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Characteristics and outcome of children with Unilateral multicystic Dysplastic Kidney Disease in Upper Egypt

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Abstract:

Background:

Unilateral multicystic dysplastic kidney is characterized by formation of multiple, non-communicating cysts with non- functioning renal parenchyma, and ureteral hypoplasia. It is a common kidney and urinary tract anomaly that can be detected via antenatal ultrasound examination. However, studies on this disease in Egypt are scarce.

Objective of the study: was to study the characteristics and outcome of the children with unilateral multicystic dysplastic kidney.

Patients and Methods: We retrospectively collected clinico-demographic, radiological and laboratory data of children with unilateral multicystic dysplastic kidney at pediatric nephrology clinic of Sohag University Hospital from January 2015 till February 2023.

Results: A total of 35 patients [18(51.4%) boys 17(48.6%) girls] were followed for a median duration of 14.7 months with Interquartile range (3-31) months. Multicystic dysplastic kidney was located on the right and left sides in 23(65.7%) and 12 (34.3%) children, respectively. Most cases (74%) were detected via an antenatal ultrasound examination. About 43% of patients had at least one episode of urinary tract infection. Associated urogenital abnormalities were detected in 4 (11.4%) patients; one (2.9%) of them had vesicoureteral reflux with hydronephrosis in the contralateral side. One (2.9%) patient had persistent proteinuria and impaired kidney function. Overall 22 (62.9%) patients underwent partial or complete kidney involution.

Conclusion: Most patients with unilateral multicystic dysplastic kidney are detected prenatally. The prognosis is generally good if the contralateral kidney is normal. Long-term follow up is essential to trace the development of proteinuria, hypertension or renal impairment.

Key words: Multicystic dysplastic kidney, children, urogenital anomalies, vesicoureteral reflux, involution.

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Introduction:

Unilateral multicystic dysplastic kidney (MCDK) is characterized by enlargement of the kidney, multiple, non-communicating cysts of varying size,

non- functioning renal parenchyma, and atresia or hypoplasia of the ureter. ⁽¹⁾ The left kidney is usually more affected than the right one and is

detected more commonly in males than females in ratio 2.4:1.⁽²⁾ Multicystic dysplastic kidney is an isolated condition in most cases; although, the contralateral side might be affected by other abnormalities such as vesicoureteral reflux (VUR), ureteropelvic junction obstruction (UPJO) and ureterovesical obstruction (UVJO).⁽³⁾ Unilateral MCDK is one of the most frequent abnormalities identified by antenatal ultrasound (US) with an incidence of approximately 1 in 3640 births.⁽⁴⁾ Nevertheless, it may be asymptomatic and undetected until the adulthood.⁽⁵⁾

In most cases, the fate of unilateral MCDK is complete or partial involution with time. It is suggested that unilateral MCDK might increase the risk of hypertension, although it was not higher than in the general pediatric population.⁽⁴⁾ It was thought that unilateral MCDK may increase the risk of malignancy (Wilms tumor); however, it is not universally accepted recently.⁽⁶⁾

Although US is the first-line and basic imaging technique for the follow-up period of MCDK, a recent study recommended reducing unnecessary US imaging scans during follow up.⁽⁷⁾ Moreover, renal scintigraphy provides additional information such as the function of renal cortical tissue in MCDK, the involvement of contralateral kidney, and/or presence of any scar or hypodysplasia.⁽⁸⁾ Therefore, various studies recommended performing the Tc-99m dimercaptosuccinic acid (DMSA) scintigraphy at least once at the follow-up period in MCDK patients.⁽⁶⁾ It is not recommended performing voiding cystourethrogram (VCUG) to the contralateral kidney on routine basis unless the initial US scan detects abnormalities, such as dilated ureters, calyces, small or abnormal appearance of the contralateral kidney.⁽⁴⁾

The management of MCDK has markedly changed over time. Previously, nephrectomy was performed to avoid infection, pain, hypertension, and malignancy.⁽⁹⁾ Recently, management is mainly conservative due to favorable outcome of patients.⁽⁴⁾

Few Egyptian studies described the clinical features of MCDK in children as a part of congenital anomalies of the kidney and urinary tract (CAKUT).⁽¹⁰⁾ However, little is known about the clinical manifestations and outcomes and associated co-

morbidities of the MCDK in children of Upper Egypt.

This work aimed to study the characters of unilateral MCDK in our pediatric patients in Sohag pediatric nephrology clinic as regard to age, method of diagnosis, variable clinical presentations, associated co-morbidities as well as outcomes of these patients.

Patients and methods:

Study design: A retrospective study

Study place: Pediatric nephrology clinic of Sohag University Hospital.

Study period: Patients followed in the period from January 2015 till February 2023 were included.

Inclusion criteria: The study included all patients diagnosed to have unilateral MCDK who were followed for at least 3 months at the pediatric nephrology clinic during the period mentioned above.

Exclusion criteria: We excluded patients with incomplete medical data.

Methods:

All patients' data were obtained from their medical records in our pediatric nephrology clinic. We evaluated the patients' clinico-demographic parameters including gender, age at diagnosis, parental consanguinity, family history for renal diseases, side of the affected kidney, renal function tests (serum urea and creatinine levels), history of urinary tract infection (UTI), blood pressure measurements, any evidence of malignancy, additional urological anomalies in the same or contralateral side, associated congenital anomalies as congenital heart diseases, previous operations, nephrectomy indications for those who underwent nephrectomy because of MCDK, and finally follow-up duration was determined.

The diagnosis of MCDK was made according to the recorded ultrasonography. The diagnosis was based on the following established US criteria: multiple cysts of varying size, absence of normal renal sinus echoes, and absence of normal renal parenchyma.⁽⁸⁾ Renal size changes of the affected side or contralateral side by renal ultrasounds during follow up were reported.

The IBM Statistical Package for the Social Sciences (SPSS version 26.0, IBM Corp., Armonk, NY, USA, 2019) software was used for statistical analysis. Categorical data were presented as frequencies and percentages. Shapiro-Wilk and Kolmogorov-Smirnov tests were applied to determine whether the distribution was normal or not. For continuous numerical data we used median with interquartile range (IQR) because the data were not normally distributed. For categorical data, frequencies and percentages were employed.

Results:

The clinical characteristics of 35 patients with MCDK in our study are outlined in table (1).

Table (1): Characteristics of patients with unilateral Multicystic dysplastic kidney

Feature	Number(35)	Percentage (%)
Gender		
Female/Male	18/17	51.4/48.6
Side of multicystic dysplastic kidney		
Right/left	23/12	65.7/34.3
Parental consanguinity	20	57.1
Prenatal diagnosis	26	74.3
Family history of urogenital anomalies	5	14.7
Extra renal anomalies:		
• Congenital heart disease	3	8.6
• Dandy Walker malformation	1	2.9
History of urinary tract infection	15	42.9
Blood pressure		
• Normal	33	94.3
• Hypertension	2	5.7
Proteinuria	1	2.9
Decreased renal function at the initial visit	3	8.6
Decreased renal function at the last follow up visit	1	2.9

Of the patients, 18 (51.4%) were male and 17 (48.6%) were female with male to female ratio was 1.1:1. The median age at presentation was 3 months with IQR^(0.6-14.5) months. The median age at last follow up visits was 22.2 months with IQR^(9.3-39.5) months. The median follow up duration was 14.7 months with IQR (3-31) months. The majority of patients 26(74.3%) were diagnosed by antenatal US examination. The remaining 9 patients were detected incidentally during US examination for

Statistical analysis:

Ethical consideration:

Approval from the Sohag Faculty of Medicine research ethics committee was obtained before study onset and all patients' data were treated according to the ethical guidelines with complete respect of patient's privacy and anonymousness. The requirement for informed consent was waived given the retrospective nature of the study.

gross hematuria, UTI and/or non-specific abdominal pain. Regarding laterality, MCDK was detected more frequently at the right side [23 (65.7%) patients] than the left side.⁽¹²⁾ (34.3%) patients] with a ratio of 1.9:1. In the present study, parenteral consanguinity was observed in 57.1% of patients. Family history of urogenital anomalies was detected in 14.7% of patients in the form of unilateral renal atrophy, epispadias, hypospadias, and simple renal cyst.

In our study, we identified 15 (42.9%) patients with at least one episode of UTI. However, recurrent episodes were detected in 5 (14.3%) patients. The highest frequency of UTI episodes was found in one patient who was a girl with contralateral infravesical ectopic ureteral opening. In addition, proteinuria was identified only in this patient. We did not observe hypertension in any of our study cohort. The median serum creatinine level at the first visits was 0.63 mg/dL with IQR (0.5-0.82) mg/dL. The median serum creatinine level at the last follow up

visits was 0.58 mg/dL with IQR (0.5-0.7) mg/dL. At presentation, we identified 3 (8.6%) patients with impaired renal function; one patient had an ipsilateral extravesical ureterocele and the other two patients had abnormal contralateral kidneys in the form of nephrocalcinosis and infravesical ectopic ureteral opening (Table 2). At the last follow up visit, the female patient with contralateral infravesical ectopic

Table (2): The associated urogenital anomalies

Feature	Number(35)	Percentage (%)
Ipsilateral extravesical ureterocele	1	2.9
Nephrocalcinosis in the contralateral side	1	2.9
Ectopic ureter in the contralateral side	1	2.9
Contralateral vesicoureteral reflux with hydronephrosis	1	2.9

ureteral opening was the only one who had persistent impairment in the renal function with an estimated glomerular filtration rate being 22 ml/min/1.73 m². Therefore, this patient was diagnosed to have stage III chronic kidney disease. The renal function of the other two patients was normalized during follow up. There was only one (2.9%) patient with VUR and hydronephrosis in the contralateral kidney identified during the US examination without performing VCUG. However, this patient had no abnormality in the renal functions, UTI, proteinuria nor hypertension at the initial or follow up visits.

In the current study, we observed a partial reduction in the size of MCDKs in 21 (60%) patients;9 of them (25.7%)had small sized MSDKs at presentation while the remaining 12 (34.3%) patients underwent reduction in size later on during follow up. Additionally, we observed complete involution of the affected kidney in one (2.9%) patient at the age of 67 months. However, we did not accurately determine the involution rates because of relatively short duration of follow up in some patients. Among 22 (62.9%) patients with partial or complete involution of MCDK;

compensatory hypertrophy in the contralateral kidneys was identified in 19 (54.3%) patients, while 3(8.6%) patients had abnormal contralateral kidneys in the form of nephrocalcinosis, VUR with hydronephrosis and ectopic ureter. The median age at which reduction of the MCDK size with concomitant hypertrophy of the other side was initially observed at 21.6 months with IQR (9.8-39.1) months. A surgical procedure was performed in our hospital for the little girl with an ectopic ureter to insert a double J stent until a corrective surgery could be performed at an older age. Another patient had undergone nephrectomy in other center. However, we could not know the indication of nephrectomy in this patient. In our center, none of the remaining patients had any surgical procedure. Malignant transformation did not occur in any of our cases.

Discussion:

In the current study, the MCDK occurred nearly equal between boys and girls. The right side was more frequently affected than the left side. Most cases were detected prenatally by ultrasound examination. Associated genitourinary

abnormalities were not common. Extra renal manifestations did not occur frequently. Most of our patients did not have hypertension, proteinuria or impaired kidney function. We observed a partial or complete involution of the MCDK in most of our patients. The prognosis was good as long as the contralateral kidney side was normal.

Our study revealed that the MCDK were presented nearly equally between boys and girls. In contrast to this observation, some studies revealed that MCDK was more common in boys than in girls.^(11,12) The rate of right side involvement was higher than the left one in our study. The previous literature showed variable findings regarding the side of involvement.^(5,6,11-13)

In our series, most of cases (74.3%) were identified antenatal via an ultrasound examination. This rate is comparable with the previous studies. Akbalik Kara et al demonstrated that prenatal diagnosis rate was 78.4%.⁽⁶⁾ Moraloğlu et al stated the prenatal diagnosis rate as 94.1% of the patients with MCDK.⁽¹⁴⁾ Despite these two high rates, Kara et al reported the prenatal diagnosis rate as 50%.⁽¹⁵⁾ In our opinion, this variability might be related the socioeconomic status of the families and the rate of the antenatal follow up.

In the present study, we detected high rate of parental consanguinity (57.1%), which was similar to a previous study.⁽⁶⁾ This seems to be related to the common consanguineous marriage in Egypt, particularly in our region.

We found that 4 (11.4%) patients had associated urogenital malformations detected by ultrasound examination: one patient had ipsilateral extravesical ureterocele and the remaining 3 patients had abnormalities in the contralateral side which were: nephrocalcinosis, VUR with hydronephrosis, and infravesical ectopic ureteral opening. Several urogenital malformations have been reported to be associated with MCDK in many studies. VUR of the contralateral kidney is the most common among them.^(6,11,13,16) Kopac et al reported that about 43.8% of patients with MCDK had associated urogenital anomalies, cryptorchidism (24%) and VUR (16.3%) of the contralateral kidney were the most common among them.⁽¹¹⁾ Dogan et al found that one in three patients with MCDK had associated urogenital

malformations with VUR of the contralateral kidney (26.6%) being the most common.⁽¹⁶⁾ The number of patients in our study is relatively small which might explain the lower rate of associated urogenital malformation compared to other studies. Moreover, because VCUG was not performed in our patients; we may not have identified all the patients with low-grade VUR. However, performing a routine VCUG in patients with MCDK is not recommended except in those with urinary tract infection or US signs suggesting VUR, such as urinary tract dilatation.⁽¹⁷⁾ This is because VCUG is an invasive process; it is stressful for both patients and their families, along with risk of exposure to radiation, urethral trauma, and iatrogenic UTI.⁽¹⁸⁾ Moreover, a spontaneous resolution is possible, especially in low-grade VUR.⁽¹⁷⁾

One important complication of MCDK is UTI and it has been reported in 5%–34.7% of the patients.⁽¹⁴⁾ In the present study, we found that 15 (42.9%) patients had at least one episode of the UTI during follow up. The highest frequency of UTI episodes was found in the little girl with contralateral infravesical ectopic ureteral opening. This anomaly could explain the higher frequency of UTI episodes in this patient. Previous studies found no statistically significant relationship between UTI and renal scar, with or without VUR.^(6,19) Unfortunately, DMSA scan was not performed in our study to investigate this relationship.

In the present series, all of our patients had normal blood pressure throughout the span of follow-up. Similarly, Alamir et al did not observe hypertension in any of their study cohort that included 50 patients.⁽¹³⁾ The incidence of hypertension with MCDK is very low and ranges from 0.6 to 17.7% in the literature.^(9,20) Hypertension is usually related to abnormalities in the contralateral kidney.⁽¹⁵⁾ Akbalik Kara et al detected hypertension in 3 out of 111 patients and hypertension was related to abnormalities in the contralateral kidney such as renal scarring secondary to high grade reflux.⁽⁶⁾ However, Sugimoto et al found that elevated serum renin and aldosterone levels due to abnormal vascular structure in an infant with MCDK was the cause of hypertension that improved dramatically after nephrectomy.⁽²¹⁾ Another important point is

that hypertension may develop overtime even in absence of abnormalities in the contralateral side as a result of compensatory hypertrophy that lead to hyperfiltration and proteinuria.⁽⁶⁾

In our study, we detected proteinuria in one case. This was the patient who had the ureteral anomaly. We thought that proteinuria in this case might result from persistent impairment in kidney function because we did not encounter compensatory hypertrophy in her contralateral kidney. Dogan et al detected proteinuria in 1 (1.7%) patient with compensatory hypertrophy in the contralateral kidney.⁽¹⁶⁾ However, relatively short follow up duration in some cases did not allow us to observe such findings. Therefore, long-term follow up of the blood pressure and proteinuria are highly recommended.

It is known that the MCDK undergoes reduction in size or complete involution predominantly in the first five years of life.⁽²²⁾ In the current series, we detected reduction in the size of MCDKs in 21 (60%) of patients at a median age of 21.6 months with IQR^(9.8-39.1) months. In addition, complete involution has been detected in one (2.8%) patient. Our finding was in line with a previous study reporting that 4 of 59 (6.7%) patients showed complete involution, and the initial length of MCDK had reduced in 26 (44%) patients during a comparable follow-up period.⁽¹⁶⁾ In contrast to our results, Alamir et al stated that the vast majority (90%) of their cohort showed some degree of involution at a longer follow up period than ours.⁽¹³⁾

The previous studies showed that initial MCDK length is the most important factor for predicting complete involution.⁽²²⁾ Hayes et al reported that the involution rates were significantly higher in patients with initial MCDK of <5 cm.⁽²³⁾

In the present study, we found that the contralateral kidney showed compensatory hypertrophy in 19 (54.3%) cases. Akbalik Kara et al reported compensatory hypertrophy in 69 (62%) patients.⁽⁶⁾ Dogan et al demonstrated compensatory hypertrophy in 36/45 (80%) patients.⁽¹⁶⁾ The lower number of cases and shorter duration of follow up might explain the lower number of compensatory hypertrophied contralateral kidneys detected in our study in comparison with other studies. We

observed that the median age of patients at which hypertrophy occurred was at 21.6 months with IQR.^(9.8-39.1) months. The age at which compensatory hypertrophy is detected is variable in different studies and hypertrophy could be started in utero.⁽²²⁾

Mansoor et al determined compensatory renal growth in 66 of 89 (74.1%) patients with MCDK and in 37% of their cohort hypertrophy started in intrauterine life.⁽²⁴⁾ In fact, the compensatory hypertrophy indicates that the function of the contralateral kidney is normal and gives a good prognosis. Therefore, if hypertrophy did not occur, the nephrologist should be suspicious of the contralateral kidney having abnormality.⁽⁶⁾

We did not detect any malignant transformation of the MCDK. This is in agreement with other studies as malignant transformation has been reported very rare.^(1,3,6) Moreover, overall 34/35 (97.1%) of our patients were managed conservatively while nephrectomy was performed for one patient in other center. The current literature supports the conservative management of MCDK giving its benign nature and very low rate of complications.⁽²⁵⁾ This study is not without limitations. Its retrospective design and the short follow-up period for some patients might underestimate the findings related to the MCDK. The relatively small numbers of included participants as well as being a single-center study are other limitations. Moreover, the ultrasound examinations were performed by different radiologists.

Conclusion:

Most children with unilateral MCDK are detected prenatally. Unilateral MCDK have a good prognosis if the contralateral kidney is normal. The size and function of the contralateral kidney, hypertension and proteinuria should be followed up regularly for long periods in all children with MCDK.

Conflicts of interest: none stated.

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Contributors: RGA, GAA: designed the study and developed the protocol; RGA: collected the data, performed the statistical analysis and drafted the article; NFB, GAA: critically reviewed the article for the important intellectual content. All authors approved the submitted version.

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