnancies between 26 and 39 weeks of gestation. Of the 11 fetuses (10 males) with megavesica, three boys underwent prenatal bladder puncture, one of them repeatedly. One fetus each underwent puncture of an abdominal cyst and ureterocele.

Extra renal diagnoses and maternal complications are listed in Table 1. The fetus with hygroma was postnatally diagnosed as Noonan syndrome; the two patients with cardiac anomalies had normal postnatal findings.

Postnatal evaluation

Ninety-one patients (22 girls, 69 boys) were in the low-risk group, and 24 (6 girls, 18 boys) fulfilled the criteria for the high-risk group: oligohydramnios (*n* = 10; 8 males), suspected PUV (*n* = 7 males), ureterocele (*n* = 2 males), megavesica and pelvic dilatation (*n* = 9; 8 males), or extrarenal anomalies (one

girl with hygroma colli and one boy with suspected cardiac malformation). Eight neonates in the low risk and three in the high-risk group were born preterm. Five patients with oligohydramnios had pulmonary complications with wet lung in four and amniotic fluid aspiration and pneumothorax in one (Table 1).

Postnatal US showed hydronephrosis in 92 patients, with 47 unilateral and 45 bilateral pelvic dilatations (i.e. 137 dilated kidneys). Pelvic dilatation was mild, moderate and severe in 58, 60 and 19 kidneys, respectively. The diagnoses at postnatal and most recent examination are summarized in Table 2.

Follow-up at study endpoints

Median follow-up time for all patients reaching their endpoint was 2.2 years (range 0.1–18).

Normalization of ultrasound findings (Table 2)

Thirty-eight children (high-risk group: *n* = 1) had normal US findings during follow-up, ranging from six patients with a

Table 1 Patients' characteristics

	Number
Sex	
Male/female	87/28
Duration of pregnancy	Number
Term/preterm	104/11
Prenatal characteristics	Number
Extrarenal diagnosis	3
Hygroma colli	1
Supraventricular extrasystoles	1
Cardiac malformation	1
Fetal intervention	5
(puncture of bladder, ureterocele, abdominal cyst)	
Maternal complications	13
Premature bleeding	4
Membrane rupture	2
Premature labour	2
Non-specified infection	5
	Median (range)
Week of gestation at first diagnosis	31 (11–38)
Postnatal characteristics	Number
Neonatal, extrarenal diagnoses	13
Wet lung	10
Meconium/amniotic fluid aspiration	2
Low birth weight (<10th percentile)	1
Follow-up: years	Median (range)
Follow-up time of all patients	2.2 (0.1–18)
Age at normalization	1.2 (0.1–9)
Age at surgery	0.4 (0.1–10.8)
Follow-up with persistent anomalies without surgery	16 (12.2–18)

Table 2 Renal diagnosis (more than one diagnosis per patient possible)

Outcome	Prenatal diagnosis		Postnatal diagnosis	Diagnosis at study endpoint	
	Total (bilateral)		Total (bilateral)	Total (bilateral)	
Normalization	Hydronephrosis	34 (14)	Normal	6	
	Megavesica	3	Mild hydronephrosis/PUJO	24 (11)	Normal
	Duplex kidney	2 (0)	POM	5 (2)	
	Renal cysts	1 (1)	Mild VUR	3 (2)	
Surgery	Hydronephrosis	28 (13)	PUJO	13 (6)	PUJO
	Ureteral dilatation	10 (4)	VUR	13 (7)	VUR
	Megavesica	6	PUV, bilateral renal dysplasia	7 (7)	PUV, bilateral renal dysplasia
	Ureterocele	1 (0)	Ureterocele	3 (0)	Ureterocele
	Renal cysts, renal dysplasia	5 (3)	POM	4 (0)	POM
	Duplex kidney	1 (0)	Others ^a	9 (0)	Others ^b
Persistent anomalies without surgery	Hydronephrosis	32 (6)	PUJO	17 (4)	PUJO
	Renal cysts, renal dysplasia	14 (2)	MCDK	11 (0)	MCDK
	Megavesica	2	VUR	7 (2)	VUR
	Others (nephromegalia, renal agenesis, intraabdominal tumour)	4 (1)	POM	4 (0)	POM
			Mild hydronephrosis	4 (2)	Mild hydronephrosis
			Others ^c	10 (6)	Others ^d

ADPKD autosomal dominant polycystic kidney disease, MCDK multicystic dysplastic kidney, POM primary obstructive megaureter, PUJO pelvi-ureteric junction obstruction, PUV posterior urethral valves, VUR vesicoureteral reflux

^a Duplex kidney ($n=4$), dysplasia of upper or lower pole ($n=2$), MCDK ($n=1$), proximal ureteral stenosis ($n=1$), sinus urogenitalis ($n=1$)

^b Duplex kidney ($n=2$), duplex kidney with PUJO and dysplasia ($n=1$), duplex kidney with dysplasia and VUR ($n=1$), POM with VUR and MCDK ($n=1$), lumbal myelomeningo-cele with VUR ($n=1$), proximal ureteral stenosis ($n=1$), sinus urogenitalis ($n=1$)

^c ADPKD ($n=3$), bilateral cysts, not ADPKD ($n=2$), duplex kidney ($n=2$), renal agenesis ($n=2$), renal dysplasia ($n=1$)

^d ADPKD ($n=3$), HNF1-beta mutation ($n=2$), duplex kidney ($n=4$), renal agenesis ($n=2$), renal dysplasia ($n=1$)

normal (first) US in the first week after birth to 9 years of age (Fig. 3a). Isolated hydronephrosis was the most frequent prenatal diagnosis ($n=33$) in this group. Rare prenatal findings were megavesica, duplex kidney, ureteric dilatation and renal cysts.

Need of surgery (Table 2)

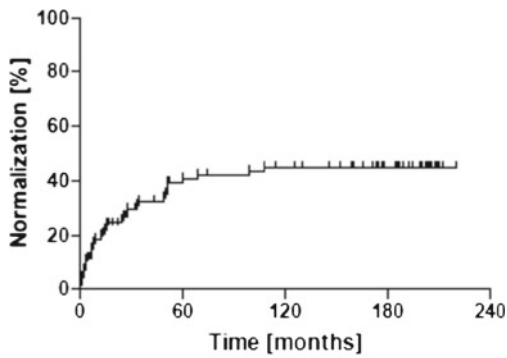
Thirty-four patients (high-risk group: $n=14$) underwent surgery, ranging from 1 month to 10.8 years of age. Thirteen patients underwent their operation within the first 3 months (Fig. 3b). Impaired renal function was noted in 19 patients (KDIGO: stage 2: $n=7$; stage 3: $n=9$; stage 4: $n=1$; stage 5: $n=2$). Unilateral or bilateral hydronephrosis was the most common prenatal diagnosis ($n=28$) in the surgery group, followed by ureteric dilatation and megavesica. Surgery included pyeloplasty ($n=10$), ureterocystoneostomy ($n=8$), transurethral resection of PUV ($n=7$), transurethral resection of ureterocele ($n=2$), nephrectomy ($n=2$), heminephrectomy ($n=2$), resection of ureteral stenosis ($n=1$), Monti-stoma ($n=1$) and dilatation of vaginal introitus ($n=1$). The majority of patients with oligohydramnios ($n=7$ out of 10) underwent

surgery. Eleven patients had break-through UTI on prophylaxis leading to re-implantation of the ureter ($n=8$), heminephrectomy ($n=2$) or nephrectomy ($n=1$). One patient with PUV died in the neonatal period due to severe extrarenal anomalies. Two operated patients with bilateral renal disease (one patient with bilateral renal dysplasia, one with PUV) developed ESRF (age 2.0 and 14.3 years) requiring dialysis with subsequent renal transplantation.

Persistent anomalies without surgery (Table 2)

Forty-three patients showed persistent renal anomalies on US without need of surgery during the observation period. In 30 patients, renal function remained normal. Thirteen patients, however, had impaired GFR. Stage 2 chronic kidney disease (GFR 62–85 ml/min per 1.73 m²) was present in 12 patients, including five with unilateral MCDK (two of them with contralateral VUR), two with autosomal dominant polycystic kidney disease (ADPKD), and one each with unilateral PUJO, bilateral PUJO, unilateral PUJO with bilateral VUR, unilateral POM with bilateral VUR, and mutation in the HNF1-beta gene; none had hypertension or proteinuria. One boy with

a Kaplan-Meier curve for patients with normalization of ultrasound (n = 38)



b Kaplan-Meier curve for patients undergoing surgery (n = 34)

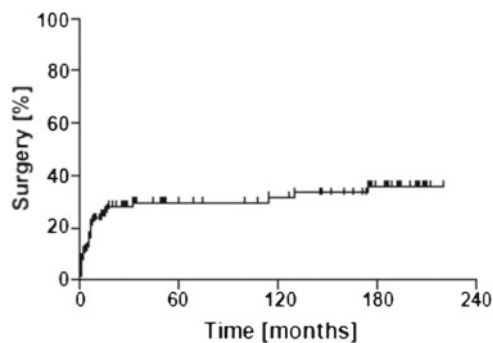


Fig. 3 **a** Kaplan-Meier curve for patients with normalization of ultrasound (n = 38). **b** Kaplan-Meier curve for patients undergoing surgery (n = 34)

ADPKD and stage 3 chronic kidney disease (GFR 58 ml/min per 1.73 m²) was on ACE-inhibitors for hypertension and proteinuria. No patient so far developed ESRF.

Outcome risk factors and high risk versus low risk group (Tables 3 and 4)

In total, 68 (58 %) patients had a favourable outcome with either normalization of the US findings or persistent renal anomalies with normal renal function.

Significantly more children in the low-risk group as compared with the high-risk group had normalized US findings (p=0.016). In contrast, non-favourable outcome

was more common in the high-risk group as compared to the low-risk group, and significantly associated with oligohydramnios and postnatal bilateral anomalies (p<0.05). Significantly more high-risk patients required surgery (p=0.005); impaired renal function was also more frequent, but without statistical significance. Forty-five episodes of UTI occurred in 26 children, both in the low-risk group (n=19; 21 %) and the high-risk group (n=7; 29 %).

Discussion

Congenital anomalies of the kidney and urinary tract (CAKUT) are the most common prenatal diagnoses with a prevalence of 1 in 70–1000 live births [5, 18, 29] accounting for 30–50% of all fetal anomalies [10, 12]. CAKUT is the most common cause for chronic kidney disease in childhood [9]. There is a broad range of fetal anomalies, ranging from mild unilateral pelvic dilatation to severe malformations of both kidneys and the urinary tract, the latter being the leading cause of paediatric end-stage renal disease [28]. Recommendations for infants with prenatally diagnosed hydronephrosis remain controversial, especially regarding diagnostic criteria, fetal interventions, risk classification and postnatal diagnostic and therapeutic management [33].

Our study deliberately encompassed a non-selected group of children with assumed prenatal renal anomalies. In addition, the follow-up time showed a broad range from 1 month to 18 years, based on the various defined endpoints. Our study showed that the majority of the patients had a favourable outcome.

One third of the children had an excellent prognosis with normalization of the US findings. Their prenatal US had mostly displayed isolated uni- or bilateral pelvic dilatation. The postnatal US most often showed unilateral or bilateral mild hydronephrosis; PUJO, POM and VUR were also reported. The time to normalization ranged from the first week of life up to 9 years. A study by John et al. reported a normalization rate of 25 % at the age of 3 months, including children with fetal hydronephrosis defined as APD ≥4 mm until 33 weeks of gestation and APD ≥7 mm thereafter [14]. It might be assumed that mild prenatal and postnatal hydronephrosis is a

Table 3 Outcome: low risk versus high risk group

Outcome	Low risk n=91	High risk n=24	Odds ratio (CI 95 %*)	p value (Fisher’s exact test)
Normalization	35 (38 %)	3 (13 %)	<i>4.38 (1.21–15.76)</i>	<i>0.016</i>
Surgery	21 (23 %)	13 (54 %)	<i>3.94 (1.54–10.08)</i>	<i>0.005</i>
Persistent anomalies without surgery	35 (38 %)	8 (33 %)	0.8 (0.31–2.06)	0.813
Impaired renal function	23 (25 %)	9 (37 %)	1.7 (0.68–4.6)	0.301

Numbers in italics are statistically relevant results

*CI confidence interval

Table 4 Outcome: risk factors for non-favourable outcome

Risk factors	Favourable outcome <i>n</i> = 61	Non-favourable outcome <i>n</i> = 54	Odds ratio (CI 95 %*)	<i>p</i> value (Fisher's exact test)
High risk group	7 (11 %)	17 (31 %)	3.5 (1.34–9.39)	0.011
Oligohydramnios	2 (3 %)	8 (15 %)	5.13 (1.04–25.33)	0.044
Preterm birth	5 (8 %)	6 (11 %)	1.4 (0.4–4.88)	0.753
Prenatal bilateral anomalies	24 (39 %)	18 (33 %)	0.75 (0.36–1.66)	0.563
Postnatal bilateral anomalies	28 (45 %)	36 (66 %)	2.36 (1.11–5.03)	0.038
Extrarenal anomalies	9 (15 %)	13 (24 %)	1.8 (0.71–4.71)	0.240

Numbers in italics are statistically relevant results

*CI confidence interval

normal variant without clinical relevance. However, (long-term) postnatal follow-up until normalization of the US is mandatory as unequivocal prenatal identification of the child with good postnatal prognosis is not possible. In 2010, the Society for Fetal Urology (SFU) defined hydronephrosis as mild (APD 7 to <9 mm), moderate (APD 9 to <15 mm) and severe (APD >15 mm) in the third trimester, similar to our study criteria. A German study suggested a pelvic dilatation in the third trimester of ≥ 7 mm as clinically significant, whereas a comparable Swiss study reported ≥ 10 mm [14, 19, 31].

Also, approximately one third of the patients underwent surgery, with the majority in early life. The most frequent procedures in the first months of life were resection of PUV and pyeloplasty in patients with PUJO. Increased risk for surgery was present in the high-risk group patients, in particular in patients with oligohydramnios. Some patients underwent surgery up to the age of 10 years including patients with persistent VUR and break-through UTI undergoing anti-reflux surgery. A substantial number of the surgical patients had impaired renal function requiring a combined urological-nephrological long-term follow-up. In an Italian study, 53 % of patients needed surgery; however, only those with solitary kidney and VUR were considered, and patients with isolated ureteral anomalies were excluded [25]. In a study of Quirino et al., surgery was needed in 28 % and PUJO was the most prevalent diagnosis leading to surgery [23].

Another third of our patients had persistent anomalies without requiring surgery. The majority of these patients had normal renal function, with the most recent evaluation taking place in adolescence. Their anomalies were generally unilateral and included mild or moderate hydronephrosis, megaureter, MCDK with normal contralateral kidney or VUR. A minority of this group had a non-favourable outcome, i.e. impaired renal function. Risk factors were the prevalence of oligohydramnios and/or postnatal bilateral anomaly. Preterm birth was not revealed as significant risk factor, as reported in other studies [17, 21], but incidence of preterm birth was low in our population.

Except two surgical patients, no other patient developed ESRF during the observation period. This favourable

outcome might result from prenatal selection as no information was available on antenatally diagnosed CAKUT leading to termination of pregnancy. However, all patients with non-favourable outcome, and also some patients with persistent renal anomalies (and still normal renal function) or successful surgery, are at risk of progressive renal failure in the long-term, requiring life-long medical follow-up. Wuhl et al. recently reported a high risk of ESRF among adult patients with congenital moderate and severe renal hypoplasia or dysplasia [32].

Based on different patient collective, other authors found a lower incidence [13] or a different distribution [25] of described nephro-uroopathies indicating the difficulty in comparing our diagnosis and outcome with others studies, as we included *any* kind of prenatal anomalies of the kidney and the urogenital tract. However, our data confirmed already known risk factors (e.g. oligohydramnios and bilateral anomalies) [3, 8, 17, 20, 30]. In addition, the results emphasized the clinical usefulness of the impact of our algorithm and stratification into low- and high-risk group.

Especially in pregnancies with identified risk factors, proactive involvement of paediatric nephrologists in prenatal counselling is valuable to discuss the range of diagnoses and the postnatal course. Prenatal counselling also includes discussion of the potential need of postnatal treatment, ranging from postnatal diagnostic imaging to antibiotic administration and (early) surgery. Parents are particularly afraid of surgery and associated risks in very young children.

Limitations

The difficulty of obtaining precise information from obstetricians is an important limitation of our study, but underlines the importance of close collaboration, communication and data exchange between obstetrician, neonatologist, paediatric urologist and nephrologist. The deliberate inclusion of a non-selected “real world” population resulted in a heterogeneous study population with a broad spectrum of findings making any statistical analysis problematic. However, our intention was to focus on *all* anomalies during pregnancy aiming to

describe the follow-up of any kind of CAKUT. This intention was based on the idea to counsel parents during pregnancy with any kind of urological anomalies on fetal US. Pre- and postnatal genetic testing for patients with CAKUT, nowadays standard in many centres, was not regularly available at the beginning of our study. Although diagnostic options have changed during the last 2 decades, indications for surgery did not change in our institution, i.e. surgical treatment for patients with VUR and break-through UTI, and for significant obstruction in case of PUJO or POM. However, antibiotic prophylaxis in patients with VUR is currently limited to high-grade reflux only.

In summary, the majority of children with prenatally assumed CAKUT had a favourable outcome, in particular children with prenatal isolated uni- or bilateral hydronephrosis. Oligohydramnios and postnatal bilateral anomalies were risk factors for non-favourable outcome, i.e. need of surgery and/or persistent renal anomalies with impaired renal function. These findings may be helpful for all involved medical professionals when counselling pregnant women and parents. Close multidisciplinary collaboration between obstetricians, neonatologists, paediatricians and paediatric urologists and nephrologists, and long-term postnatal follow-up is mandatory.

Authors' contributions Samuel Nef: paediatric nephrologist, main author Thomas Neuhaus, Prof., M.D.: paediatric nephrologist, nephrological counselling, writing, revision Giuseppina Sparta, M.D.: paediatric nephrologist, nephrological counselling Marcus Weitz, M.D.: paediatric nephrologist, nephrological counselling Kathrin Buder, M.D.: statistics Josef Wissner, Prof., M.D.: obstetrician, prenatal counselling Rita Gobet, Prof., M.D.: paediatric urologist, urological counselling, revision Ulrich Willi, Prof., M.D.: paediatric radiologist, radiological counselling Guido F. Laube, PD, M.D.: paediatric nephrologist, nephrological counselling, writing, revision, man in charge.

Compliance with ethical standards All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Conflict of interest The authors declare that they have no competing interests.

Informed consent Written informed consent was obtained from all parents or guardians of each child included in the study.

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