

Unilateral multicystic dysplastic kidney complicated with urinary tract infection by *E. coli* in a premature newborn

Gabriela-Maria Chifa¹, Laura-Mihaela Suci¹, Cristina Oana Marginean²

¹Department of Neonatology, Country Clinical Hospital-Mures, Targu Mures, Romania

²Department of Pediatrics 1, "George Emil Palade" University of Pharmacy, Medicine, Sciences and Technology, Targu Mures, Romania

ABSTRACT

Autosomal recessive polycystic kidney disease is a renal development anomaly characterized by cystic transformation in renal parenchyma. ARPKD is more common in children. We present the case of a premature newborn, female, 36-37 weeks gestation, small for gestational age (SGA) originating from a completely unmonitored pregnancy, diagnosed upon admission to the clinic with unilateral multicystic dysplastic kidney. The condition complicated by a urinary tract infection with *E. coli*. This newborn displayed no clinical symptoms, was carefully monitored during hospitalization, and received antibiotic treatment. Antenatal ultrasound screening can aid in the early diagnosis of congenital anomalies and determining the appropriate course of action.

Keywords: polycystic, kidney, newborn, *E coli*, antibiotic therapy, ultrasound

INTRODUCTION

The multicystic dysplastic kidney, also known as renal multicystosis, is a renal congenital anomaly described like cystic lesions in renal parenchyma. This pathology can be unilateral or bilateral. When it affects a congenital solitary kidney or is bilateral, it is incompatible with life, and the only treatment is renal transplantation. Polycystic kidney disease are the common cause to end-stage renal disease in adults, children, and newborns [1].

Renal multicystic dysplasia, a rare congenital anomaly, found in 1.1% urinary anomalies in children, yet, represents a widespread cystic pathology in newborns. As a unilateral condition, it occurs in 1:2500 - 1:4000 cases, while as a bilateral pathology, it is found in 1:3600 cases. In 55% of cases, it affects the left side, in 45% cases the right side. Regarding sex predisposition, it is more common in males [1]. ARPKD is infrequent and more common in children, while ADPKD is more frequent and predominantly affects adults [1].

Polycystic kidney disease - PKD - represents a small part of renal cystic diseases (CKD) which over time reduce kidney function and can lead to complete renal failure with the onset of renal insufficiency. PKD can also lead the appearance of other complications: high blood pressure, development of hepatic cystic formations, pathologies related to blood vessels, brain, or heart [2].

A genetic relationship or a structural defect can lead to PKD. In most cases of PKD, the child inherits the condition from one parent. In very few cases, PKD appears without a detectable cause, without either parent being carriers of the gene - a situation in which the condition is idiopathic [2].

The aim of the study is to highlight the importance of the antenatal ultrasound of PKD in context of the absence of the abnormal clinical features in the case of SGA preterm infant with mild hypoxic perinatal event and non specific symptoms in the early neonatal time.

Corresponding author:
Gabriela-Maria Chifa
E-mail: gabrielachifa16@gmail.com

Article History:
Received: 10 June 2024
Accepted: 28 June 2024

PRESENTING CONCERNS

We present the case of a premature newborn, female, 36-37 weeks gestation, small for gestational age (SGA), from an unappropriate antenatal care during pregnancy. The mother, a 17-year-old primigravida and primipara, was admitted to our clinic with painful uterine contractions every 5-6 minutes, lasting 15 seconds each. An obstetric ultrasound performed upon admission raised the suspicion of a fetal multicystic left kidney. The delivery was vaginal, with cephalic presentation, opalescent amniotic fluid, and membranes that ruptured spontaneously 40 minutes before delivery. At birth, the newborn weighed 2590 grams (<50th percentile) - SGA, with a measurement of 49 cm, head boundary of 32 cm, and chest boundary of 30 cm. The score Apgar was 7 at 1 minute and 9 at 5 minutes. Reanimation in delivery room: tactile stimulation, upper airway clearance, VPP (positive pressure ventilation) with Neopuff 25/5 cmH₂O - 30 seconds then free flow oxygen 45 seconds with appropriate postpartum adaptation.

There were no documented renal or other malformative pathologies in the family histories of the mother and father.

CLINICAL FINDING

Upon immediate postpartum examination, the newborn presented with mild hypotonia and slight hyporeactivity, which resolved after resuscitation maneuvers. The skin and mucous membranes were intact, with acrocyanosis and abundant vernix, generalized. There was plantar reflex elicited on the anterior 1/3, intact skull without facial dysmorphism, normotensive anterior fontanelle measuring 2.5 × 2 cm, normal-shaped chest participating symmetrically in respiratory movements, bilateral present vesicular murmur, symmetric, with fine transmission rales. Preductal oxygen saturation in ambient air at 5 minutes of life was 85%, respiratory rate was 45 breaths per minute, temperature was 36.5 degrees Celsius, rhythmic cardiac sounds well-auscultated without added murmurs, palpable bilateral symmetric femoral pulses, Average arterial pressure: 50 mmHg, systolic/diastolic blood pressure: 66/41 mmHg, Heartbeat: 135-140 bpm, supple, elastic abdomen, without palpable formations. Liver and spleen were within normal limits, external genitalia were consistent with gestational age and female sex. The nervous system demonstrated normal tone and reflexes after resuscitation maneuvers.

Considering the renal pathology, it was decided to conduct a comprehensive biological assessment, a complete urine analysis, and a urine culture, with careful monitoring of blood pressure values, vital functions, and diuresis in NICU - Neonatal Intensive Care Unit.

The clinical examination in NICU: General condition good, afebrile, pink skin, intact, without peripheral edema, normal chest conforming symmetrically participating in respiratory movements, vesicular murmur present bilaterally, fine transmission rales, O₂ sat in ambient air 98-100% without episodes of apnea or desaturation, respiratory rate 45 breaths/minute, rhythmic heart sounds, well beaten, without extra breaths, peripheral pulses palpable bilaterally, symmetrical, TAM: 50 mmHg, BP: 66/41 mmHg, heart rate: 124-135 beats per minute, supple, elastic abdomen, without palpable formations, intestinal transit present, spontaneous micturitions, tone and reactivity corresponding to gestational age, normotensive anterior fontanel.

THERAPEUTIC FOCUS AND ASSESSMENT

Considering the low birth weight for gestational age together with prematurity we perform a capillary blood glucose test at 2 hours of life, which resulted in 74 mg/dL.

Considering the prenatal ultrasound suspicion of polycystic kidney, a postpartum abdominal ultrasound was performed, revealing the following findings: The right kidney measured 4.59 × 2.78 cm with preserved echogenicity and renal parenchymal structure (Figure 1). The left kidney showed multiple cystic formations with variable diameters, the largest cystic formation of 4.52 × 2.60 cm, anechoic without intracystic formations. The urinary bladder appeared semi-filled with sonolucent content (Figure 2).

Liver ultrasound - within normal limits;

Pulmonary ultrasound - within normal limits;

Transfontanel ultrasound - normal relations.

During the hospitalization period, diuresis was monitored (Table 1) and laboratory tests were conducted dynamically (Table 2).

TABLE 1. Urinary Output

	Day I	Day II	Day III
Urinary output	3,2 ml/kgc/ 15 h	2,83 ml/kgc/ 24 h	2,61 ml/kgc/ 24h

Urine summary: Negative.

Blood pressure values: Within normal limits during hospitalization.

The urine culture result was positive for *E. coli*. Pediatric nephrology consultation was requested and recommending antibiotic treatment with Ampicillin 2 × 100 mg/kg/24 hours IV for 5 days and Gentamicin 4 mg/kg/24 hours for 5 days. After completing the antibiotic treatment, negative urine culture was confirmed. Probiotic treatment was initiated during the antibiotic administration period and

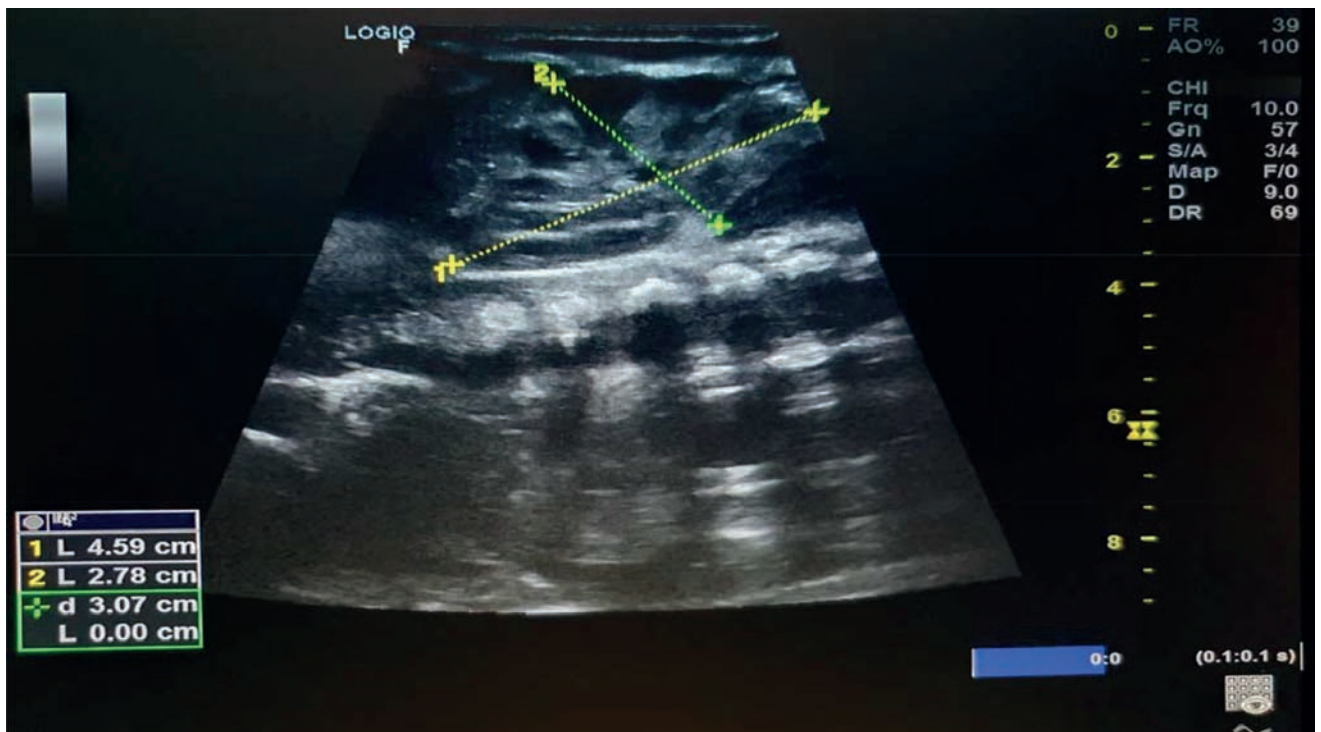


FIGURE 1. Right kidney ultrasound

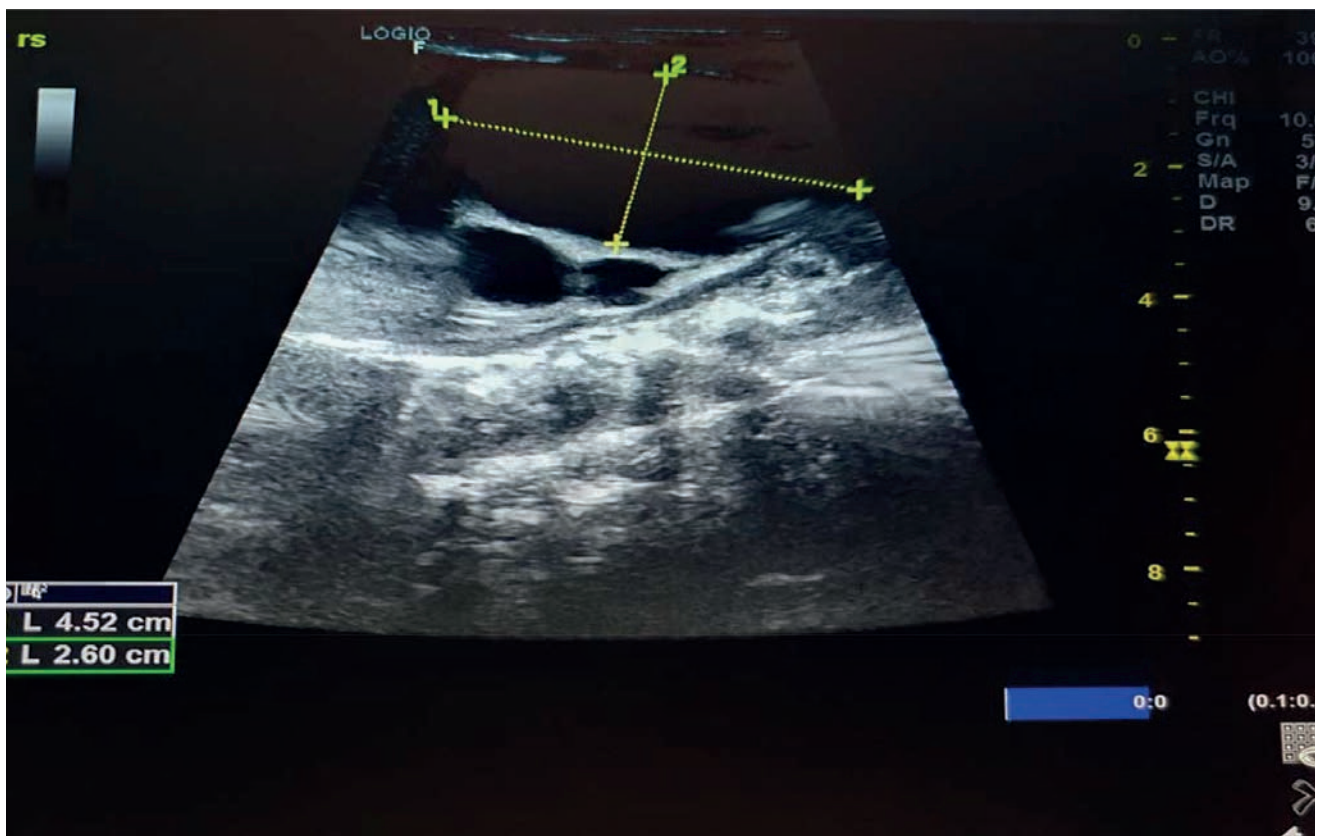


FIGURE 2. Left kidney ultrasound

continued for an additional 5 days at home. Hospitalization and monitoring in the NICU were continued.

During the hospitalization, blood pressure values remained within normal limits - with average blood pressure: 50-51 mmHg.

DIAGNOSTIC DIFFERENTIATION

Glomerulocystic kidney disease. A rare cause of cystic kidney disease that affects any age. Pathology that is characterized by the dilatation of Bowman’s capsule and normal tubes. [3].

TABLE 2. Laboratory analyses in dynamics

Variable	The first collection on day 1 of admission	Second collection on day V of hospitalization	Reference newborns
White cell count (per microl)	19,540	12,660	9,100-24,000
Hemoglobin (g/dl)	15.20	17.3	15-24
Hematocrit (%)	41.20	47.20	44-70
Platelet count (per microl)	519,000	488,000	84,000-478,000
Urea nitrogen (mg/dl)	30.82	21.14	10-50
Creatinine (mg/dl)	0.50	0.22	0-5
Alanine aminotransferase (U/liter)	12.83	12.85	4-52
Aspartate aminotransferase (U/liter)	50.35	52.25	4-110
Sodium (mmol/liter)	3.25	3.1	3.5-5.0
Potassium (mmol/liter)	5.7	5.1	5-20
Calcium (mg/dl)	8.7	9	8.5-10.5
Chloride (mmol/liter)	95	97	98-106

Dominant polycystic kidney disease (ADPKD).

Adult cystic renal pathology [4].

Diffuse cystic dysplasia refers to large reniform kidney that often have a patent ureter and a recognizable collecting system. The renal parenchyma is characterized by agenesis pyramids, diffuse cysts of the cortex, which are uniform and rounded.

Hepatocyte nuclear factor-1-beta (HNF1B). An cystic pathology that is associated with cortical renal cysts and diabetes in adulthood [6].

Nephronophthisis (NPHP). Genetically heterogenic disorder with variants in genes that involved in the function of centrioles. The abdominal ultrasound examination reveals hyperechoic renal structure with loss of corticomedullary differentiation, kidneys of normal or slightly reduced size, in contrast to the large kidneys observed in patients with ARPKD.

Is an autosomal recessive genetic pathology that affects the genes responsible for the proteins involved in the function of primary cilia, basal bodies and centrosomes. Ultrasonography detects an increased renal echogenicity with the impossibility of detecting the renal cortico-medullary border and small-sized kidneys, in contrast to the large-sized kidneys detected in patients with ARPKD [6].

FOLLOW-UP AND MONITORING

The newborn was discharged at 11 days of age with a weight of 2650 grams, negative Ortolani test, and bilateral PASS auditory testing. Being a progressive pathology, it is recommended to carefully monitor constants on a regular basis [5]:

Ultrasound re-evaluation at discharge. The annual abdominal ultrasound examination is indicated for the evaluation of signs of portal hypertension. [14]. However, this examination must be performed

every time there is a suspicion or detectable sign during the objective examination of splenomegaly. At the age of 5 years at the latest, it must be performed to evaluate the degree of liver damage (ultrasound evaluation of intra- and extrabiliary tracts and signs of portal hypertension) [12]. If the examined patient falls within the normal stage, it is possible to move on to a subsequent reevaluation at 2-3 years intervals to monitor liver function.

Blood pressure (BP). The frequency of arterial pressure measurement varies depending on the degree of kidney impairment in the hypertensive patient. It is mandatory to measure blood pressure at each clinical examination. If blood pressure values are elevated in the medical office, home monitoring of blood pressure is recommended to distinguish between fixed hypertension and white coat blood pressure [6].

Kidney function. Kidney function – Renal biological constants should be evaluated at least once a year: monitoring of serum creatinine is recommended [6]. Monitoring symptoms of polyuria and polydipsia due to a reduced ability to concentrate urine represents an early sign of kidney dysfunction that precedes a decrease in glomerular filtration rate (GFR) [7]. In most patients, the maximum urine osmolality is less than 500 mosmol/kg.

Liver status. Annual hepatic evaluation involves a physical examination that can detect splenomegaly, indicative of portal hypertension, and laboratory constants – full blood count and hepatic function tests (serum transaminases, coagulation studies, and serum albumin) [9,12,13].

Pediatric nephrology consultation: is recommended if symptoms indicating kidney failure appear: loss of appetite accompanied by weight loss, swelling of the ankles, feet, or hands (edema), breathing difficulties, frequent urination, especially at night (nocturia), hives, nausea, vomiting [7].

Genetic consultation. The majority of cases of ARPKD are caused by variations in the PKHD1 gene (polycystic kidney and hepatic disease 1 gene), located on chromosome 6p21. This gene encodes the protein fibrocystin, found in the epithelial cells of renal tubules and bile ducts; deficiency of this gene leads to polycystic dilation affecting both structures [8].

Growth and nutrition. Feeding intolerance can be significant and may necessitate aggressive nutritional support, including supplemental feeding and intravenous infusions, to optimize weight gain and optimal [9]. Some patients require replacement therapy with recombinant growth hormone [15].

DISCUSSIONS

ARPKD is part of a category of congenital fibrocystic illness that frequently cause comorbidities in children. Most patients present enlarged kidneys, and 50% progress to end-stage renal disease requiring renal transplantation [9].

Ultrasound examination is the primary method for diagnosing and further evaluating disease both in the neonatal and perinatal periods [8].

Ultrasonography remains the most important tool in diagnosing kidney pathology both prenatally and postnatally, but we also have other alternatives: MRI examination and computer tomography scan [9]. Prenatal ultrasound examination, although reliable, remains challenging due to numerous factors: examiner expertise, maternal obesity, inconsistent timing of examinations which may not coincide with optimal fetal positioning, thereby affecting detailed visualization of fetal parts and potential associated malformations.

The management of these patients is individualized based on the severity of the disease stage. Due to these factors, a screening ultrasound examination for all newborns in the first month of life would be highly beneficial for accurately determining the incidence of various pathologies and preventing complications, both in terms of multicystic renal pathology and other associated comorbidities.

A study involving 264 patients from 40 countries demonstrated that 13% of neonatal end-stage renal disease cases were attributed to cystic kidney disease, 55% had congenital anomalies of the kidney and urinary tract as contributing factors, 11% had cortical necrosis, and only 6% had congenital nephrotic syndrome. Within 2 years of initiating Renal Replacement Therapy (RRT), 69 children required dialysis and 53 underwent renal transplantation. After 7 months, 45 children had died, primarily due to associated infections, resulting in a 2-year survival rate of 81% and a 5-year survival rate of 76%.

Growth retardation was observed in 63% of cases, anemia in 55%, and arterial hypertension in 57%. [10].

Fortunately, our newborn had a favorable outcome without associated extrarenal pathology, alongside treatment for the urinary tract infection associated with the pathology, and without aggravation of the pathology during hospitalization.

In our case, prenatal ultrasound was only performed upon the pregnant woman's admission, as it was an unscheduled pregnancy, and the woman had not attended any obstetrical consultations or ultrasound evaluations until the time of admission.

Unfortunately, the incidence of premature births is steadily increasing globally, representing a significant risk factor for neonatal and perinatal incidence of sickness and death. In addition to premature births, the rising incidence of morbidity and mortality is associated with the comorbidities that accompany premature birth. A study has shown that approximately 500,000 neonatal lives could be saved each year if antenatal steroids are administered to all mothers at risk of preterm birth [11].

Urinary tract infections are commonly associated with patients with ARPKD [16,17]. For this reason, patients presenting with symptoms such as fever, dysuria, or flank pain are recommended to undergo clinical examination accompanied by urine culture collection. Empirical antibiotic treatment is initiated and adjusted based on the results of the urine culture.

End-stage renal disease along and poor prognosis are associated with situation where a person has two copies of a particular type of genetic mutation [18,19]. The mortality rate is much higher in patients diagnosed in infancy with severe kidney disease associated with respiratory failure, with rates of approximately 30% [16,20]. Patients who survive the first month of life have significantly higher chances, around 80%, of surviving until 15 years of age [20-23]. In a longitudinal study of 164 patients with ARPKD who survived the neonatal period, renal function evaluation was approximately 85% at 5 years, 70% at 10 years, and 40% at 20 years [20]. Three-quarters of the cohort developed systemic arterial hypertension, 44% acquired liver fibrosis and hypertension portal. Improved management of renal insufficiency and end-stage renal disease (ESKD) has led to an increase in the number of patients developing portal hypertension [24].

CONCLUSIONS

The use of antenatal intrauterine and postnatal ultrasound screening during hospitalization in maternity wards is helpful in detecting congenital

anomalies and intrauterine growth restrictions with establishing appropriate management and individualized therapeutic conduct for each case. With high-resolution ultrasound equipment, professional examiners, and systematic ultrasound screening throughout pregnancy, a variety of fetal malformations can now be diagnosed. However, a small percentage of them still escape detection. Nevertheless, there are pregnant women who do not benefit from

any ultrasound screening during pregnancy, as was the case with a completely unsupervised pregnancy like ours with parents coming from a socio-economically disadvantaged background, the incidence of congenital malformative anomalies remains constant.

Conflict of interest: none declared
Financial support: none declared

REFERENCES

1. „Nicolae Testemitanu” University of Medicine and Pharmacy. Renal multi-cystic lazia in child. National clinical protocol. (1st edition). [Rom]. Available: <https://ms.gov.md/wp-content/uploads/2022/06/PCN-Displazia-multichistica-renala-la-copil.pdf>
2. National Institute of Diabetes and Digestive and Kidney Diseases. What Is Polycystic Kidney Disease? Available: <https://www.niddk.nih.gov/health-information/kidney-disease/polycystic-kidney-disease/what-is-pkd>
3. Sahay M, Gowrishankar S. Glomerulocystic disease. *NDT Plus*. 2010 Aug;3(4):349-50. <http://doi.org/10.1093/ndtplus/sfq048>. Epub 2010 Apr 13. PMID: 25949428; PMCID: PMC4421520.
4. Gaillard F, Sharma R, Kogan J, et al. Autosomal dominant polycystic kidney disease. Reference article, Radiopaedia.org (Accessed on 20 Jun 2024) <https://doi.org/10.53347/rID-10257>
5. Sweeney WE, Avner ED. Polycystic kidney disease, autosomal recessive. GeneReviews. 2014. www.ncbi.nlm.nih.gov/books/NBK1326/#pkd-ar. REF.roy.1997.302 (Accessed on December 02, 2014).
6. Niaudet P. Autosomal recessive polycystic kidney disease in children. Available: <https://www.uptodate.com/contents/autosomal-recessive-polycystic-kidney-disease-in-children>
7. Seeman T, Bláhová K, Fencí F, et al. Kidney concentrating capacity in children with autosomal recessive polycystic kidney disease is linked to glomerular filtration and hypertension. *Pediatr Nephrol*. 2023;38:2093. <http://doi.org/10.1007/s00467-022-05834-5>
8. https://en.wikipedia.org/wiki/Autosomal_recessive_polycystic_kidney_disease
9. Sweeney WE, Avner ED. Polycystic kidney disease, autosomal recessive. In: GeneReviews® [Internet]. Seattle: University of Washington; 2019.
10. van Stralen KJ, Borzych-Dużalka D, Hataya H, et al. Survival and clinical outcomes of children starting renal replacement therapy in the neonatal period. *Kidney Int*. 2014;86:168-74. <http://doi.org/10.1038/ki.2013.561>
11. Mitchell HK, Thomas R, Hogan M, Bresges C. Miracle baby: managing extremely preterm birth in rural Uganda. *BMJ Case Rep*. 2014;bcr2013200949–bcr2013200949.
12. Guay-Woodford LM, Bissler JJ, Braun MC, et al. Consensus expert recommendations for the diagnosis and management of autosomal recessive polycystic kidney disease: report of an international conference. *J Pediatr*. 2014;165:611. <http://doi.org/10.1016/j.jpeds.2014.06.015>
13. Turkbey B, Ocak I, Daryanani K, et al. Autosomal recessive polycystic kidney disease and congenital hepatic fibrosis (ARPKD/CHF). *Pediatr Radiol*. 2009; 39:100. <http://doi.org/10.1007/s00247-008-1064-x>
14. Gimpel C, Avni EF, Breysem L, et al. Imaging of Kidney Cysts and Cystic Kidney Diseases in Children: An International Working Group Consensus Statement. *Radiology*. 2019;290:769. <http://doi.org/10.1148/radiol.2018181243>
15. Lilova M, Kaplan BS, Meyers KE. Recombinant human growth hormone therapy in autosomal recessive polycystic kidney disease. *Pediatr Nephrol*. 2003;18:57. <http://doi.org/10.1007/s00467-002-0986-z>
16. Guay-Woodford LM, Desmond RA. Autosomal recessive polycystic kidney disease: the clinical experience in North America. *Pediatrics*. 2003; 111:1072. <http://doi.org/10.1542/peds.111.5.1072>
17. Zerres K, Rudnik-Schöneborn S, Deget F, et al. Autosomal recessive polycystic kidney disease in 115 children: clinical presentation, course and influence of gender. Arbeitsgemeinschaft für Pädiatrische Nephrologie. *Acta Paediatr*. 1996;85:437. <http://doi.org/10.1111/j.1651-2227.1996.tb14056.x>
18. Burgmaier K, Brinker L, Erger F, et al. Refining genotype-phenotype correlations in 304 patients with autosomal recessive polycystic kidney disease and PKHD1 gene variants. *Kidney Int*. 2021;100:650. <http://doi.org/10.1016/j.kint.2021.04.019>
19. Benz EG, Hartung EA. Predictors of progression in autosomal dominant and autosomal recessive polycystic kidney disease. *Pediatr Nephrol*. 2021;36:2639. <http://doi.org/10.1007/s00467-020-04869-w>
20. Bergmann C, Senderek J, Windelen E, et al. Clinical consequences of PKHD1 mutations in 164 patients with autosomal-recessive polycystic kidney disease (ARPKD). *Kidney Int*. 2005;67:829. <http://doi.org/10.1111/j.1523-1755.2005.00148.x>
21. Adeva M, El-Youssef M, Rossetti S, et al. Clinical and molecular characterization defines a broadened spectrum of autosomal recessive polycystic kidney disease (ARPKD). *Medicine (Baltimore)*. 2006;85:1. <http://doi.org/10.1097/01.md.0000200165.90373.9a>
22. Roy S, Dillon MJ, Trompeter RS, Barratt TM. Autosomal recessive polycystic kidney disease: long-term outcome of neonatal survivors. *Pediatr Nephrol*. 1997;11:302. <http://doi.org/10.1007/s004670050281>
23. Dorval G, Boyer O, Couderc A, et al. Long-term kidney and liver outcome in 50 children with autosomal recessive polycystic kidney disease. *Pediatr Nephrol*. 2021; 36:1165. <http://doi.org/10.1007/s00467-020-04808-9>
24. Khan K, Schwarzenberg SJ, Sharp HL, et al. Morbidity from congenital hepatic fibrosis after renal transplantation for autosomal recessive polycystic kidney disease. *Am J Transplant*. 2002;2:360. <http://doi.org/10.1034/j.1600-6143.2002.20412.x>