CHAPTER 88
Cystic Diseases of the Kidney

Osarumwense David Osifo
Edward Hannon

Introduction

Cystic diseases of the kidney are common lesions worldwide.[1–5] They are broadly divided into genetic and nongenetic cysts. A renal cyst is a fluid-filled sac arising from dilatation in any part of the nephrons or collecting ducts. The cysts may eventually separate from the nephrons or ducts and continue to enlarge. Although most are simple cysts, about one-third of people older than 50 years of age are said to have renal cysts.[1–3] Depending on the type, symptoms can occur at any age, and many cases may manifest symptoms in utero. Undiagnosed or untreated cases ultimately progress to end-stage renal disease (ESRD) and death. The outcome of the disease varies between developed and developing countries, due mainly to late presentation, lack of facilities required for prompt diagnosis, and a lack of facilities and manpower required for intrauterine interventions in developing countries, especially in children who manifest symptoms in utero.[3] Table 88.1 shows the classifications of cystic diseases of the kidney. This chapter discusses the common types, which include:

- multicystic kidney or multicystic dysplastic kidney (MCDK);
- autosomal dominant polycystic kidney disease (ADPKD); and
- autosomal recessive polycystic kidney disease (ARPKD).

Table 88.1: Classification of cystic diseases of the kidney.

Nongenetic	Genetic
Acquired disorders	***Autosomal dominant***
Simple renal cysts (solitary or multiple)	Autosomal dominant polycystic kidney disease*
Cysts of the renal sinus (or peripelvic lymphagiectasis)	Tuberous sclerosis complex
Acquired cystic kidney disease (in patients with chronic renal impairment)	von Hippel-Lindau disease
Multilocular cysts (or multilocular cystic nephroma)	Medullary cystic disease
Hypokalemia-related cysts	Glomerulocystic disease
Developmental disorders	***Autosomal recessive***
Medullary sponge kidney	Autosomal recessive polycystic kidney disease*
Multicystic dysplastic or multicystic kidney*	Nephronophthisis
Pyelocalyceal cysts	***X-linked***
	Orofaciodigital syndrome type 1

*Common type of cystic disease of the kidney

Source: Pirson Y, Chauveau D, Grunfeld JP. Autosomal dominant polycystic kidney disease. In: Davison AM, Cameron JS, Grunfeld JP, eds. Oxford Textbook of Clinical Nephrology. Oxford University Press, 1998, Pp 2393-2415.

Demographics

Incidence

No conclusive African figures on cystic kidney disease are available due especially to a poor database. There is, however, geographical variation in incidence as well as variation in incidence among the subtypes.[2,3] Available literature[1–6] from more developed countries suggests that:

- Multicystic kidney or MCDK has an incidence of 1 per 1,000–4,000 live births.
- ADPKD has an incidence of 1 per 400–1,000 among whites and accounts for 8–10% of all cases of ESRD.
- ARPKD has an incidence of 1 per 6,000–55,000 live births, with a heterozygous carrier frequency of 1 per 70.

Race

ADPKD is found worldwide in all races and ethnic groups, whereas acquired cystic renal disease is reported to be most common in white and African American men.

Gender

MCDK is more common in males than females, and symptomatic progression of ADPKD appears to be more rapid in men.

Age

ADPKD has a bimodal distribution of onset. It usually presents in infancy or childhood and adulthood, with rare occurrence in middle age. ARPKD often presents in infancy, childhood, or adolescence. In contrast, simple cysts are very rare in children but increase in frequency with age.

Aetiology/Pathophysiology

Generally, cysts develop due to increased tubular epithelial proliferation.[1–3] Many of the cysts may detach from the parent tubule after growing to a few millimeters in size.

Multicystic kidney is usually a sporadic, nonsyndromal, congenital anomaly. It occurs as a result of ureteropelvic dysplasia or atresia that results in an enlarged kidney and the formation of cysts of varying sizes that do not communicate. There is no demonstrable pelvis and calyces, but microscopic examination shows rudimentary lobes with no corticomedullary differentiation.

ADPKD occurs due to mutations in the genes PKD1 and PKD2, which encode polycystin proteins. It may require a second "hit" to result in ADPKD later in life.[5]

ARPKD occurs following mutations in PKHD1, a large gene that encodes fibrocystin/polyductin, which plays a critical role in collecting-tubule and biliary development.

Clinical Presentation

Clinical presentation depends on the type of cystic disease.[1–3]

Multicystic kidney is the second most common cause of a flank mass in the newborn. The diagnosis may be made in utero by ultrasonography (US) or palpation of an abdominal mass during examination for other conditions in neonates. Clinical symptoms are rarely seen unless it is

complicated by infection. The contralateral kidney is usually normal but may be absent, hydronephrotic, ectopic, refluxing, or dysplastic.

Patients with ADPKD usually present in the fourth decade of life with flank pain or intermittent haematuria. Renal size increases exponentially with an equal growth rate in both kidneys over time due to the increase in cyst volume. The disease course varies significantly among affected individuals. Hepatic cysts are the most common extrarenal manifestation that increases with age. Recent reports[1,2] revealed an incidence of 20% and 75%, respectively, at the third and sixth decades of life. Patients with PKD1 genoytpe appear to develop more rapid disease progression.

ARPKD affects renal and hepatic development with varying degrees of organ involvement with age. It may be a cause of neonatal death due to pulmonary disease resulting from nephromegaly and oligohydraminios. Symptoms in infants include hypertension, diminished urine concentrating ability, and renal insufficiency. Almost half of affected individuals develop ESRD in the first decade of life. Occurrences in children between 4 and 8 years of age are predominantly hepatic involvement with kidneys often less severely affected.

Investigation

Cystic diseases of the kidney are usually diagnosed by imaging investigations, such as the following:

- *Ultrasonography:* US is a common investigation with high diagnostic accuracy. It is used for both diagnosis and follow-up of the patient. A US scan shows the cystic nature of the mass, but critical for the diagnosis of a renal cyst is the loss of internal echoes; rounded outline; sharply demarcated, smooth walls; and bright posterior wall echo.[4,6] Multiple cysts show similar features that are separated by septa with a lobulated appearance (Figure 88.1).
- *Intravenous urography:* Intravenous urography may show a nonfunctioning kidney in ESRD, loss of tubular connection in MCDK, and multiple cystic collections in polycystic kidney disease.[3,5]
- *Computerised tomography (CT) scan:* A CT scan gives better resolution than US or intravenous urography, which is especially useful when the US finding is not conclusive.
- *Magnetic resonance imaging (MRI):* MRI has a very high diagnostic accuracy and is quite useful for follow-up, but its nonavailability is a major drawback to its use in developing countries.
- *Nonimaging investigations:* Other investigations include genetic testing for polycystic kidney disease, serum electrolytes, urea and creatinines, and urine for microscopy culture and sensitivity.

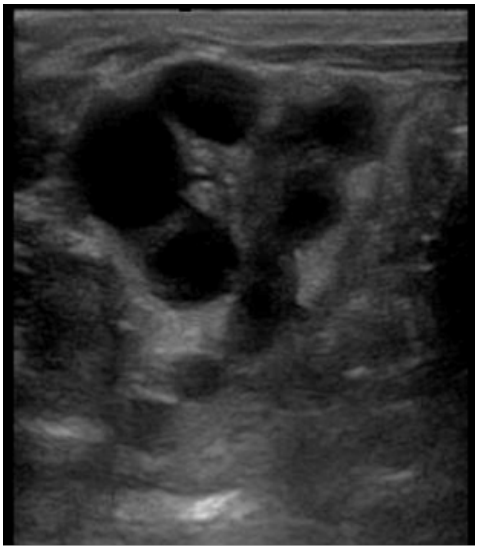

Figure 88.1: Ultrasound of a multicystic dysplastic kidney.

Management

The management of cystic disease of the kidney in the developed world, as in Africa, involves a multidisciplinary team approach involving paediatric urologists, paediatric nephrologists, and (as required and/or available) transplant surgeons and dialysis teams. The main differences in the management of these conditions is obviously influenced by the availability of resources in these locations, including antenatal scanning, availability of specialists, and, more specifically to renal disease, the availability of renal replacement therapy and transplantation. These key factors obviously play a role in the long-term outcomes of each of these conditions.

Multicystic Dysplastic Kidneys

The management of MCDK[7,8] in the developed world remains controversial, especially as the numbers of asymptomatic patients being picked up on routine antenatal screening increases. The most common presentation in developed countries is on antenatal US scan, with fewer cases now being picked up clinically. US scans remain the first-line investigation of choice and are usually diagnostic, but postnatal isotope scanning (dimercaptosuccinic acid (DMSA) or mercaptuacetyltriglycine (MAG3)) is being used increasingly to confirm a total absence in isotope uptake in the affected kidney and hence a diagnosis of MCDK. US also has a role in imaging the contralateral kidney, in which pelviureteric junction obstruction or vesicoureteric reflux may be demonstrated and may subsequently require investigation with a micturating cystourethrogram (MCUG) and/or MAG3 scanning.

Nephrectomy is the treatment of choice for large MCDK presenting clinically with a palpable mass in the neonatal period. Surgery is also indicated in those with smaller lesions and symptoms such as pain, haematuria, and hypertension. Management of asymptomatic patients is more controversial. Up to 50% of MCDK cases have been shown to involute by 5 years of age; however, for the remaining patients the role of "prophylactic" nephrectomy to minimise the risk of hypertension and malignancy is debatable. Hypertension is a rare but recognised complication of MCDK, and malignancy (Wilms' and renal cell carcinoma) is also documented; many authors and clinicians suggest the rarity of these complications makes prophylactic nephrectomy unnecessary in the asymptomatic patient, but opinion on this remains divided.

Autosomal Dominant Polycystic Kidney Disease

ADPKD is essentially a disease of adulthood but may be brought to the attention of the paediatric surgeon in developed countries, with occasional cases being picked up on antenatal scan or following US screening of family members of a patient. Management during childhood is typically expectant, managing any early complications of hypertension or infection as they occur. Rarely, nephrectomy may be required if these complications cannot be managed medically.

Autosomal Recessive Polycystic Kidney Disease

ARPKD,[7–9] in contrast to ADPKD, is a disease of childhood with a generally poor prognosis in both the developing and developed world due to the combination of end-stage renal failure and significant hepatic disease, which most patients experience. The mainstay of management is directed at treating the complications of renal and hepatic failure. The main difference in the developed world compared to developing countries is the wider availability of specialist medical care, dialysis, and transplantation; some studies suggest the prognosis may not be as poor as originally thought and that it is organ- and disease type-specific.[9] The survival rate therefore depends on many factors, including age of onset, presence of pulmonary disease, and relative degree of hepatic and renal involvement. Although severe perinatal disease has a universally poor prognosis, a survival rate of 46% at 15 years has been reported.[8]

Prognosis

The prognosis for cystic kidney diseases depends on the type of disease and age at presentation. Early diagnosis and surgical treatment of unilateral multicystic kidney disease is usually curative with an excellent outcome. The prognosis is good in patients with ADPKD, but those with PKD1 genoytpe appear to develop a more rapid disease progression, resulting in end-stage renal disease. The worst prognosis is in patients with ARPKD. Life expectancy is poor, as almost half of the affected individuals progress to ESRD and death in the first decade of life.

Prevention

There is no known preventive measure for cystic kidney diseases, but genetic counselling of couples intending to become parents may help in the prevention of polycystic kidney diseases.

Key Summary Points

1. Cystic disease of the kidneys is a common problem worldwide.
2. The three most common types of cystic kidney disease are:
   - multicystic kidney or multicystic dysplastic kidney (MCDK);
   - autosomal dominant polycystic kidney disease (ADPKD); and
   - autosomal recessive polycystic kidney disease (ARPKD).
3. MCDK is commonly sporadic and is usually diagnosed antenatally or neonatally on ultrasound. Nephrectomy may be required if patients are symptomatic; prognosis is excellent.
4. ADPKD is associated with the PKD1 and PKD2 genes, which encode for polycystin proteins. ADPKD usually presents in adulthood, but may be seen in the paediatric population antenatally or following screening of family members.
5. ARPKD is a disease of the liver and kidneys presenting in childhood. The prognosis of ARPKD is universally poor and depends on the disease type, organ involvement, and availability of renal replacement therapy.
6. Involvement of a multidisciplinary team with nephrologists is important for all cystic kidney lesions.

References

1. Grantham JJ, Nair V, Winklhoffer F. Cystic diseases of the kidney. In: Brenner BM, ed. Brenner and Rector's The Kidney, 6th ed. WB Saunders Company, 2000, Pp 1699–1730.
2. Trout AT, Siegal J. Cystic diseases of the kidney. Overview-eMedicine, updated 27 June 2006; accessed 25 May 2009. Available at: emedicine.medscape.com/article/453831-overview.
3. Kaplan BS, Mouriquand P, Ewalt DH, et al. Genitourinary and related disorders. In: O'Neill JA, Rowe MI, Grosfeld JI, Fonkalsrud EW, Coran GA, eds. Pediatric Surgery, 5th ed. Mosby Year Book Inc, 1998.
4. Pirson Y, Chauveau D, Grunfeld JP. Autosomal dominant polycystic kidney disease. In: Davison AM, Cameron JS, Grunfeld JP, eds. Oxford Textbook of Clinical Nephrology. Oxford University Press, 1998, Pp 2393–2415.
5. Germino CC. Autosomal dominant polycystic kidney disease: a two hit model. Hospital Pract 1997; 2:81–102.
6. Ravine D, Gibson RN, Walker RG. Evaluation of ultrasonographic diagnostic criteria for autosomal dominant polycystic kidney disease. Lancet 1994; 343:824–827.
7. Wu HY, Snyder HM III. Developmental and positional anomalies of the kidneys. In: Ashcraft KW, Holcomd GW, Murphy JP. Pediatric Surgery, 4th ed. Elsevier Saunders, 2005, Pp 723–731.
8. Thomas DFM. Cystic renal disease. In: Thomas DFM, Rickwood AMK, Duffy PG. Essentials of Paediatric Urology, 2nd ed. Informa UK Ltd, 2008, Pp 97–104.