



## Autosomal Recessive Polycystic Kidney Disease

### Alternative Names

ARPKD  
Polycystic Kidney and Hepatic Disease 1  
PKHD1  
Polycystic Kidney Disease, Infantile, Type I  
Formerly PKD3  
Infantile Polycystic Kidney Disease Type 1  
Congenital Hepatic Fibrosis  
Caroli Disease  
Renal-Hepatic-Pancreatic Dysplasia  
Potter Disease Type 1

### WHO International Classification of Diseases

Congenital malformations, deformations and chromosomal abnormalities

### OMIM Number

263200

### Mode of Inheritance

Autosomal recessive

### Gene Map Locus

6p21.1-p12

### Description

Autosomal recessive polycystic kidney disease is one of the most common pediatric, hereditary nephropathies, with an estimated incidence of 1 in 20,000 live births. The clinical spectrum is variable and depends on the age at presentation, ranging from stillbirth and neonatal demise to survival into adulthood. The most severely affected fetuses have enlarged echogenic kidneys and oligohydramnios attributable to poor fetal renal output. These fetuses develop the "Potter" phenotype, characteristic facies (consists of wide-set eyes, squashed nose, micrognathia, and large, floppy, low-set ears deficient in cartilage) with pulmonary hypoplasia, and deformities of the spine and limbs. A critical degree of pulmonary hypoplasia is often present at birth in these neonates. Renal function is rarely a cause of neonatal death and for infants who survive the

perinatal period, a wide range of associated morbidities can evolve, including hypertension, renal failure, and portal hypertension. In the case of Potter syndrome, autosomal recessive inheritance has been suggested in familial cases. However, the syndrome most probably develops as a pattern of multiple anomalies derived from one single, mechanical factor. The initiating event of this syndrome is oligohydramnios.

It is important to note that a considerable portion of children with autosomal recessive polycystic kidney disease have associated asymptomatic Caroli disease of the liver. Caroli disease is a rare disorder of the liver, characterized by saccular and cystic dilatation of intrahepatic biliary ducts. This abnormality may remain asymptomatic and undetected throughout life but often presents in adolescence or later with episodes of bacterial cholangitis, complicated by multiple biliary calculi.

### Molecular Genetics

Autosomal recessive polycystic kidney disease is caused by mutation in the polycystic kidney and hepatic disease 1 (PKHD1) gene, mapped to chromosome 6p21.1-p12. PKHD1 is a large gene, approximately 470 kb, with 67 exons from which multiple transcripts may be generated by alternative splicing. It is highly expressed in kidney, with lower levels in liver and pancreas. The ARPKD protein, fibrocystin: 4074-amino acids and 447 kDa, is predicted to be an integral membrane, receptor-like protein containing multiple copies of an Ig-like domain (TIG).

### Epidemiology in the Arab World

#### Kuwait

Ninan et al. (2002) described a 25-year-old female who had been diagnosed with autosomal recessive polycystic kidney disease at the age of 15 years. Over the subsequent years of follow



up, her renal function declined progressively and at the age of 20 years she was started on maintenance hemodialysis. She underwent renal transplantation and post-transplant an ultrasound of the abdomen was carried out. This analysis revealed multiple cysts in the liver with no localized symptoms. She remained stable and asymptomatic on follow up till 5 years post-transplant when she was admitted with fever, upper abdominal pain, and vomiting. On physical examination, an enlarged tender liver was palpable. Computerized tomography of the abdomen showed dilated intra- and extra-hepatic ducts with multiple biliary calculi. An endoscopic retrograde cholangiopancreatography (ERCP) revealed a dilated common bile duct (CBD) and intra-hepatic ducts with marked saccular dilatation, involving both lobes of the liver. These features were consistent with Caroli disease of the liver. In a span of about 4 months she was admitted into the hospital five times with fever. An orthotopic liver transplantation from a cadaveric source was successfully carried out and she has remained well over the subsequent 4 years of follow up.

#### **Lebanon**

Barbari et al. (2003) surveyed all the dialysis centers in Lebanon to study the effect of consanguineous marriages and their impact on the repartition of kidney diseases and on the risk for familial nephritis. Diabetes, polycystic kidney disease (PKD), chronic pyelonephritis and nephrosclerosis (NS) were the most commonly documented diagnoses in 925 patients reviewed. More than half of the hemodialysis (HD) patients had an unknown etiology of their kidney disease. Consanguinity was present in 26% of the total HD population. Consanguinity-associated kidney diseases pattern differed from that of the general HD population by disease diagnosis and initiation at a younger age and a significantly higher risk for familial renal disease. Certain geographical areas were more involved than others such as the North, South and the Bekaa with the highest percentage (40%) in the latter.

#### **Palestine**

Finer et al. (2004) conducted a retrospective analysis for autosomal recessive polycystic kidney disease cases to establish a genetic method for prenatal diagnosis of the disease. Eighteen ARPKD patients from 7 extended Bedouin families were identified (perinatal manifestation = 9; neonatal = 2; infantile = 2; juvenile = 5). Inter- and intra-familial phenotypic variability was found in several families. Finer et al. (2004) observed a

considerable phenotypic variability in their patients with autosomal recessive polycystic kidney disease with supposedly homozygous mutations in the PKHD1 gene.

#### **Saudi Arabia**

Patel (1992) evaluated 17 patients, age 1 day to 6 years with infantile polycystic kidney disease with ultrasound and other imaging techniques. Most patients showed bilaterally enlarged kidneys with hyperechoic renal parenchyma, which had poor differentiation in outlines as well as between renal sinus, cortex and medulla. Cysts of various sizes were also identified in the kidneys. However, a third of these cases showed well-defined renal outlines, normal echogenic cortical rim, whilst dilated renal collecting systems were seen in another third of the cases. Twelve cases showed hepatomegaly. Few rare findings such as liver cysts, associated Meckel syndrome, renal stone, bilateral vesicoureteric reflux and renal calcification were also noted.

Mattoo et al. (1994) described 15 Arab children (8 males, 7 females) with autosomal recessive polycystic kidney disease (ARPKD) whose ages at diagnosis ranged from 2 days to 7 years (median 10 months). Eleven (73.3%) patients were hypertensive on admission and one developed hypertension 4 months later; five patients became normotensive after receiving treatment for 18-36 months (mean 23.2 months). Patients were followed for a period of 1-48 months (mean 20.9 months). Glomerular filtration rate remained normal in seven patients, improved in four and deteriorated in one. Two patients died soon after diagnosis and one was lost to follow-up and was assumed dead. Of the four patients less than 6 months old at the time of diagnosis, only one was alive compared with 10 of 11 presenting after 6 months of age. Mattoo et al. (1994) highlighted the reversible nature of hypertension in ARPKD indicating that survival is better in patients older than 6 months at the time of diagnosis and those surviving the 6 months follow-up.

#### **Tunisia**

Boutheina et al. (2000) carried out 43 prenatal diagnoses of lethal urinary tract abnormalities during a five-year-period. Among the abnormalities observed there were bilateral renal agenesis (56%), autosomal recessive polycystic kidney disease (16%), autosomal dominant polycystic kidney disease (14%), Meckel-Gruber syndrome, and Prune-Belly syndrome (4%). The pregnancy in 35 cases was interrupted (81.4%).



### United Arab Emirates

Al Talabani et al. (1998) studied the pattern of major congenital malformations in 24,233 consecutive live and stillbirth in Corniche hospital, which is the only maternity hospital in Abu Dhabi, between January 1992 to January 1995. A total of 401 babies (16.6/1,000), including 289 Arabs, were seen with major malformation. Single gene disorders accounted for 24% of the cases, 76% were due to autosomal recessive disorders. In their study, Al Talabani et al. (1998) observed nine case of bilateral polycystic kidney disease and eight cases of Potter syndrome born to first cousin couples from the United Arab Emirates. Recurrence was reported in all families with bilateral polycystic kidney disease and in three families with Potter syndrome. Al Talabani et al. (1998) concluded that their study was very close to representing the true incidence of congenital abnormalities in the whole United Arab Emirates, as they investigated over 98% of deliveries in Abu Dhabi, the capital of United Arab Emirates.

Abouchacra et al. (2004) described a female patient with autosomal recessive polycystic kidneys as well as a rare condition of Caroli disease. Despite advanced cystic transformation of the biliary tree with striking architectural changes, there was no evidence of portal hypertension or hepatic fibrosis. Moreover, the patient did not suffer a single episode of cholangitis, a most interesting feature of this case. Her clinical course was punctuated by repeated episodes of gastrointestinal and urinary tract infections with resistant organisms; but fortunately, she had no evidence of septicemia. Recurrent Salmonella gastroenteritis indicated a chronic carrier state with the dilated bile ducts possibly acting as a potential reservoir. This has significant implications considering the immune suppression associated with renal transplantation.

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