

## RENAL CYSTS AND ASSOCIATED MALFORMATIONS IN PEDIATRIC AUTOPSY MATERIAL

Radi M.A. Hamed, MD; Salah Tamimi, MD; Abdelkader Al-Shamayleh, MD;  
M. Faisal Kamal, MD; Mosleh Tarawneh, MD; Samir Amr, MD; Amjad Toffaha, MD

Autosomal recessive polycystic kidney disease (ARPKD), also known as infantile polycystic kidney disease (or Potter type I), and autosomal dominant polycystic kidney disease (ADPKD), an adult form of polycystic kidney disease (or Potter type III), are the two main types of genetic polycystic kidney diseases encountered in infants and children. The clinical spectrum of ARPKD is variable, however, it presents mainly in infancy and most affected viable neonates die within the first few hours of extrauterine life. Some of the clinical variability is accounted for by differences in the genotypes responsible for the clinical syndrome of ADPKD. At least three different gene codes for the development of ADPKD have been identified, with loci mapped to chromosome 16 (polycystic kidney disease or PKD1),<sup>1,2</sup> to chromosome 4 (PKD2),<sup>3</sup> and recently a small number of families with ADPKD that are not linked to the PKD1 and PKD2 loci.<sup>4,5</sup> A single ARPKD gene is identified and is linked to chromosome 6.<sup>6</sup>

The morphologic criteria applied to make distinctions among the different types of chronic renal disease (CRD) involve the cyst size, number, cyst distribution within the kidney, the site along the nephron from which the cysts arise, and the possible involvement of other organs. CRD may present as a non-syndromal heritable and sporadic form, or as a component of a malformation syndrome.<sup>7</sup> The aim of this study was to determine the relative frequency of the different types of CRD, and to study the frequency of associated extrarenal disorders and congenital malformations. In this report, we emphasize the latter as an important consideration in cases presenting in the neonatal period.

### Subjects and Methods

We reviewed the records of all infants who presented to

Jordan University Hospital in the neonatal period with CRD or renal dysplasia, over the period 1980-1990 inclusive. The search also included all newborns who were found at autopsy to have CRD or renal dysplasia during the same period. Histological assessment was performed on all organs, with special emphasis on the kidneys and liver. Clinical findings and associated malformations were also reviewed. The classification of renal cysts was based on that of Kissane,<sup>8</sup> and Potter and Craig<sup>9</sup> (Table 1).

The following data were obtained from the clinical and autopsy records: gestational age in weeks, age at the time of death, sex, clinical presentation, clinical progression, kidney weight, and the family history. Chromosomal analysis was not performed, due to the fact that it has only been available at our institution in recent years.

TABLE 1. *Classification of renal cysts.*

Polycystic kidney disease (PKD)
Infantile polycystic disease: autosomal recessive PKD: Potter type I
Adult type polycystic disease: autosomal dominant PKD: Potter type III
Renal cystic dysplasia: multicystic dysplastic kidney: Potter type II
- Large kidney (type IIA)
- Small kidney (type IIB)
Cystic disease with intrauterine urethral obstruction: Potter type IV
Medullary cystic disease, juvenile nephronophthisis
Glomerulocystic renal disease
Simple renal cysts
Cortical cysts in syndromes of multiple malformations

TABLE 2. *The relative frequency of the different types of cystic kidney disease in infant autopsies at JUH (1980-1990).*

Type	Number
Potter type I	12
Potter type IIA	3
Potter type IIB	3
Potter type III	3
Potter type IV	2
Simple solitary cyst	1
Cortical cysts	1
Medullary cystic disease	1
Total	26

From the Departments of Pediatrics and Pathology, Faculty of Medicine, University of Jordan, Amman, Jordan.

Address reprint requests and correspondence to Dr. Hamed: Department of Pediatrics, Faculty of Medicine, University of Jordan, Amman, Jordan.

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TABLE 3. Associated malformations with cystic kidney disease in infant autopsies at JUH (1980-1990).

System	Number of cases	Total
Genital		4
Apenia	1	
Phimosis	1	
Cryptorchidism	1	
Ambiguous genitalia	1	
Cardiac		4
Ventricular septal defect	1	
Hypoplastic left heart syndrome	1	
Patent ductus arteriosus	2	
Gastrointestinal		10
Liver disease	9	
Imperforate anus	1	
Facial system abnormalities		4
Depressed nasal bridge	1	
Fish mouth	1	
Abnormal facial features	2	
Ophthalmologic		4
Microphthalmia	1	
Slanting eyes	1	
Exophthalmos	1	
Epicanthal folds	1	
Musculoskeletal		8
Polydactyly	2	
Congenital hip dislocation	1	
Talipes deformity	2	
Arthrogyposis	3	
Auditory		4
Accessory auricle	1	
Large ear helix	1	
Low set ears	2	
Pulmonary		3
Hypoplastic lungs	3	
Other		9
Hernias	3	
Agenesis of corpus callosum	2	
Supernumerary spleen	1	
Choanal atresia	1	
Situs inversus	1	
Hydrocephalus	1	

### Results

During the study period (1980-1990), there were 26 autopsies of CRD patients, comprising 16 females and 10 males. Table 2 shows the relative frequency of CRD in our cases. The largest group consisted of 12 cases of ARPKD (Potter type I).

Seventeen cases completed 38 weeks of gestation and the rest were premature. Abdominal mass was the most common presenting sign, occurring in 16 cases. Respiratory manifestations were common among our patients—respiratory distress occurred in 10, spontaneous pneumothorax in one, and cyanosis in six cases. At the time of presentation, poor sucking was a feature in four patients, and three had jaundice. Three other patients presented with either abdominal distention, vomiting or edema, and four had symptoms of sepsis. All patients

except one died before three months of age. The cause of death was renal failure in 10 cases, culture-proven sepsis in three, respiratory failure in four, intraventricular hemorrhage in two, and congestive heart failure in two. Five others died soon after birth.

Single or multiple malformations were encountered in 14 (54%) (Table 3). A total of 50 congenital anomalies and extrarenal abnormalities were seen in these cases. Due to the small number of affected subjects with malformations in the different groups of CRD, statistical analysis was not feasible. Liver abnormalities were notable in ARPKD cases. Nine of these cases had evidence of bile duct proliferation and the rest had normal liver architecture.

### Discussion

Autopsy material continues to provide suitable guidance for the classification and typing of cystic renal disorders. The perinatal autopsy is clearly an undervalued source of information. Little or no information is available from developing countries.<sup>10</sup> CRD presenting in the neonatal and early infancy period is often incompatible with long survival, hence the incidence of renal cysts is usually much higher in autopsy material than in clinical studies. The association of CRD with extrarenal malformations and congenital anomalies of other organs is well known,<sup>7,11</sup> however, there is paucity of literature in the description of this association. At least 45 syndromes with a well-recognized cystic renal disorder have been described in the literature.<sup>11,12</sup> This conforms with the high association between CRD and extrarenal malformations in this study. In one study,<sup>7</sup> extrarenal malformations were encountered in 75% of pediatric autopsy material with renal cysts, a much higher frequency than what was observed in our series. Gastrointestinal malformations very often appear to be associated with CRD,<sup>7</sup> however, this was not noted in the present series. An associated CRD should be suspected in infants presenting with multiple congenital malformations.

With the developments in ultrasound technology in recent years, the use of ultrasound has increased our awareness of these disorders in suspected pregnancies. The terms “cystic kidneys” or renal cystic disease are morphologic descriptions for an etiologic heterogeneous group of disorders ranging from solitary cysts to several forms of multicystic and polycystic kidneys. The combination of examination of the kidneys and liver, clinical data, family history, and the presence of associated anomalies is mandatory in obtaining a final diagnosis. The use of prenatal ultrasound to monitor pregnancies at risk for ARPKD is limited because a recurrence can be diagnosed early in pregnancy but may not be excluded.<sup>13</sup> For pregnancies at risk for ADPKD, a reliable prenatal diagnosis can be obtained by DNA studies after chorionic

villus sampling<sup>13</sup> and other DNA-based techniques.<sup>14,15</sup> Despite the wide variability in clinical phenotypes, there is a single ARPKD gene. Linkage data and the absence of genetic heterogeneity in all families tested to date have important implications for DNA-based prenatal diagnosis.<sup>16</sup>

In order to be able to provide for proper genetic counseling, there is a continuous need to subject most polycystic kidney disease variants to the utmost morphologic scrutiny, using all available techniques. Both genetic factors and the study of genes are extremely useful in defining discrete disease entities. Such efforts and developments in this field have provided significantly for gene mapping to chromosomes, with its important implications to DNA-based prenatal diagnosis and genetic counseling.

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