Supplementary Table 1: Demographic, clinical and laboratory findings of the patients with ARPKD

Patient number	Gender	Age at Diagnosis	Consanguinity	Family History	Creatinine at diagnosis (mg/dL)	eGFR at diagnosis (ml/min/1.73 m^2)	Creatinine at last visit (mg/dL)	eGFR at last visit (ml/min/1.73 m^2)	USG Findings
PN1556	F	prenatal	+	-	0.64	21.25	NA	NA /died	Increased renal echogenicity, CM cysts
PN772	M	10 years	-	-	0.58	124	0.98	69.5	Increased renal echogenicity, Nephrocalcinosis, Medullary sponge kidney, CM cysts
PN778	M	7 months	+	-	0.60	82	1.41	51.2	Increased renal echogenicity, Nephrocalcinosis, CM cysts, splenomegaly
PN1483	F	11 months	-	-	0.38	63.5	0.53	95.7	Increased renal echogenicity, Nephrocalcinosis, CM cysts, increased liver echogenicity
PN1540 II1[†]	F	14 years	+	+	0.69	95.7	0.83	81	Increased renal echogenicity, CM cysts
PN1540 II2[†]	M	2 years	+	+	0.90	39	1.34	39.7	Increased renal echogenicity, CM cysts and multiple cysts in the liver
PN1680*	F	12 months	-	-	1.30	29.8	1.31	48.2	Increased renal echogenicity, CM cysts, PF, ascites, splenomegaly
PN1700	M	11.5 months	-	-	0.20	81.6	0.20	81.6	Renal cortical cysts
PN1671	M	prenatal	-	-	0.63	86.5	0.78	74	Increased renal echogenicity, renal cortical cysts
PN1855	M	9 years 3 months	+	-	0.37	147	0.5	132	Renal cortical cysts
PN1820	M	3 years 9 months	-	+	0.42	105	0.52	123	Increased renal echogenicity, CM cysts and multiple cysts in the liver
PN1831	M	5 months	-	-	0.23	122	0.53	102	Increased renal echogenicity, Medullary sponge kidney, CM cysts
PN1881	F	6 years	-	-	0.54	116	0.66	98	Increased renal echogenicity, Medullary sponge kidney, multiple medullary cysts
PN2107*	M	7 months	+	+	1.25	16.5	0.19	165	Increased renal echogenicity, CM cysts, PF
PN2285	F	1.5 months	+	+	0.52	30.7	4.29	7.6	Increased renal echogenicity, CM cysts, PF, ascites
PN2261	M	4 months	+	+	0.26	83.6	0.26	82	Increased renal echogenicity, CM cysts and liver cysts, PF, dilated bile ducts
PN2040	F	15 years	+	-	0.80	75.88	1.08	56	Increased renal echogenicity, CM cysts
PN2044	F	prenatal	+	+	0.38	27.6	0.34	65	Increased renal echogenicity, CM cysts and liver cysts, PF, dilated bile ducts
PN1967	F	prenatal	+	-	1.12	6.7	NA	NA /died	Increased renal echogenicity, CM cysts
PN1963	M	10 months	-	-	0.21	119.8	0.51	76.7	Increased renal echogenicity, CM cysts, PF, dilated bile ducts, splenomegaly
PN2325	F	prenatal	-	+	0.86	14.5	0.64	19 /died	Increased renal echogenicity, CM cysts

CM, corticomedullary; F, female; M, male; NA, not available; PF, periportal fibrosis; USG, ultrasonography

*: Patients with the renal transplantation

[†]: PN1540 II1 and II2 are siblings.

Supplementary Table 2: Genetic characteristics of the patients with ARPKD

Patient number	*PKHD1* allele 1 Variant (predicted aminoacid change)*	Reference/dbSNP database	ClinVar[a] or *In slico* prediction for previously unpublished variations	Aachen database[b]	*PKHD1* allele 2 Variant (predicted aminoacid change)*	Reference/dbSNP database	ClinVar[a] or *In slico* prediction for previously unpublished variations	Aachen database[b]
PN1556	c.707+1G>A (splice site)	Melchionda (2016) J Hum Genet 61: 811 [1]		NA	c.707+1G>A (splice site)	Melchionda (2016) J Hum Genet 61: 811 [1]		NA
PN772	Exon 12: c.788_789delCT (p.Ser263fs*22)	rs1045491786	ClinVar: Not reported MT: Disease causing	NA	Exon 60: c.10036T>C (p.Cys3346Arg)	Rossetti (2003) Kidney Int 64: 391 [2]	(-)	Pathogenic
PN778	Exon 58: c.9524A>G (p.Asn3175Ser)	Furu (2003) J Am Soc Nephrol 14: 2004 [3]	(-)	Pathogenic	Exon 36: c.5785_5790delTCCAGG (p.Ser1929_Arg1930del)	rs1045491786	ClinVar: Not reported MT: Disease causing SIFT: Deleterious	NA
PN1483	Exon 33: c.5275G>C (p.Gly1759Arg)	rs398124488	ClinVar: Uncertain significance MT: Disease causing SIFT: Damaging; PolyPhen-2: Possibly damaging	NA	Exon33: c.5365G>T (p.Val1789Phe)	Novel	ClinVar: Not reported MT: Polymorphism SIFT: Damaging; PolyPhen-2: Possibly damaging	NA
PN1540 II1	Exon32: c.4870C>T (p.Arg1624Trp)	Onuchic (2002) Am J Hum Genet 70: 1305 [4]	(-)	Pathogenic	Exon 58: c.9189C>A (p.Asn3063Lys)	Novel	ClinVar: Not reported MT: Polymorphism SIFT: Damaging; PolyPhen2: Probably damaging	NA
PN1540 II2	Exon32: c.4870C>T (p.Arg1624Trp)	Onuchic (2002) Am J Hum Genet 70: 1305 [4]	(-)	Pathogenic	Exon 58: c.9189C>A (p.Asn3063Lys)	Novel	ClinVar: Not reported MT: Polymorphism SIFT: Damaging; PolyPhen2: Probably damaging	NA
PN1680	Exon 35: c.5735G>A (p.Trp1912*)	Novel	ClinVar: Not reported MT: Disease causing	NA	Exon 33: c.5353T>C (p.Phe1785Leu)	Bergmann (2005) Kidney Int 67: 829 [5]	(-)	Pathogenic
PN1700	c.4870C>T (p.Arg1624Trp)	Onuchic (2002) Am J Hum Genet 70: 1305 [4]	(-)	Pathogenic	Exon 22: c.2279G>A (p.Arg760His)	Onuchic (2002) Am J Hum Genet 70: 1305 [4]	(-)	Pathogenic
PN1671	Exon 53: c.8315T>C (p.Leu2772Pro)	Furu (2003) J Am Soc Nephrol 14: 2004 [3]	(-)	Pathogenic	Exon16: c.1397G>A (p.Gly466Glu)	Gunay-Aygun (2010) Mol Genet Metab 99: 160 [6]	(-)	Probably pathogenic
PN1855	Exon 57: c.8863C>T (p.Arg2955*)	Liang (2020) Clin Chim Acta 501: 207[7]	ClinVar: Pathogenic	NA	Exon 32: c.5134G>A (p.Gly1712Arg)	Gunay-Aygun (2010) Mol Genet Metab 99: 160 [6]	(-)	Probably pathogenic
PN1820	Exon 40: c.6610G>A (p.Val2204Met)	rs747645373	ClinVar: Not reported MT: Disease causing SIFT: Damaging PolyPhen2: Probably damaging	NA	Exon 35: c.5735G>A (p.Trp1912*)	Novel	ClinVar: Not reported MT: Disease causing	NA
PN1831	Exon 50: c.7912T>A (p.Tyr2638Asn)	Denamur (2010) Kidney Int 77: 350 [8]	(-)	NA	Exon 32: c.5134G>A (p.Gly1712Arg)	Gunay-Aygun (2010) Mol Genet Metab 99: 160 [6]	(-)	Probably pathogenic
PN1881	c.8441-1G>A (splice site)	Novel	HSF: Broken WT acceptor site	NA	Exon 61: c.10658T>C (p.Ile3553Thr)	Ward (2002) Nat Genet 30: 259 [9]	(-)	Pathogenic
PN2107	Exon 59: c.9945delG (p.Met3316fs*2)	Novel	ClinVar: Not reported MT: Disease causing	NA	Exon 14: c.1116C>G (p.Phe372Leu)	Bergmann (2005) Kidney Int 67: 829 [5]	(-)	Pathogenic
PN2285	c.602+5G>T (splice site)	Brinkert (2013) Transpl Int 26: 640 [10]	(-)	NA	c.602+5G>T (splice site)	Brinkert (2013) Transpl Int 26: 640 [10]	(-)	NA
PN2261	Exon 41: c.6771T>G (p.Asn2257Lys)	rs1315333212	ClinVar: Uncertain significance SIFT: Damaging, PolyPhen-2: Probably damaging	NA	Exon 41: c.6771T>G (p.Asn2257Lys)	rs1315333212	ClinVar: Uncertain significance MT: Polymorphism SIFT: Damaging, PolyPhen-2: Probably damaging	NA
PN2040	Exon 61: c.10910G>A (p.Arg3637His)	rs371329493	ClinVar: Uncertain significance MT: Polymorphism; SIFT: Tolarated; PolyPhen2: Benign	NA	Exon 24: c.2539G>A (p.Val847Met)	rs778864835	ClinVar: Uncertain significance MT: Polymorphism SIFT: Tolarated	NA

							PolyPhen2: Probably damaging	
PN2044	Exon 14: c.1116C>G (p.Phe372Leu)	Bergmann (2005) Kidney Int 67: 829 PubMed: 15698423 [5]	(-)	Pathogenic	Exon 14: c.1116C>G (p.Phe372Leu)	Bergmann (2005) Kidney Int 67: 829 PubMed: 15698423 [5]	(-)	Pathogenic
PN1967	Exon 59: c.9945delG (p.Met3316fs*2)	Novel	ClinVar: Not reported MT: Disease causing	NA	Exon 59: c.9945delG (p.Met3316fs*2)	Novel	ClinVar: Not reported MT: Disease causing	NA
PN1963	Exon 61: c.10623C>A (p.Asn3541Lys)	Novel	ClinVar: Not reported MT: Polymorphism; SIFT: Tolarated; PolyPhen-2: Probably damaging	NA	Exon 3: c.107C>T (p.Thr36Met)	Ward (2002) Nat Genet 30: 259 PubMed: 11919560 [9]	(-)	Pathogenic
PN2325	Exon 34: c.5513A>G (p.Tyr1838Cys)	Rossetti (2003) Kidney Int 64: 391 [2]	(-)	Pathogenic	Exon 34: c.5513A>G (p.Tyr1838Cys)	Rossetti (2003) Kidney Int 64: 391 [2]	(-)	Pathogenic

*Variations and predicted aminoacid changes have been named according to the guidelines of the Human Genome Variation Society using Mutalyzer software (https://mutalyzer.nl) of *PKHD1* (transcript # NM_138694.4). Minor allele frequencies of those variations not previously reported are either less than 1% or not present in both The Genome Aggregation Database (gnomAD) (https://gnomad.broadinstitute.org/) and our in-house database comprising >100 exome data.
[a]ClinVar (https://www.ncbi.nlm.nih.gov/clinvar). MT, Mutation Taster (http://www.mutationtaster.org); PolyPhen2: Polymorphism Phenotyping v2 (http://genetics.bwh.harvard.edu/pph2/index.shtml); SIFT, Sorting Tolerant From Intolerant (http://provean.jcvi.org/index.php); HSF, Human Splicing Finder (https://hsf.genomnis.com/home) [b]RWTH Aachen database (http://www.humgen.rwth-aachen.de/index.php), NA, non-available, WT, wild-type

Supplementary Table 3: Demographic, clinical and laboratory Findings of patients with ADPKD

Patient number	Gender	Age at Diagnosis	Consanguinity	Family History	Creatinine at diagnosis (mg/dL)	eGFR at diagnosis (ml/min/1.73 m^2)	Creatinine at last visit (mg/dL)	eGFR at last visit (ml/min/1.73 m^2)	USG Findings
PN1698	M	4 months	-	+	0.31	66.8	0.32	115.6	Increased renal echogenicity, CM cysts
PN1608 II1‡	M	20 days	-	+	0.19	125	0.2	216	CM cysts, cysts in the liver, PF, dilated bile ducts
PN1608 II2‡	M	5 months	-	+	0.58	100	0.58	105	CM cysts
PN1582	F	4 years	+	+	0.36	117	0.5	96	CM cysts
PN1605	M	7.5 years	-	-	0.38	136	0.53	146	Increased renal echogenicity, CM cysts
PN1571	M	2 years	-	+	0.31	165	0.31	165	CM cysts
PN1519	F	11 years	-	+	0.43	136	0.51	127	CM cysts
PN1613	F	6 years	-	+	0.53	93.5	0.39	133	Cortical cysts
PN1533	M	3 months	-	+	0.3	75	0.4	102	Cortical cysts
PN1843-II1‡	M	16 years	-	+	0.57	131	0.67	112	Cortical cysts
PN1843-II2‡	M	3 years 3 months	-	+	0.34	132	0.45	104	Cortical cysts
PN1843-II3‡	F	9.5 years	-	+	0.38	122.8	0.51	113	CM cysts
PN1822-II1‡	F	6 years	-	+	0.4	112.5	0.39	145	CM cysts
PN1822-II2‡	F	8 months	-	+	0.22	104	0.37	135	Cortical cysts
PN1746	M	5 years 5 months	+	-	0.42	128	0.45	145	Increased renal echogenicity, CM cysts, medullary nephrocalcinosis
PN1747	M	9 years 9 months	+	-	0.5	66.3	0.6	86	Increased renal echogenicity, CM cysts, medullary nephrocalcinosis
PN1652	F	5 years 9 months	-	+	0.32	148.4	0.4	132	Renal cysts
PN1794	F	4 years 9 months	-	+	0.3	150	0.38	134.7	Increased renal echogenicity, CM cysts
PN1590-II1*‡	F	1.5 months	+	+	0.9	27.5	0.58	70.4	Increased renal echogenicity, CM cysts
PN1590-II2‡	M	10 years 1 month	+	+	0.5	113.9	0.47	121	Renal cysts
PN1821†	M	2 years 5 months	+	+	4.6	9.4	0.9	77	Increased renal echogenicity, CM cysts
PN1872	M	9 years	-	-	0.6	87.4	0.65	85	Increased renal echogenicity, CM cysts
PN1878	F	12 years 8 months	-	+	0.54	118.5	0.66	102	Cortical cysts, splenomegaly
PN1889	F	9 months	-	+	0.43	122	0.65	82.6	Cortical cysts

PN2124	M	5 years 6 months	-	+	0.37	129	0.46	129	Cortical cysts
PN1711	F	2.5 months	-	+	0.26	90.5	0.45	102	Increased renal echogenicity, cortical cysts
PN1724	F	5 months	+	+	0.5	54	0.43	88.3	Increased renal echogenicity, cortical cysts
PN1743	F	7 years	-	-	0.2	249	0.45	132	CM cysts
PN1915	M	5 years	-	+	0.32	160	0.27	203	Medullar cysts, multiple cysts in the liver
PN1922	M	3 years 2 months	-	+	0.27	151.4	0.35	123.9	Cortical cysts
PN2131	F	6 years 10 months	+	+	0.35	139.2	0.32	152	CM cysts
PN2086	M	8 years	-	-	0.38	152	0.51	136	CM cysts
PN2064	F	3 years 2 months	-	+	0.22	187	0.19	230	CM cysts
PN2042	F	3 years 11 months	-	+	0.3	166	0.57	102	Cortical cysts
PN2201	F	2.5 months	-	-	1.00	19	0.78	52	Increased renal echogenicity, cortical cysts
PN2222	M	12 years 3 months	-	+	0.6	117	0.79	90	CM cysts, splenomegaly
PN2216	M	5 years 4 months	-	-	0.42	101	0.34	151	Cortical cysts
PN2142	F	8 months	-	+	0.39	85	0.2	154	Increased renal echogenicity, CM cysts
PN2283	F	14 years	-	+	0.79	85	0.56	122	Increased renal echogenicity, CM cysts
PN1991*	F	2 months	+	+	0.2	117.7	0.3	101	Increased renal echogenicity, medullar cysts
PN1980	F	2 years	-	+	0.28	140	0.41	151	Increased renal echogenicity, cortical cysts
PN2336	F	4 years 7 months	+	+	0.52	98.4	0.63	97.6	Increased renal echogenicity, CM cysts
PN1668	F	10 months	-	-	0.38	73.9	0.27	113	Increased renal echogenicity, CM cysts
PN1583	M	6 years	-	+	0.41	117	0.55	108	Increased renal echogenicity, medullary nephrocalcinosis
PN1824	F	8 years 2 months	-	+	0.36	153	0.69	98	CM cysts
PN2269-II1‡	F	10 years 5 months	-	+	0.45	126	0.61	102	Increased renal echogenicity, medullary cysts
PN2269-II2‡	F	15 years 4 months	-	+	0.60	110	0.71	93	Medullar cysts, splenomegaly
PN2270	F	15 years	-	+	0.68	151	0.66	99	Increased renal echogenicity, cortical cysts

CM, corticomedullary; F, female; M, male; PF, periportal fibrosis. *Patient with a homozygous variation in *PKD1* †: Patient with the renal transplantation

‡: PN1608 II1 and II2; PN1843 II1, II2 and II3; PN1822 II1 and II2; PN1590 II1 and II2; PN2269 II1 and II2 are siblings.

Supplementary Table 4: Genetic characteristics of the patients with ADPKD

Family-Patient number	*PKD1* variant (predicted aminoacid change)[a]	Reference	ClinVar[c] or *In slico* prediction for previously unpublished variations	Mayo PKDB database[d]
PN1698-II1	Exon 46: c.12682C>T (p.Arg4228*)	Peral (1996) Am J Hum Genet 58: 86 [(11)]	(-)	Pathogenic
PN1608-II1	Exon 23: c.8311G>A (p.Glu2771Lys)	Rossetti (2001) Am J Hum Genet 68: 46 [(12)]	(-)	Likely pathogenic
PN1608-II2	Exon 23: c.8311G>A (p.Glu2771Lys)	Rossetti (2001) Am J Hum Genet 68: 46 PubMed: 11115377 [(12)]	(-)	Likely pathogenic
PN1582-II1	Exon 23: c.8614del (p.Ile2872Serfs*3)	Yu (2011) BMC Med Genet 12, 164 [(13)]	(-)	Pathogenic
PN1605-II1	Exon 29 c.9914_9915delCT (p.Ser3305fs*84)	Neumann (2013) Nephrol Dial Transplant 28: 1472 [(14)]	(-)	Pathogenic
PN1571-II1	Exon 5: c.679C>T (p.Gln227*)	Rossetti (2001) Am J Hum Genet 68: 46 [(12)]	(-)	Pathogenic
PN1519-II1	Exon 42: c.11563_11564delAC (p.Thr3855AlafsTer105)	rs1555445585	ClinVar: Pathogenic	NA
PN1613-II1	Exon 9: c.1839_1842delCAGC (p.Ser614fs*170)	Novel	MT: Disease causing	NA
PN1533-II1	Exon 15: c.5099_5101delCCA (p.Thr1700del)	Novel	MT: Disease causing	NA
PN1843-II1	Exon 43: c.11935C>T (p.Gln3979*)	Hoefele (2010) Nephrol Dial Transplant 26: 2181 [(15)]	(-)	Pathogenic
PN1843-II2	Exon 43: c.11935C>T (p.Gln3979*)	Hoefele (2010) Nephrol Dial Transplant 26: 2181 [(15)]	(-)	Pathogenic
PN1843-II3	Exon 43: c.11935C>T (p.Gln3979*)	Hoefele (2010) Nephrol Dial Transplant 26: 2181 [(15)]	(-)	Pathogenic
PN1822-II1	Exon 23: c.8614del (p.(Ile2872Serfs*3)	Yu (2011) BMC Med Genet 12, 164 [(13)]	(-)	Pathogenic
PN1822-II2	Exon 23: c.8614del (p.(Ile2872Serfs*3)	Yu (2011) BMC Med Genet 12, 164 [(13)]	(-)	Pathogenic
PN1746-II1	Exon 23: c.8464G>A (p.Val2822Met)	Hwang (2016) J Am Soc Nephrol 27: 1861 [(16)]	(-)	VUS
PN1747-II1	Exon10: c.1910C>T (p.Ala637Val)	rs1324355778	ClinVar: Not reported MT: Polymorphism SIFT: Tolarated PolyPhen2: Benign MAF: 0 (ALFA, gnomAD)	Likely benign
PN1652-II1	Exon 15: c.4551C>G (p.Tyr1517*)	Audrézet (2012) Hum Mutat 33: 1239 [(17)]	(-)	Pathogenic
PN1794-II1	Exon 15: c.5860A>T (p.Asn1954Tyr)	Novel	ClinVar: Not reported MT: Disease causing SIFT:Damaging PolyPhen2: Probably damaging	NA
PN1590-II1[b]	Exon 30: c.10033C>T (p.Arg3345Trp) (homozygous)	rs986431548	ClinVar: Not reported MT: Disease causing SIFT: Damaging PolyPhen2: Probably damaging	NA
PN1590-II2	Exon 30: c.10033C>T (p.Arg3345Trp)	rs986431548	ClinVar: Not reported MT: Disease causing	NA

			SIFT: Damaging PolyPhen2: Probably damaging	
PN1821-II1	Exon10: c.1910C>T (p.Ala637Val)	rs1324355778	ClinVar: Not reported MT: Polymorphism; SIFT: Tolarated; PolyPhen2: Benign MAF: 0 (ALFA, gnomAD)	Likely benign
PN1872-II1	Exon18: c.7418G>A (p.Gyl2473Glu)	Novel	ClinVar: Not reported MT: Disease causing SIFT: Deleterious PolyPhen-2: Probably damaging	NA
PN1878-II1	Exon23: c.8447_8448insA (p.Ala2817fs*5)	Novel	ClinVar: Not reported MT: Disease causing MAF: Not reported (ALFA, gnomAD)	NA
PN1889-II1	c.10618+2T>C (splice site)	Audrézet (2012) Hum Mutat 33: 1239 [17]	(-)	Pathogenic
PN2124-II1	Exon 37: c.10842delC (p.Phe3615fs*17)	Novel	ClinVar: Not reported MT: Disease causing MAF: Not reported (ALFA, gnomAD)	NA
PN1711-II1	Exon 12 c.2896C>T (p.Arg966Trp)	Laleye (2012) Genet Couns 23: 435 [18]	(-)	NA
PN1724-II1	Exon 15: c.4639C>T (p.Arg1547Cys)	rs1487713442	ClinVar: Not reported MT: Disease causing SIFT:Damaging PolyPhen-2: Probably damaging MAF: 0 (ALFA), 0.000008 (gnomAD)	NA
PN1743-II1	Exon 15: c.3451dupC (p.Leu1151fs*60)	Novel	ClinVar: Not reported MT: Disease causing MAF: Not reported (ALFA, gnomAD)	NA
PN1915-II1	Exon 44: c.12010C>T(p.Gln4004*)	Gao (2006) Zhonghua Yi Xue Yi Chuan Xue Za Zhi 23: 23 [19]	(-)	Pathogenic
PN1922-II1	Exon 15: c.5014_5015delAG (p.Arg1672fs*98)	rs1555455457	ClinVar: Pathogenic	Pathogenic
PN2131-II1	Exon 38: c.11082C>A (p.Cys3694*)	Mizoguchi (2001) J Hum Genet 46: 511 PubMed: 11558899 [20]	(-)	Pathogenic
PN2086-II1	Exon 46: c.12910T>A (p.*4304Lys) (stop loss)	Novel	ClinVar: Not reported MT: Polymorphism MAF: Not reported (ALFA, gnomAD)	NA
PN2064-II1	Exon 23: c.8311G>A (p.Glu2771Lys)	Rossetti (2001) Am J Hum Genet 68: 46 PubMed: 11115377 [12]	(-)	Likely pathogenic
PN2042-II1	Exon 15: c.5995G>A (p.Gly1999Ser)	Rossetti (2007) J Am Soc Nephrol 18: 2143 [21]	(-)	Likely pathogenic
PN2201-II1	Exon 18: c.7418G>A (p.Gly2473Glu)	Novel	ClinVar: Not reported MT: Disease causing SIFT: Deleterious PolyPhen2: Probably damaging MAF: Not reported (ALFA, gnomAD)	NA
PN2222-II1	Exon 15: c.4306C>T (p.Arg1436*)	Garcia-Gonzalez (2007) Mol Genet Metab 92: 160 [22]	(-)	Pathogenic
PN2216-II1	Exon 29: c.9895T>A (p.Tyr3299Asn)	Novel	ClinVar: Not reported MT: Disease causing SIFT: Damaging	NA

			PolyPhen2: Probably damaging MAF: Not reported (ALFA, gnomAD)	
PN2142-II1	Exon 24: c.8914G>A (p.Asp2972Asn)	rs150189496	ClinVar: Not reported MT: Disease causing SIFT: Damaging PolyPhen2: Probably damaging MAF: 0.00045 (ALFA), 0.000104 (gnomAD)	Likely benign
PN2283-II1	Exon 37: c.11000T>C (p.Leu3667Pro)	Novel	ClinVar: Not reported MT: Disease causing SIFT: Damaging PolyPhen-2: Probably damaging MAF: Not reported (ALFA, gnomAD)	NA
PN1991-II1[b]	Exon 20: c.7852G>A (p.Val2618Met) (homozygous)	rs376969316	ClinVar: Not reported MT: Disease causing SIFT: Damaging PolyPhen2: Probably damaging MAF: 0.00009 (ALFA), 0.000043 (gnomAD)	NA
PN1980-II1	Exon 15: c.5014_5015delA G (p.Arg1672fs*98)	Watnick (1999) Am J Hum Genet 65: 1561 [(23)]	(-)	Pathogenic
PN2336-II1	Exon 39: c.11258G>A (p.Arg3753Gln)	Rossetti (2007) J Am Soc Nephrol 18: 2143 PubMed: 17582161 [(21)]	(-)	Likely pathogenic
	PKD2 variant (predicted aminoacid change)[a]			
PN1668-II1	Exon 8: c.1859G>T (p.Gly620Val)	Novel	ClinVar: Not reported MT: Disease causing SIFT: Damaging PolyPhen-2: Probably damaging MAF: Not reported (ALFA, gnomAD)	NA
PN1583-II1	Exon6: c.1445T>G (p.Phe482Cys)	Dedoussis (2008) Eur J Clin Invest 38: 180 [(24)]	(-)	Likely benign
PN1824-II1	Exon 6: c.1445T>G (p.Phe482Cys)	Dedoussis (2008) Eur J Clin Invest 38: 180 [(24)]	(-)	Likely benign
PN2269-II1	Exon 5: c.1281_1282delAG (p.Tyr429fs*5)	Novel	ClinVar: Not reported MT: Disease causing MAF: Not reported (ALFA, gnomAD)	NA
PN2269-II2	Exon 5: c.1281_1282 delAG (p.Tyr429fs*5)	Novel	ClinVar: Not reported MT: Disease causing MAF: Not reported (ALFA, gnomAD)	NA
PN2270-II1	Exon 6: c.1372C>T (p.Gln458*)	Novel	ClinVar: Not reported MT: Disease causing MAF: Not reported (ALFA, gnomAD)	NA

[a]Variations and predicted aminoacid changes have been named according to the guidelines of the Human Genome Variation Society using Mutalyzer software (https://mutalyzer.nl) of *PKD1* (transcript # NM_001009944.3) or *PKD2* (transcript # NM_000297.4). All but PN1590-II1 and PN1991 are heterozygous. [b]Homozygous *PKD1* variation. Patients with the same family number represent siblings.
[c] ClinVar (https://www.ncbi.nlm.nih.gov/clinvar). [d]https://pkdb.mayo.edu/variants
MAF, minor allele frequency MT, Mutation Taster (http://www.mutationtaster.org); PolyPhen2, Polymorphism Phenotyping v2 (http://genetics.bwh.harvard.edu/pph2/index.shtml); SIFT, Sorting Tolerant From Intolerant (http://provean.jcvi.org/index.php)
ALFA, Allele Frequency Aggregation (https://www.ncbi.nlm.nih.gov/snp/docs/gsr/alfa), gnomAD, The Genome Aggregation Database (https://gnomad.broadinstitute.org); NA, non-available; VUS, Variant of Uncertain Significance (VUS)

Supplementary Table 5: 3-Year and 6-Year renal survival according to clinical and genetic features in the entire study cohort

	Patient number (n)	3 year RS* % (SE)	6 year RS* % (SE)	p value
Variant				
PKHD1	n=21	51.6 (11.1)	32.8 (11.2)	0.001
PKD1	n=42	83.8 (6.2)	74.5 (10.4)	(PKHD1-PKD1: 0.001
PKD2	n=6	100 (-)	100 (-)	PKD1-PKD2: 0.28
				PKHD1-PKD2: 0.02)
Diagnosis				
ADPKD	n=48	86.2 (5.3)	77.6 (9.5)	0.001
ARPKD	n=21	51.6 (11.2)	32.8 (11.1)	
Gender				
Female	n=38	69.4 (7.8)	64.1 (8.8)	0.72
Male	n=31	82.3 (7.4)	52.6 (15.2)	
Hypertension				
Yes	n=22	61.5 (10.8)	26.9 (12.5)	0.002
No	n=47	81.8 (5.9)	81.8 (5.9)	
Growth retardation				
Yes	n=12	50 (14.4)	16.7 (14.4)	0.001
No	n=57	80.4 (5.7)	71.5 (7.8)	
Malnutrition				
Yes	n=19	40.9 (11.5)	0 (0)	0.0001

No	n=50	88.8 (4.8)	79.4 (7.6)	
USG renal echogenicity				
Normal	n=28	95.5 (4.4)	76.4 (17.4)	0.04
Increased	n=32	64.3 (14.6)	64.3 (14.6)	

*GFR<90 ml/dk/1.73 m^2 (RS: Renal survival, SE: Standart error, USG: Ultrasonography)

Supplementary Table 6: 3-Year and 6-Year renal survival according to clinical and genetic features in patients with ARPKD

	Patient number (n)	3 year RS* % (SE)	6 year RS* % (SE)	p value
Age at diagnosis				
<1	n=13	50 (14.4)	33.3 (16.7)	0.62
≥1	n=8	55.6 (16.6)	33.3 (15.7)	
Gender				
Female	n=10	30 (14.5)	20 (12.6)	0.046
Male	n=11	71.6 (14)	47.7 (16.6)	
Hypertension				
Yes	n=13	44 (14.3)	17.6 (11.2)	0.15
No	n=8	62.5 (11.1)	62.5 (11.1)	
Growth retardation				
Yes	n=7	28.6 (17.1)	0 (0)	0.01
No	n=14	64.3 (12.8)	45.9 (14.3)	
Malnutrition				
Yes	n=11	27.3 (13.4)	13.6 (11.7)	0.03
No	n=10	78.8 (13.4)	52.5 (17.6)	

USG renal echogenicity				
Normal	n=4	100 (-)	100 (-)	0.019
Increased	n=17	43.8 (12.4)	18.2 (11)	
Phenotypic presentation				
Renal	n=10	50 (15.8)	40 (15.5)	0.85
Renal+Liver	n=11	53 (15.5)	19.9 (16.3)	
***PKHD1* variant**				
Exon 1-15	n=5	40 (21.9)	0 (0)	
Exon 16-30	n=2	50 (35.4)	50 (35.4)	0.42†
Exon 31-45	n=11	54.5 (15)	34.1 (15)	
Exon 46-67	n=12	64.8 (14.3)	43.2 (15.7)	
Variant type				
Homozygous	n=6	0 (0)	0 (0)	0.0001
Compound heterozygous	n=15	72.2 (11.9)	45.9 (14.4)	
Variant function				
T+	n=3	0 (0)	0 (0)	
T-	n=11	36.4 (14.5)	36.4 (14.5)	0.017**
T+ and **T-**	n=7	100 (-)	50 (20.4)	

(SE: Standard error, T+: Truncating mutation, T-: Non-truncating mutation)

*: eGFR<90 ml/min/1.73 m^2 †: p = 0.42 for Exon 1-15 and 16-30, p = 0.25 for Exon 1-15 and 31-45, p = 0.08 for Exon 1-15 and 46-67, p=0.76 for Exon 16-30 and 31-45, p=0.91 for Exon 16-30 and Exon 46-67, p=0.75 for Exon 31-45 and 46-67.

**: p = 0.103 for T + with T-, p = 0.003 for T + with T + and T-, p = 0.08 for T- with T + and T-

Supplementary Table 7: 3-Year and 6-Year renal survival according to clinical and genetic features in patients with ADPKD

	Patient number (n)	3-year RS* % (SE)	6-year RS* % (SE)	p value
Age at diagnosis				
<2	n=13	59 (17)	59 (17)	0.04
≥2	n=35	94 (3.9)	83 (11)	
Gender				
Female	n=28	84.1 (7.4)	84.1 (7.4)	0.75
Male	n=20	90 (6.7)	45 (32)	
Hypertension				
Yes	n=9	88.9 (10.5)	44.4 (31.9)	0.49
No	n=39	85.5 (6.1)	85.5 (6.1)	
Growth retardation				
Yes	n=5	80 (17.9)	40 (29.7)	0.15
No	n=43	86.8 (5.6)	86.8 (5.6)	
Malnutrition				
Yes	n=8	60 (18.2)	0 (0)	0.002
No	n=40	92 (4.4)	92 (4.4)	
USG renal echogenicity				
Normal	n=34	95.5 (4.4)	76.4 (17.4)	0.04
Increased	n=12	64.3 (14.6)	64.3 (14.6)	

***PKD1* variant**				
Exon 1-15	n=14	83.6 (10.8)	62.7 (19.8)	
Exon 16-30	n=16	81.3 (9.8)	81.3 (9.8)	0.73†
Exon 31-46	n=12	88.9 (10.5)	88.9 (10.5)	
Variant function (PKD1)				
T+	n=23	94.4 (5.4)	94.4 (5.4)	0.03
T-	n=19	71.1 (11.3)	59.2 (14.3)	
Variant function (PKD2)				
T+	n=3	100 (-)	-	
T-	n=3	100 (-)	-	

(SE: Standard error, T+: Truncating mutation, T-: Non-truncating mutation)

*: eGFR<90 ml/min/1.73 $m^{2.}$ †: PKD1 p=0.95 for exon 1-15 and 16-30, p=0.59 for exon 1-15 and 31-46, p=0.54 for exon 16-30 and 31-46.

Supplementary Table 8: Comparison of Clinical and Laboratory Findings by Variant Function in PKHD1

	T+ (n=3)	**T- (n=11)**	**T+ and T- (n=7)**	**p value**
Diagnosis age				
<1 year	3 (100)	7 (63.6)	3 (42.9)	0.058
≥1 year	0 (0)	4 (36.4)	4 (57.1)	
Growth retardation	2 (66.7)	3 (27.3)	2 (28.6)	0.41
Malnutrition	3 (100)	6 (54.5)	2 (28.6)	0.11
eGFR at diagnosis	19.5 ± 12	73.6 ± 34.9	88.6 ± 48.9	0.055
Follow-up eGFR	5.2 ± 4.3	75.3 ± 18.3	94.7 ± 34.3	0.02

(T+: Truncating mutation, T-: Non-truncating mutation)

References Supplementary Data

1. Melchionda S, Palladino T, Castellana S, Giordano M, Benetti E, De Bonis P, et al. Expanding the mutation spectrum in 130 probands with ARPKD: identification of 62 novel PKHD1 mutations by sanger sequencing and MLPA analysis. Journal of human genetics. 2016;61(9):811-21.
2. Rossetti S, Torra R, Coto E, Consugar M, Kubly V, Málaga S, et al. A complete mutation screen of PKHD1 in autosomal-recessive polycystic kidney disease (ARPKD) pedigrees. Kidney international. 2003;64(2):391-403.
3. Furu L, Onuchic LF, Gharavi A, Hou X, Esquivel EL, Nagasawa Y, et al. Milder presentation of recessive polycystic kidney disease requires presence of amino acid substitution mutations. Journal of the American Society of Nephrology : JASN. 2003;14(8):2004-14.
4. Onuchic LF, Furu L, Nagasawa Y, Hou X, Eggermann T, Ren Z, et al. PKHD1, the polycystic kidney and hepatic disease 1 gene, encodes a novel large protein containing multiple immunoglobulin-like plexin-transcription-factor domains and parallel beta-helix 1 repeats. American journal of human genetics. 2002;70(5):1305-17.
5. Bergmann C, Senderek J, Windelen E, Küpper F, Middeldorf I, Schneider F, et al. Clinical consequences of PKHD1 mutations in 164 patients with autosomal-recessive polycystic kidney disease (ARPKD). Kidney international. 2005;67(3):829-48.
6. Gunay-Aygun M, Tuchman M, Font-Montgomery E, Lukose L, Edwards H, Garcia A, et al. PKHD1 sequence variations in 78 children and adults with autosomal recessive polycystic kidney disease and congenital hepatic fibrosis. Molecular genetics and metabolism. 2010;99(2):160-73.
7. Liang N, Jiang X, Zeng L, Li Z, Liang D, Wu L. 28 novel mutations identified from 33 Chinese patients with cilia-related kidney disorders Clim Chim Acta 2020; 501: 207-215.
8. Denamur E, Delezoide AL, Alberti C, Bourillon A, Gubler MC, Bouvier R, et al. Genotype-phenotype correlations in fetuses and neonates with autosomal recessive polycystic kidney disease. Kidney international. 2010;77(4):350-8.
9. Ward CJ, Hogan MC, Rossetti S, Walker D, Sneddon T, Wang X, et al. The gene mutated in autosomal recessive polycystic kidney disease encodes a large, receptor-like protein. Nature genetics. 2002;30(3):259-69.
10. Brinkert F, Lehnhardt A, Montoya C, Helmke K, Schaefer H, Fischer L, et al. Combined liver-kidney transplantation for children with autosomal recessive polycystic kidney disease (ARPKD): indication and outcome. Transplant international : official journal of the European Society for Organ Transplantation. 2013;26(6):640-50.
11. Peral B, San Millán JL, Ong AC, Gamble V, Ward CJ, Strong C, et al. Screening the 3' region of the polycystic kidney disease 1 (PKD1) gene reveals six novel mutations. American journal of human genetics. 1996;58(1):86-96.
12. Rossetti S, Strmecki L, Gamble V, Burton S, Sneddon V, Peral B, et al. Mutation analysis of the entire PKD1 gene: genetic and diagnostic implications. American journal of human genetics. 2001;68(1):46-63.
13. Yu C, Yang Y, Zou L, Hu Z, Li J, Liu Y, et al. Identification of novel mutations in Chinese Hans with autosomal dominant polycystic kidney disease. BMC medical genetics. 2011;12:164.

14. Neumann HP, Jilg C, Bacher J, Nabulsi Z, Malinoc A, Hummel B, et al. Epidemiology of autosomal-dominant polycystic kidney disease: an in-depth clinical study for south-western Germany. Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2013;28(6):1472-87.
15. Hoefele J, Mayer K, Scholz M, Klein HG. Novel PKD1 and PKD2 mutations in autosomal dominant polycystic kidney disease (ADPKD). Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2011;26(7):2181-8.
16. Hwang YH, Conklin J, Chan W, Roslin NM, Liu J, He N, et al. Refining Genotype-Phenotype Correlation in Autosomal Dominant Polycystic Kidney Disease. Journal of the American Society of Nephrology : JASN. 2016;27(6):1861-8.
17. Audrézet MP, Cornec-Le Gall E, Chen JM, Redon S, Quéré I, Creff J, et al. Autosomal dominant polycystic kidney disease: comprehensive mutation analysis of PKD1 and PKD2 in 700 unrelated patients. Human mutation. 2012;33(8):1239-50.
18. Laleye A, Awede B, Agboton B, Azonbakin S, Biaou O, Sagbo G, et al. Autosomal dominant polycystic kidney disease in University Clinic of Nephrology and Haemodialysis of Cotonou: clinical and genetical findings. Genetic counseling (Geneva, Switzerland). 2012;23(4):435-45.
19. Gao DX, Cao QW, Ding KJ, Zhao YR, Wang LC, Niu ZH, et al. [An analysis for the phenotype and genotype of autosomal dominant polycystic kidney disease from two Chinese families]. Zhonghua yi xue yi chuan xue za zhi = Zhonghua yixue yichuanxue zazhi = Chinese journal of medical genetics. 2006;23(1):23-6.
20. Mizoguchi M, Tamura T, Yamaki A, Higashihara E, Shimizu Y. Mutations of the PKD1 gene among Japanese autosomal dominant polycystic kidney disease patients, including one heterozygous mutation identified in members of the same family. Journal of human genetics. 2001;46(9):511-7.
21. Rossetti S, Consugar MB, Chapman AB, Torres VE, Guay-Woodford LM, Grantham JJ, et al. Comprehensive molecular diagnostics in autosomal dominant polycystic kidney disease. Journal of the American Society of Nephrology : JASN. 2007;18(7):2143-60.
22. Garcia-Gonzalez MA, Jones JG, Allen SK, Palatucci CM, Batish SD, Seltzer WK, et al. Evaluating the clinical utility of a molecular genetic test for polycystic kidney disease. Molecular genetics and metabolism. 2007;92(1-2):160-7.
23. Watnick T, Phakdeekitcharoen B, Johnson A, Gandolph M, Wang M, Briefel G, et al. Mutation detection of PKD1 identifies a novel mutation common to three families with aneurysms and/or very-early-onset disease. American journal of human genetics. 1999;65(6):1561-71.
24. Dedoussis GV, Luo Y, Starremans P, Rossetti S, Ramos AJ, Cantiello HF, et al. Co-inheritance of a PKD1 mutation and homozygous PKD2 variant: a potential modifier in autosomal dominant polycystic kidney disease. European journal of clinical investigation. 2008;38(3):180-90.