10.5152/turkjnephrol.2019.3240

Original Article

Turkish Journal of Nephrology

Cystic Renal Disease in Children: A Broad Spectrum from Simple Cyst to End Stage Renal Failure

Neslihan Çiçek, Nurdan Yıldız, Tuğba Nur Daşar, İbrahim Gökce, Harika Alpay

Division of Pediatric Nephrology, Marmara University School of Medicine, İstanbul, Turkey

Abstract

Objective: Renal cystic diseases consist of a broad spectrum of hereditary or acquired conditions that may lead to end stage renal disease. We aimed to evaluate our patients diagnosed as renal cystic disease in terms of their diagnosis, demographic findings and clinical follow-up.

Materials and Methods: The patients followed between 1993-2015 in our pediatric nephrology outpatient department with renal cystic diseases were evaluated retrospectively.

Results: In 237 patients, 110 (46.41%) were female, 127 (53.59%) were male. One hundred-eight (45.56%) patients were diagnosed antenatally, the mean age at diagnosis was 7.23±4.72 (0-17) years in 129 patients. The diagnosis were simple-cyst in 36 (15.18%), multicystic displastic kidney disease in 112 (47.25%), autosomal dominant polycystic kidney disease in 56 (23.62%), autosomal recessive polycystic kidney disease in 22 (9.28%), cyst hydatic in three (1.26%), Joubert sydrome in two, nephronophthisis in one, tuberosclerosis in two, Bardet-Biedl syndrome in three patients. Five patients (2.1%) died and ten (4.21%) patients progressed to chronic kidney injury. Proteinuria was found in 15 (6.32 %) and hypertension in 10 (4.21%) patients.

Conclusion: Renal cystic disease is an important group that can lead to proteinuria, hypertension and end stage kidney failure. Periodic follow-up is important in these patients to avoid and treat the complications early and properly.

Keywords: Renal cyst, kidney failure, proteinuria, hypertension

Corresponding Author: Neslihan Çiçek ✉ drneslihancicek@yahoo.com

Received: 22.02.2018 **Accepted:** 04.02.2019

Presented in: This study was presented at the 3rd Marmara Pediatrics Congress, 18-20 February 2016, İstanbul, Turkey.

Cite this article as: Çiçek N, Yıldız N, Daşar TN, Gökce İ, Alpay H. Cystic Renal Disease in Children: A Broad Spectrum from Simple Cyst to End Stage Renal Failure. Turk J Nephrol 2019; 28(4): 239-43.

INTRODUCTION

Renal cyst formation can be seen in different kidney diseases. While most of these diseases are genetically transmitted, some of them are developmental or acquired. Renal cysts may be a part of a syndrome or may be accompanied by extra-renal symptoms. In genetically inherited cystic kidney diseases, defects in the epithelial cilia structure or function of the kidney have been implicated in cyst formation. While earlier kidney cysts have been classified according to their morphological features, in the recent years, clinical, radiological, and genetic characteristics are considered during classification. In simple cysts, the mechanism of cyst formation is not fully understood (1, 2).

While kidney cysts in children can be simple cortical cysts, they may also include a large group of diseases that can cause hypertension, proteinuria, and chronic kidney disease (CKD). Therefore, early diagnosis of cystic kidney diseases is very important to prevent complications and protect renal functions.

This study aimed to evaluate the demographic characteristics, diagnosis, and follow-up results of patients with renal cysts in our pediatric nephrology clinic.

MATERIALS AND METHODS

The records of 237 patients who were followed up for cystic kidney disease between 1998 and 2015 were retrospectively reviewed. Family history, comorbid diseases, physical examination findings, complete urinalysis, protein excretion in 24-h urine, serum BUN, creatinine, electrolytes, ALT and AST levels, and antenatal and/or postnatal radiological examination results were recorded. The diagnosis of simple cysts was made by ultrasonography (USG), and of multicystic dysplastic kidney (MCDK) by the presence of cysts in USG and the absence of renal function in the same kidney via dimercaptosuccinic acid (DMSA) scintigraphy. Zerres criteria were used as the diagnostic criteria for autosomal recessive polycystic kidney disease (ADPKD) (3). In the diagnosis of autosomal dominant polycystic kidney disease (ADPKD), the presence of bilateral large kidneys and cysts, extra-renal organ involvement, and family history were evaluated. The diagnosis of nephronophthisis was made according to clinical, laboratory, pathological, and radiological findings (4).

The diagnosis of hypertension was made when the blood pressure measurements performed three times using the appropriate cuff with the oscillometric method in the policlinic controls were above the 95th percentile according to age, sex, and height (5).

Proteinuria was defined as a protein excretion of 4 mg/m^2/h in 24-h urine or a protein/creatinine ratio of more than 0.2 in spot urine. Proteinurine 4-40 mg/m^2/h or protein/creatinine ratio of 0.2-2 levels was accepted as nephritic, while ≥40 mg/m^2/h or protein/creatinine ratio ≥2 was accepted as nephrotic level proteinuria.

Estimated glomerulofiltration rate (eGFR) was calculated via the Schwartz formula using patient height and serum creatinine values (6). Ethics Committee approval was received for this study from the Ethics Committee of Marmara University School of Medicine (approval no: 09.2016.240). Informed consent is not necessary due to the retrospective nature of this study.

RESULTS

Of the 237 patients with renal cysts under observation, 110 were female (46.41%) and 127 were male (53.9%). While 108 patients (45.56%) had antenatal diagnosis, the average age of the remaining 129 patients was 7.23±4.72 (0-17) years, and the average follow-up period of all patients was 4.41±3.76 (0-17.7) years. When the patients were examined according to their diagnoses, 36 (15.18%) were diagnosed with simple cysts; 112 (47.25%) with MCDK; 56 (23.62%) with ADPCKD; 22 (9.28%) with ARPCKD; 3 (1.26%) with hydatid cyst; 3 nephronophthisis, 2 of which were Joubert syndrome; 2 with tuberous sclerosis; and 3 with Bardet–Biedl syndrome (Table 1).

There was a family history of renal cyst in 63 patients (26.58%). Of these patients, 45 (71.42%) were followed with the diagnosis of ADPKD, 6 (9.52%) of MCDK, 10 (15.87%) of simple cyst, and 2 (3.17%) of nephronophysis.

Nine patients (40.9%) with ARPCKD and 90 patients (80.35%) with MCDK had prenatal pre-diagnosis (Table 1).

Hypertension was detected in ten patients (4.21%). Hypertension was most commonly seen in our patients with ARPCKD and nephronophthisis, and it was detected in only 1 of 112 patients with MCDK. Hypertension was not observed in any of the patients with simple cysts. Proteinuria was detected in 15 patients (6.32%), including nephritic level in 12 patients and nephrotic level in 3 patients. Proteinuria and hypertension rates according to the diagnoses of the patients are shown in the Table 1.

Table 1. The characteristics of the patients with cystic kidney disease

Diagnosis	Number	Family History n (%)	Antenatal Diagnosis n (%)	Hypertension n (%)	Proteinuria n (%)	CKD n (%)	Death n (%)
ADPKD	56	45 (80.35%)	6 (10.71%)	1 (1.78%)	6 (10.71%)		
ADPKD	22	-	9 (40.9%)	5 (22.72%)	2 (9%)	6 (27.27%)	3 (13.63%)
MCDK	112	6 (5.35%)	90 (80.4%)	1 (0.89%)	3 (2.7%)	1* (0.89%)	2# (1.78%)
Simple cyst	36	10 (27.7%)	3 (8.33%)		2 ¥ (5.55%)		
Nephronophthisis (Joubert syndrome)	3	2 (66.66%)		2 (66.66%)		2 (66.66%)	
Tuberous sclerosis	2						
Bardet–Biedl syndrome	3			1 (33.33%)		1 (33.33%)	
Hydatid cyst	3						
Total	237						

ADPCKD: Autosomal dominant polycystic kidney disease; ARPCKD: Autosomal recessive polycystic kidney disease; MCDK: Multicystic dysplastic kidney
*contralateral kidney hypodysplastic, # ex for non-renal reasons, ¥ unilateral renal agenesis

Proteinuria was detected in approximately 10% of children with ADPCKD and ARPCKD. Proteinuria was seen in two patients (5.55%) with simple cyst but additional pathologies were detected in both cases (Table 1).

Ten patients (4.21%) had CKD due to cystic kidney disease. Six of these patients were diagnosed with ARPCKD, one with MCDK, two with nephronophthisis, and one with Bardet–Biedl syndrome. While CKD developed during the first decade of life in all the patients with ARPCKD, three of them entered end-stage renal disease (ESRD) and underwent peritoneal dialysis (PD). The contralateral kidney of the patient with MCDK was hypodysplastic. In all patients with ADPCKD, eGFR was within normal limits. Five patients (2.10%), two of whom had MCDK and three had ARPCKD, died during follow-up. While one of the two patients diagnosed with MCDK had comorbid adrenal insufficiency, esophageal atresia, anal atresia, the other patient had hydroureteronephrosis in the contralateral kidney and congenital heart disease. Both patients died due to extra-renal causes.

Bilateral nephrectomy was performed in a patient with ARPCKD at the age of 36 days due to respiratory problems, and PD was successfully performed; however, the patient died at the age of 10 months due to sepsis and lung complications. Bilateral nephrectomy was performed in one patient because of respiratory problems and the presence of large kidneys. Afterwards, the patient's body weight reached 7 kg, and she underwent renal transplantation from a live donor at the age of 16 months. The patient is still being followed up with normal graft function.

Hepatic fibrous liver was detected in three of the patients (13.63%) with ARPCKD.

Among the patients with MCDK, MCDK was detected on the right in 52 patients (46.43%) and on the left in 60 patients (53.57%). Ninety-eight patients (87.5%) underwent voiding cystourethrography (VCUG); vesicoureteral reflux (VUR) was detected in 19 (16.96%) patients where 15 patients (13.39%) had VUR in the contralateral kidney, two patients (1.78%) had VUR in the MCDK and two patients (1.78%) had bilateral VUR. Nine patients (8%) underwent nephrectomy. In 86 patients (76.8%), renal atrophy was observed on USG images.

Three patients were diagnosed as juvenile nephronophthisis syndrome. One of these patients was 12-year-old male with CKD, and the diagnosis was confirmed by renal biopsy. Two patients were siblings followed with the diagnosis of the Joubert syndrome. The older sister is a 10-year-old girl who has been under PD treatment for five years, and her 3-year-old brother is still followed up with normal eGFR.

Bilateral cysts in the kidneys were detected in three patients with the Bardet–Biedl syndrome. Two patients were followed up with normal renal function, while one patient had been followed under PD treatment for five years.

Bilateral renal cysts were detected in two patients with tuberous sclerosis, and renal functions are still within normal limits. The cysts of 36 patients who had simple cysts were unilateral except one. Ten patients (27.77%) had a family history of simple cyst. Two patients with proteinuria had unilateral agenesis, and one of them had hypodysplasia in the contralateral kidney and CKD developed during follow-up. The patient is still being followed up under hemodialysis treatment. Proteinuria of the second patient with renal agenesis is monitored under control with angiotensin converting enzyme therapy.

The renal hydatid cysts were detected in three patients (1.1%). The patients were successfully treated with mebendazole treatment and cyst resection.

DISCUSSION

Cystic kidney disease includes a large group of inherited or acquired diseases that can lead to ESRD. In our study, a high number of patients with renal cysts in our department were evaluated to draw attention to cystic kidney diseases in our country and to emphasize the importance of early diagnosis and treatment.

While ADPKD is generally an adult disease, ADPKD is diagnosed in infancy. With the routine use of antenatal ultrasonography, patients with ARPCKD can be frequently detected in the prenatal period. In our study, 40.9% of the patients with ARPCKD were pre-diagnosed. The prognosis is more severe, and the survival is shorter in patients with ARPCKD than in patients with ADPCKD. ARPCKD should be monitored for CKD starting from the first years. In these patients, kidneys increases in size, as well as lung hypoplasia, may cause respiratory problems in the postnatal period. In this case, PD treatment with unilateral and/or bilateral nephrectomy may be the treatment option to keep the patient alive (3,7). In our case series, two patients with ARPCKD underwent bilateral nephrectomy due to respiratory distress, and PD and hemodialysis treatments were applied. While one patient was lost, the second patient underwent successful live donor kidney transplantation after PD and hemodialysis treatments. All patients with ADPCKD had normal eGFR and did not develop CKD at an early age.

Multicystic dysplastic kidney disease is a cystic kidney disease whose hereditary transmission is not fully understood. In our case series, the most common renal cysts were MCDK, and the rate of antenatal diagnosis of the patients was high. In children with MCDK, different urinary tract abnormalities may accompany. Among these, VUR is the most common one (8). Unilateral VUR accompanied, mostly to the contralateral kidney, in 19.4% of our patients. In addition, one patient with hypodysplasia of the contralateral kidney developed CKD. Therefore, clinical and ultrasonographic findings should be carefully evaluated in children with MCDK, and further examination of VUR should be considered when necessary. Detection of concomitant urinary system abnormalities in patients with MCDK is very important

to prevent or slow the development of CKD. Routine nephrectomy in MCDK is not recommended except for limited indications such as hypertension, persistent infection, and mass effect (8, 9). Our patients who have undergone nephrectomy mostly belong to the year 2000 and do not undergo routine nephrectomy in our center.

Renal cysts may accompany some congenital syndromes, and ESRD may develop. Three patients were diagnosed with Bardet–Biedl syndrome, three with nephronophthisis, and three with tuberous sclerosis. ESRD developed in one patient with Bardet–Biedl syndrome and in two of the three patients with nephronophthisis. Renal lesions including cysts and angiomyolipomas can be seen in approximately 40% of patients with tuberous sclerosis (10, 11). Renal cysts in our patients were also bilateral and renal functions were within normal limits.

A different cause of cyst in the kidney is hydatid cyst. Renal involvement in hydatid cyst is seen in only 2%-4% of cases (12, 13). Three patients admitted from Eastern and Southeastern Anatolian countryside were diagnosed with hydatid cyst in the kidney. Hydatid cyst should be kept in mind in the differential diagnosis especially in patients presenting from endemic region.

Simple kidney cysts are the most common acquired renal cysts and are rarely seen in children. Cysts can be single or multiple that increase with age. The diagnosis is made by USG (14). There was a family history of simple cyst in 10 of 36 patients who were followed up with a simple cyst diagnosis. However, because of the simple cyst in the family, the number of cysts should be monitored in the long term, and their diagnosis should be reviewed in time.

Among our patients, hypertension was most commonly seen in patients with ARPCKD and nephronophysis, while hypertension was found to be low in patients with MCDK. The patients with simple cysts were considered not at risk for hypertension unless there was any additional concomitant factor.

Proteinuria was found in approximately 10% of our patients with ARPCKD and ADPCKD and 2.7% of patients with MCDK. Proteinuria was not detected in any patient with simple renal cyst except two patients who had renal agenesis and hypodysplasia. It was considered that patients with simple renal cyst were not at risk for proteinuria and CKD unless there was concomitant renal anomaly. The children with hereditary cystic kidney disease and MCDK should be monitored for proteinuria and CKD in the long term.

In our study, because of the retrospective evaluation of the clinical and radiological findings of the patients who were referred due to the detection of renal cysts on USG, they were shown to have differences in terms of occurrence mechanisms, clinical findings, prognosis, and follow-up characteristics. For this reason, the presence of cysts in the kidney should be well evaluated, and it should be known that under the presence of a single cyst, important diseases may arise.

To confirm the diagnosis of cystic kidney disease, genetic, clinical, morphological, and radiological features of the patients should be evaluated together. Ultrasonography is a reliable and good radiological method in the diagnosis and follow-up of renal cysts (14). Genetic analysis opportunities in our country, especially in recent years, can be reached more easily. For this reason, genetic analysis of our patients could not be performed except for a small number of PCKD. However, the clinical and radiological evaluations were sufficient in most patients for the diagnosis of our patients.

CONCLUSION

We believe that simple cysts, which are observed in abdominal and/or urinary system USGs performed for different reasons, and which have normal laboratory findings and no additional urinary anomalies, can be closely monitored by pediatric health and diseases specialists. This is important for patients with limited opportunities for access to pediatric nephrology or pediatric urology. However, it should be kept in mind that these patients should be efficiently evaluated in the beginning in terms of accompanying renal anomalies, syndromic diseases, hypertension, proteinuria, and renal functions.

The early diagnosis of the patients, early and effective treatment of hypertension, and proteinuria are important in slowing the progression to CKD. Dialysis and transplantation are the main treatment modalities in patients with CKD.

Ethics Committee Approval: Ethics Committee approval was received for this study from the Ethics Committee of Marmara University School of Medicine (approval no: 09.2016.240)

Informed Consent: Informed consent is not necessary due to the retrospective nature of this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – N.Ç, N.Y., H.A.; Design – N.Ç, I.G, H.A.; Supervision - NY, HA; Resource – No; Materials – T.D., N.Ç.; Data Collection and/or Processing – T.D., N.Ç.; Analysis and/or Interpretation – N.Y., İ.G., H.A.; Literature Search – N.Y., N.Ç., İ.G.; Writing – N.Ç., N.Y.; Critical Reviews – N.Ç., N.Y., T.D., İ.G., H.A.

Conflict of Interest: The authors have no conflict of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Greenbaum LA, Avner ED. Cystic kidney disease. Kher KK, Schnaper HW, Makker SP (Ed); Clinical Pediatric Nephrology. Informa UK Ltd., London 2007; p.261-9. [CrossRef]

2. Dell KM. The role of cilia in the pathogenesis of cystic kidney disease. Curr Opin Pediatr 2015; 27: 212-8. [CrossRef]
3. Zerres K, Rudnik-Schoneborn S, Deget F, Holtkamp U, Brodehl J, Geisert J, et al. Autosomal recessive polycystic kidney disease in 115 children: clinical presentation, course and influence of gender. Acta Paediatr 1996; 85: 437-45. [CrossRef]
4. Wolf MTF, Hildebrant F. Nephronophthisis. Pediatr Nephrol 2011; 26: 181-94. [CrossRef]
5. Flynn JT, Kaelber DC, Baker-Smith CM, Blowey D, Carroll AE, Daniels SR, et al. Clinical Practice Guideline for Screening and Management of High Blood Pressure in Children and Adolescents. Pediatrics 2017; 140: pii: e20171904. [CrossRef]
6. Schwartz GJ, Work DF. Measurement and estimation of GFR in children and adolescents. Clin J Am Soc Nephrol 2009; 4: 1832-43. [CrossRef]
7. William E, Sweeney J, Avner ED. Diagnosis and management of childhood polycystic kidney disease. Pediatric Nephrol 2011; 26: 675-92. [CrossRef]
8. Cardona-Grau D, Kogan BA. Update on Multicystic Dysplastic Kidney. Curr Urol Rep 2015; 16: 67. [CrossRef]
9. Kuwertz-Broeking E, Brinkmann OA, Von Lengerke HJ, Sciuk J, Fruend S, Bulla M, et al. Unilateral multicystic dysplastic kidney: experience in children. BJU Int 2004; 93: 388-92. [CrossRef]
10. Ewalt DH, Sheffield E, Sparagana SP, Delgado MR, Roach ES. Renal lesion growth in children with tuberoussclerosis complex. J Urol 1998; 160: 141-5. [CrossRef]
11. Robert A, Leroy V, Riquet A, Gogneaux L, Boutry N, Avni FE. Renal involvement in tuberoussclerosis complex with emphasis on cystic lesions. Radiol Med 2015; 121: 402-8. [CrossRef]
12. Blanton R. Echinococosis. Kliegman RM, Stanton BF, St. Geme JW, Schor NF, Behrman RE (eds); Nelson Textbook of Pediatrics 19th edition. Philadelphia: Elsevier Saunders; 2011: p.1237-9.
13. Amrani A, Zerhouni H, Benabdallah FF, Belkacem R, Outarahout O. Renal hydatid cyst in children: report of six cases. Ann Urol 2003; 37: 8-12. [CrossRef]
14. Bulas D, Markle B, Shalaby-Rana E. Diagnostic imaging of the urinary tract. Kher KK, Schnaper HW, Makker SP (Ed); Clinical Pediatric Nephrology. Informa UK Ltd., London 2007: p.95-109. [CrossRef]