DIAGNOSIS AND CLINICAL CONSEQUENCES OF URINARY TRACT MALFORMATION IN CHILDREN

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Abstract

Congenital alterations of the kidney and urinary tract have been grouped under the name of CAKUT, although it includes a large spectrum of malformations. Early diagnosis of CAKUT is important. During pregnancy, the third trimester threshold value for the antero-posterior renal pelvis diameter measurement and should be followed by postnatal ultrasound. Children with CAKUT often have comorbidities, as CAKUT may lead in time to Chronic Kidney Disease (CKD) due to reduced nephron number at birth or progressive nephron loss, as well as recurrent urinary tract infections. We analyzed 42020 patient files between January 2015 and June 2017 admitted in "Louis Turcanu" Clinical Emergency Children Hospital in Timisoara, and we identified and analyzed 252 individual patients with CAKUT in a cross sectional study. Prevalence of CAKUT was 0.6%, with a male: female ratio of 1.35. 14% of cases had prenatal diagnosis determined by abdominal ultrasound performed in the third trimester of pregnancy, while 66 patients were diagnosed with congenital anomalies by accident, during a screening abdominal ultrasound. Unilateral kidney agenesis (URA) was found in 20 patients, with a male/female ratio = 1 and right/left ratio of 2.33. In 25% of cases, URA was associated with dilatation of the urinary tract on the contralateral kidney. Treatment options included medical/observational treatment and surgical options. Early diagnosis of CAKUT using a simple abdominal ultrasound screening allows early and proper treatment and reduces the risk of parenchymal complications and CKD.

Keywords: hydronephrosis, ureter, kidney disease, ultrasound, CAKUT

Introduction

Congenital alterations of the kidney and urinary tract have been grouped under the name of CAKUT, includes a large spectrum of malformations [1]. Given the complex development process of genitourinary system it is no surprise that CAKUT are among the most common congenital abnormalities in children [2], occurring in 1 in every 500 live births [3] and represent a major cause of CKD in children. Severity of CAKUT varies between incompatible with life malformations (bilateral renal agenesis) to minor abnormalities that are often asymptomatic for long periods of time [4].

Early diagnosis of CAKUT is important, during pregnancy, the third trimester threshold value for the antero-posterior renal pelvis diameter measurement and should be followed by postnatal ultrasound [5]. Prenatal urinary tract dilatation is common, present in 1-4% of pregnancies. Hydronephrosis is the most common anomaly identified on prenatal ultrasound, affecting 1–5 % of all pregnancies, but usually mild and resolves by itself [6, 7, 8]. Postnatal, the most common cause of pelvic and calyceal dilatation is ureteropelvic junction obstruction (PUJO) [9]. Prenatal diagnosis and supportive or corrective surgical inventions have improved survival rate of affected newborns. As a consequence, children with CAKUT often have comorbidities, as CAKUT may lead in time to Chronic Kidney Disease (CKD) due to reduced nephron number at birth or progressive nephron loss, as well as recurrent urinary tract infections (UTIs) [10,11]. Despite recent improvement in prenatal diagnosis and early surgical interventions, CAKUT remains the primary cause of kidney failure in infants. Almost 70% of pediatric patients with CKD progress to end stage renal disease (ESRD) before reaching adulthood. The care of patients with CKD focuses on interventions in order to preserve renal function [11]. In addition, adequately identifying, treating and preventing UTIs is another important goal to spare the remaining kidney.

Materials and Methods

We analyzed 42020 patient files between January 2015 and June 2017 admitted in "Louis Turcanu" Clinical Emergency Children Hospital in Timisoara, and we identified and analyzed 252 individual patients with CAKUT in a cross sectional study over a period of 30 months.

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	Male	Female		M:F ratio
Antenatal n=34	22 (64.7%)	12 (35.29%)		**1.83**
Neonatal n=48	28 (58.33%)	20 (41.66%)		**1.4**
UTI n=104	61 (58.65%)	43 (41.34%)		**1.41**
Ultrasound screening n=66	34 (51,51%)	32 (48.48%)		1.06

Tabel 1. Sex distribuiton correlated with moment of diagnosis

	Left	Right	Bilateral
Renal agenesis (n=20)	6 (30%)	14 **(70%)**	-
Renal hypoplasia (n=13)	7 (53.84%)	5 (38.46%)	1 (7.69%)
Renal ectopy/malrotation (n=14)	4 (28.57%)	10 **(71.42%)**	
Kidney fusion anomalies (n=7)	-	-	7
Displastic kidney (n=22)	7 (31.81%)	9 **(40.90%)**	6 (27.27%)
Total (n=76)	24 (31.57%)	**38 (50%)**	14 (18.42%)

Tabel 2. Uniterality of renal malformations

	Left	Right	Bilateral
Hydronephrosis PUJO (n=131)	59 **(45.03%)**	50 (38.16%)	22 (16.79%)
Ureterohydronephrosis (n=56)	20 **(35.71%)**	10 (17.95%)	26 (46.42%)
Uretheral duplicity (n=21)	7 (33.33%)	8 (38.09%)	6 (28.57%)
Total = 208	**86 (41.34%)**	68 (32.69%)	54 (25.96%)

Tabel 3. Unilaterality of ureteral malformations

Inclusion criteria were age between 1 month and 18 years and presence of any type of CAKUT by abdominal ultrasound examination. We excluded from our study children with urinary tract dilatations due to external compression or lithiasis (secondary hydronephrosis). We collected data about the age of the patient, age at the time of diagnosis, prenatal ultrasound, sex of the patient, type of diagnosis, clinical manifestations at the time of diagnosis and evolution, malformation type, severity and treatment options. For statistical analysis we used Microsoft Office Excel

Results

Prevalence of CAKUT in Children Pediatric Emergency Hospital Timisoara admissions over a 30 months survey time was 0.6%, with 252 patients presenting the required criteria to be included in our study out of 42020 hospital admissions, with a male: female ratio 1.35. About 14% of cases had prenatal diagnosis determined by abdominal ultrasound performed in third trimester of pregnancy, while 66 patients were diagnosed with congenital anomalies during a screening abdominal ultrasound.

Golden standard for structural malformations of kidney and urinary tract is abdominal ultrasound and it was performed for all patients, considered to be an inclusion criteria in our study. One third of patients, though, required further and more detailed imaging of the structural malformation of urinary tract including CT urography or retrograde cystography to evaluate the complexity, possible complications and comorbidities like as vesico-ureteral reflux (VUR). Over 40% of patients were diagnosed with CAKUT with the occasion of their first urinary tract infection.

Analyzing sex distribution correlated with moment of diagnosis we revealed that more boys are diagnosed with CAKUT in prenatal screening with a male (M): female (F) ratio of 1.83, as well in the neonatal period (M: F=1.4) and simultaneously to their first UTI (M: F=1.41). Gender equality was to be found in children diagnosed accidentally

(M: F=1.06) (Table 1). Age at the time of diagnosis within the group (252 patients) had two peaks of incidence: less than 1 year (81patients) and children over 6 years of age (99).

We divided CAKUT in three major groups based on anatomic level of the defect: renal malformations (76 patients), uretero-pelvic malformations (208patients) and vesical/subvesical malformations (20 patients). Out of all the patients, 20.23% had complex renal-ureteral malformations, affecting more than one anatomic level based of our classification.

Unilateral kidney agenesis (URA) was found in 20 patients, with a male/female ratio=1 and right/left ratio of 2.33. In 25% of cases, URA was associated with dilatation of urinary tract on the contralateral kidney. Compensatory hypertrophy (renal length greater than two standard deviations above the mean), is commonly observed in patients with a congenitally solitary kidney. In our study one quarter of patients were found with Hypertrophic contralateral kidney.

Other renal malformations included renal hypoplasia (13 patients), renal ectopy/malrotation, double kidney, renal fusion anomalies and dysplastic kidney (22patients) (Table 2). More than 80% of renal malformations were unilateral, predominantly affecting the right side, with a right/left ratio of 1.58.

Ureteropelvic malformations included patients with Hydronephrosis due to ureteropelvic junction obstruction (PUJO), Hydronephrosis associated with ureteral distension and ureteral duplicity/double collecting system (Table 3). Out of 208 patients with ureteropelvic defect, 154 (74.03%) had unilateral defect with a Left: Right ratio = 1.26. Severity of hydronephrosis was scored I-V grade depending on the dilatation of the renal pelvis and calyces, bilateral involvement, dilatation of the ureter and management of case was according to guidelines. Congenital obstruction in urine flow, referring to PUJO, obstructive megaureter, obstructive ureterocelle, ureteral stenosis were found in 140 patients out of 252 (55.55%). Reflux anomalies including primary or secondary vesicoureteral reflux (VUR) were found in 41 patients (16.26%). Double collecting urinary system consists of both obstructive and reflux anomaly as one or both ureters have modified structure leading to slow drainage of urine flow and incompetent ureterovesical valve and was found in 21 cases (8.3%). Lower urinary tract malformations involving the bladder and the urethra were found in 20 patients (7.93%).

Almost half of our patients were diagnosed with anomalies of urinary tract with the occasion of their first UTI. UTI has a high incidence among patients with abnormal urinary tract, especially when associating VUR or when UTI becomes recurrent. Half of our patients (56.34%) had at least one episode of UTI during our observation time, while several patients had more than one episode in the case of reflux anomalies. Each UTI episode received antibiotic treatment according to antibyogram. Antibiotic prophylaxis was recommended in 13 patients that had recurrent episodes of infection associated with high grade (III/IV) VUR.

Treatment options included medical/observational treatment and surgical options (Hynes-Anderson pyeloplasty, percutaneous ureterostomy, unilateral nephrectomy, endoscopic PUV removal, and endoscopic correction using Vantris. Surgical treatment is required in case of high grade VUR, progressive renal scarring associating any VUR grade, solitary kidney associating high grade VUR. Repeated renal scarring leads to Chronic Kidney Disease (CKD), as encounter in 12% of patients.

Discussion

Congenital anomalies of kidney and urinary tract are one of the most frequent malformations to be found in children, considered among the top 5 anomalies. In our study CAKUT prevalence was slightly lower (0.6%) compared to other studies Salento, Italy 0.96% (171 CAKUT out of 17783 children) and Beijing 1.67% incidence (489 CAKUT din 26989) [12], most probably due to our selection of patients. The patients were selected from our hospital admitted patients, not being able to take under consideration the asymptomatic ones, or diagnosed outside the hospital within the same area.

Significant maternal factors associated with CAKUT are being searched and proved to be linked, like maternal age (30–39 years), gestational diabetes, polyhydramnios/oligohydramnios, thalassemia/hemochromatosis and other illness. Infants with CAKUT are more likely to be boys and born at small gestational age (SGA) [13].

Renal agenesis may occur as an isolated finding or, commonly, in association with other anomalies or syndromes conditions. Unilateral renal agenesis is thought to occur in approximately 1 in 1000–3000 live births [14]. There is a slight predilection for the left side and almost twofold higher incidence in males than in females [14]. In our study, surprisingly, right side was more frequently affected with a right/left ratio of 2.33 and a male/female ratio of 1.

Unilateral renal agenesis may occur by itself or, commonly, in association with other congenital genitourinary and non-genitourinary anomalies. Anomalies of the contralateral kidney and collecting system have been reported to occur in 32–50 % of patients with unilateral renal agenesis. The most common abnormality affecting the contralateral kidney is vesicoureteral reflux, which occurs in approximately 24 % of patients with unilateral renal agenesis. Other less common associated urinary tract anomalies include ureteropelvic junction obstruction (6 %), megaureter (7 %), and duplicated collecting system (3 %) [14]. in our study, 25% of patients with unilateral renal agenesis had urinary tract dilatation (hydronephrosis or megaureter) on the contralateral kidney, and one had dysplastic contralateral kidney. Right kidney anomalies are more frequent in our group. Unilateral right kidney anomalies represented 50% of all renal malformations. Left unilateral hydronephrosis is the most frequent anomaly regarding the urinary collecting system (51.98%).

CAKUT is more frequent in symptomatic male children compared to symptomatic female children. Male

pediatric patients with UTI symptoms should be further investigated for CAKUT. The diagnosis of VUR often follows the diagnosis of febrile UTI. According to NICE guidelines, children with atypical UTI or under the age of 6 months at their first UTI should have ultrasound of the urinary tract during the acute infection in order to identify eventual malformations of the urinary tract [14]. In case of atypical or recurrent UTI in children, with the suspicion of an underlying vesicoureteral reflux, micturition cystourethrogram is recommended to be performed [15]. The procedure should be performed on the second day of a 3 day antibiotic prophylaxis [15]. In our study VUR was identified in 41 patients out of 52 cystography performed.

Conclusions

The proportion of children with CAKUT is high among pediatric population. Positive prenatal ultrasound should be followed by a postnatal abdominal ultrasound examination in order to diagnose CAKUT and reduce the risk of complications. Early diagnosis of CAKUT using a simple abdominal ultrasound screening allows early and proper treatment and reduces the risk of parenchymal complications and CKD. Male pediatric patients that have UTI should be further investigated. Crucial for diagnosing VUR in complete flow of urinary bladder.

Abbreviations

CAKUT – Congenital Anomalies of Kidney and Urinary Tract
VUR – Vesico-Ureteral reflux
UTI – Urinary tract infection
CKD – Chronic Kidney Disease
URA – Unilateral renal agenesis
UTD – urinary tract dilatatition

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