*Urinary and Renal Research* (2022) Volume 3 Issue 2, 8 pages.
doi: 10.54517/urr.v3i2.2123

ORIGINAL RESEARCH ARTICLE

# Ultrasound screening and follow-up study of congenital anomalies of the kidney and urinary tract in neonates

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## ABSTRACT

**Objective:** To investigate the incidence of congenital anomalies of the kidney and urinary tract (CAKUT)in neonates, and to evaluate the value of urinary ultrasound screening in the early postnatal period. **Methods:** The neonates born or treated in Beijing Tsinghua Changgung Hospital affiliated to Tsinghua University between January 2016 and December 2018 accepted the urinary ultrasound screening, and the neonates with problem were followed up. In the meanwhile, the maternal pregnancy data were analyzed to screen out the risk factors associated with the onset of CAKUT. **Results:** (1)A total of 2655 neonates were screened by ultrasonography, of whom 82 neonates had been diagnosed with CAKUT (male: 60 cases, female: 22 cases), the positive rate was 3. 1% (82 /2655). There were 66 cases of hydronephrosis, 6 cases of duplicate kidney, 2 cases of multiple renal cysts, 2 cases of renal cystic dysplasia, 1 case of medullary sponge kidney, 3 cases of small kidney, 1 case of isolated kidney, and 1 case of horseshoe kidney. (2)Of the 66 children with hydronephrosis, 4 cases were lost to the follow-up; 8 cases were followed for less than six months with no significant changes found, and still in the follow-up observation; 54 cases were followed up for 1 year, among which 32 cases were returned to normal within 1 year, 3 cases were alleviated, 7 cases were aggravated, and 12 cases were unchanged. One case underwent surgery for repeated urinary tract infections and decreased renal function. (3)Abnormal fetal urinary ultrasound in the late pregnancy was found to be the most common in the high risk factors of CAKUT. There were 44 high-risk newborns with abnormal fetal urinary ultrasound, and 35 cases of CAKUT were diagnosed after birth. The incidence rate was 795% (35 /44). (4)Among the 2655 newborns screened, 2611 newborns had normal antenatal urinary ultrasonography. Among these neonates with normal urinary ultrasound during pregnancy, 47 cases of CAKUT were diagnosed after birth, with an incidence of 18% (47 /2611). **Conclusion:** The most common CAKUT in neonates is hydronephrosis and most cases with hydronephrosis had a good prognosis, but they should be followed up regularly. Urinary ultrasound screening for neonates, especially those high-risk neonates with abnormal fetal urinary ultrasound, has important clinical implications for the early detection of CAKUT.

***Keywords:*** anomalies; kidney and urinary tract; congenital; ultrasonography; neonates

**ARTICLE INFO**
Received: May 4, 2022 | Accepted: June 11, 2022 | Available online: June 30, 2022

**CITATION**
Li N, Ji L, Chao S et al. Ultrasound screening and follow-up study of congenital anom-alies of the kidney and urinary tract in neonates. Urinary and Renal Research 2022; 3(2): 8 pages.

# 1. Introduction

The concept of congenital malformations of the kidney and urinary tract (CAKUT) was first proposed by scholars in related fields in 1999. It refers to a series of diseases caused by various reasons and characterized by congenital anatomical abnormalities of the urinary system [1]. The clinical phenotype of CAKUT is diverse, including renal abnormalities (such as hydronephrosis, renal agenesis, polycystic renal dysplasia, solitary kidney, absence of kidney, duplication of kidney, ectopic kidney, horseshoe kidney, etc.), ureteropelvic abnormalities (such as megaureter, vesicoureteral reflux, ureteropelvic junction obstruction, ureterovesical junction obstruction, etc.), and bladder and urethra abnormalities (such as posterior urethral valve). The incidence of children's CAKUT is reported differently at home and abroad. Foreign studies have found that CAKUT accounts for 30%~40% of all congenital malformations in prenatal examination, and the incidence of CAKUT in healthy newborns and infants is 0.96%~4.10% [2–4]. There are few reports on the incidence of CAKUT in China. Most of the previous studies on CAKUT were conducted before delivery. During the "melamine milk powder incident" in 2008, many children's hospitals nationwide carried out large-scale ultrasonic screening of asymptomatic children's urinary system, screening a large number of children with CAKUT (1.67%~2.87%)[5–6], which caused concern about ultrasonic screening of postpartum children's urinary system. Sun Qi et al. [7] performed urinary system ultrasonic screening on 5428 newborns born in Ningbo Women and Children's Hospital in 2012, and found that the positive rate of CAKUT was 1.0%. In addition, ultrasonic screening of the urinary system was conducted for high-risk infants in some areas, and the positive rate of CAKUT was found to be as high as 5.65%~14.40% [8–10]. CAKUT often has no clinical manifestations in the early stage, and some patients may progress to end-stage renal failure, which is the main cause of end-stage renal disease in children and adolescents. At present, among the known causes of chronic kidney disease in children, CAKUT accounts for 50%~70% [11–12]. According to statistics, up to 47% of children receiving renal replacement therapy had the primary disease of CAKUT [13]. In addition, the probability of growth retardation, reproductive system abnormality and cardiovascular disease in children with CAKUT is also much higher than that in normal children of the same age [14]. Therefore, early detection of CAKUT and early intervention are of great significance to prevent its development into end-stage renal disease and improve the quality of life of children. This study is intended to understand the incidence and follow-up results of neonatal CAKUT by means of urinary system ultrasound screening and follow-up of neonates born in some areas of Beijing, evaluate the value of early post natal B-ultrasound screening of the urinary system, and analyze the risk factors related to the incidence of children's CAKUT, so as to achieve the purpose of early diagnosis, timely intervention and improved prognosis.

# 2. Data and methods

## 2.1. Screening objects

2655 newborns born and treated in Beijing Tsinghua Changgeng Hospital affiliated to Tsinghua University from January 2016 to December 2018 were selected as screening objects. This study was approved by the Ethics Committee of Beijing Tsinghua Changgeng Hospital affiliated to Tsinghua University (batch number: 20150911–06). Before ultrasonic examination, the guardians of all newborn infants signed the informed consent form of "cohort study on the incidence and risk factors of congenital renal and urethral malformations in children".

## 2.2. Methods

Within 28 days after birth, the patient was examined by a doctor at or above the attending level in the Ultrasound Department of Beijing Tsinghua Changgeng Hospital affiliated to Tsinghua University when his condition was stable. The B-ultrasound model Aplio300 (Toshiba Medical Equipment Company of Japan) was selected, and the probe frequency was 3.5~5.0MHz. The structure and morphology of

the kidney, ureter and bladder were observed in the supine position of the child. The maximum anteroposterior diameter of the renal pelvis in the transverse section was measured and recorded in the unfilled bladder state.

### 2.3. Diagnostic criteria and grading of hydronephrosis

There is still no unified international standard for the diagnosis of congenital hydronephrosis. After the 1990s, the anteroposterior dimension (APD) of the renal pelvis was considered to be the most sensitive diagnostic indicator of congenital hydronephrosis. Referring to the standard of literature [1516], this study takes the APD ≥ 7mm of the renal pelvis as the diagnostic standard of congenital hydronephrosis, and divides hydronephrosis into four grades: Grade I, only with the dilation of the renal pelvis of 7–11mm; Grade II, the dilatation of the renal pelvis extends to the renal calices, 11mm<the diameter before and after the separation of the renal pelvis ≤ 15mm; Grade III, dilatation of renal pelvis and calices, 15mm<diameter before and after separation of renal pelvis ≤ 21mm; Grade IV, the renal pelvis and calices are dilated, and the diameter before and after the separation of the renal pelvis is>21mm.

### 2.4. Analysis of high risk factors

According to the diagnostic criteria for high-risk neonates in Pediatrics (8th Edition)[17], the high-risk factors of children with positive CAKUT screened by B-ultrasound were analyzed to evaluate the risk factors related to the incidence of children with CAKUT.

### 2.5. Follow up

For children with CAKUT screened by B-ultrasound, it is recommended to continue to follow up in our hospital or go to a children's special hospital according to the patient's condition. It is recommended to have ultrasound and urine routine examinations every 3 months, and the follow-up time lasts for 1 year.

### 2.6. Statistical analysis

Use Epidata3.0 software to establish the database, and use double entry check and logical error detection methods to collate the data. SPSS20.0 software was used for statistical analysis. The mean of the two groups of data was compared by independent sample t test, and the rate was compared by $\chi$ 2 Test, $P<0.05$ indicates that the difference is statistically significant.

## 3. Results

### 3.1. Incidence rate of CAKUT and distribution of various malformations

Among 2655 newborns screened, 82 were positive, with a positive rate of 3.1% (82/2655), including 60 males and 22 females, with a male female ratio of 2.7 : 1. Among 82 cases of CAKUT, 66 cases were hydronephrosis, 6 cases were duplicate kidney, 2 cases were multiple renal cysts, 2 cases were cystic dysplasia, 1 case was medullary sponge kidney, 3 cases were small kidney, 1 case was solitary kidney, and 1 case was horseshoe kidney. The proportion of hydronephrosis was the largest, accounting for 80.5% (66/82), including 51 cases of grade I, 11 cases of grade II, 3 cases of grade III, and 1 case of grade IV. Hydronephrosis occurred on the left in 45 cases (68.2%, 45/66), on the right in 8 cases (12.1%, 8/66), and on both sides in 13 cases (19.7%, 13/66). The prevalence of left side was higher than that of right side and both sides. Among 13 children with bilateral hydronephrosis, 1 case was grade II hydronephrosis, 1 case was grade III hydronephrosis, and the other 11 cases were grade I hydronephrosis. There were 48 male children, the prevalence rate was 1.8% (48/2655), and 18 female children, the prevalence rate was 0.7% (18/2655). The prevalence rate of male children was higher than that of female children, with a statistically significant difference($\chi^2=5.97$, $P<0.05$).

### 3.2. Follow up results

Follow up and monitor the urine routine of children with CAKUT regularly, and recheck the urinary

system B ultrasound of children with hydronephrosis every 3 months. Among the 62 children with grade I and II mild to moderate hydronephrosis, 3 cases lost the follow-up. Up to now, 8 cases have been followed up for less than 6 months, and hydronephrosis has not changed significantly. During the follow-up, 51 cases have completed 1-year follow-up, of which 33 cases returned to normal or reduced, accounting for 64.7% (33/51). Among the three children with grade III hydronephrosis, one male patient (left renal pelvis dilated by 17mm, right renal pelvis dilated by 8mm) lost the follow-up, and two patients completed a one-year follow-up. One male patient (right renal pelvis dilated by 16mm) was followed up for half a year, and hydronephrosis disappeared at the age of half a year. The other male patient (left renal pelvis dilated by 16mm) suffered from urinary tract infection at 5 months after birth. After anti infection treatment, parents were recommended to further perform angiography to exclude obstruction and reflux, Concerned about invasive operation and radiation exposure, parents refused to check, and chose conservative treatment for observation. At 11 months, they suffered from urinary tract infection again. Monitoring ultrasound found that hydronephrosis was aggravated (left renal pelvis was expanded by 21mm) with thinner renal cortex. Parents agreed to conduct intravenous pyelography and enhanced CT examination. The results showed that the left renal pelvis ureter junction was narrow, and nuclide scanning showed that the left renal divider function was reduced. Therefore, at the age of 1, they underwent surgical treatment of amputated pyeloureteroplasty, the urine routine test was normal after the operation. One year after the operation, the ultrasound showed that the left renal pelvis expansion was reduced to 12 mm, and the radionuclide showed that the left renal function was improved. One child with grade IV hydronephrosis (left renal pelvis dilated by 22mm) had less hydronephrosis at the age of 1 year (left renal pelvis dilated by 16mm). The urine routine test and renal function were normal. The urine routine test was normal in the follow-up of other types of children with CAKUT.

### 3.3. Analysis of B-ultrasound results of urinary system in high-risk neonates

There were 44 high-risk neonates with abnormal fetal urinary system revealed by maternal ultrasound during pregnancy, and 35 cases of CAKUT were found by postnatal screening, including 28 cases of hydronephrosis, 3 cases of duplicate kidney, 2 cases of cystic renal dysplasia, 1 case of multiple renal cyst, and 1 case of solitary kidney. The incidence of urinary system malformations in high-risk neonates was 79.5% (35/44).

### 3.4. Analysis of B-ultrasound screening results of postnatal urinary system in neonates with normal prenatal ultrasound examination

Among 2655 neonates screened this time, 2611 neonates had normal prenatal ultrasound examination of urinary system. Among these neonates with normal prenatal ultrasound examination of urinary system, 47 neonates with CAKUT diagnosis were screened by postnatal ultrasound of urinary system, including 38 hydronephrosis, 3 duplicate kidneys, 1 multiple renal cyst, 1 medullary sponge kidney, 3 small kidneys, and 1 horseshoe kidney. The diagnostic rate of CAKUT in postpartum ultrasound was 1.9 : 1 (82 : 44)higher than that in prenatal ultrasound screening. About 1.8% (47/2611) of the neonates with normal prenatal ultrasound examination of urinary system were screened by ultrasound, and CAKUT was detected.

### 3.5. Analysis of CAKUT high risk factors

The analysis of high risk factors in 82 children with CAKUT showed that 65 cases had high risk factors, including 35 cases of late pregnancy with abnormal fetal urinary system ultrasound, which was the most common high risk factor for children with CAKUT (53.9%, 35/65), followed by cesarean section (30.8%, 20/65), premature delivery (9.2%, 6/65), full-term baby (4.6%, 3/65), neonatal asphyxia (1.5%, 1/65), etc.

## 4. Discussion

CAKUT is one of the main causes of end-stage renal disease in children and adolescents. The onset of such diseases is hidden, and it is not easy to be found in the early stage. Once clinical symptoms occur, renal insufficiency, even renal failure and uremia often exist, requiring dialysis and renal transplantation treatment, which brings huge harm and economic burden to children and families, including obstructive kidney disease, such as severe hydronephrosis caused by various reasons, It is a common and important type of CAKUT and also the main cause of chronic renal failure in children. Therefore, early detection and treatment of CAKUT is expected to avoid the occurrence of obstructive kidney diseases such as severe hydronephrosis as far as possible, which is expected to reduce and prevent the occurrence of chronic renal failure caused by CAKUT. Prenatal ultrasound screening of fetal CAKUT was proposed and implemented as early as 1981 [18]. The results of color Doppler ultrasound examination of 11753 pregnant women by Zhang Xiaoying et al. [19] showed that color Doppler ultrasound has high sensitivity and specificity in diagnosing fetal urinary system abnormalities, and is a safe, non-invasive, simple, accurate and reliable prenatal diagnostic method. At present, a considerable number of economically developed countries have or are carrying out screening and prevention of chronic kidney disease in children, so as to achieve early detection, early diagnosis, early intervention and early treatment.

Foreign research data show that hydronephrosis is the most common in CAKUT, accounting for 60.0%~93.6% [20]. This study found that 66 out of 82 children with CAKUT had hydronephrosis, accounting for 80.5% of all children with CAKUT, which was consistent with the results reported above. Among them, males are significantly higher than females, with the ratio of males to females being 2.7:1, which is similar to the 2.4:1 reported by Broadley et al. [21]. With regard to the high incidence of hydronephrosis in male infants, it is currently believed that it may be the anatomical cause. Male fetuses have higher urination pressure in utero than female fetuses, which is easy to cause distortion and deformation of the ureter bladder junction, which can lead to dilatation of the ureter and renal pelvis [22]. This study found that left kidney hydronephrosis was more than right kidney, and the ratio of left kidney hydronephrosis to right kidney hydronephrosis was 6.4 : 1, which was consistent with the fact that left kidney hydronephrosis accounted for 88% of hydronephrosis in newborn health examination reported by Miyakita et al. [15] of Japan, and its cause was still unclear.

Woodward et al. [23]'s research on neonatal and fetal hydronephrosis shows that 48% of them are transient hydronephrosis, 15% are physiological hydronephrosis, 11% are obstruction of the ureteropelvic junction, 9% are vesicoureteral reflux, 4% are megaureterosis, 2% are duplicate kidneys, and 1% are posterior urethral valves. The remaining causes are unknown, indicating that 63% of cases can recover by themselves. Liu Liping et al. [16] in China followed up and observed that hydronephrosis in neonates found that most of the cases with hydronephrosis in grade I and II naturally subsided or alleviated within two years; Children with grade III hydronephrosis may have gradually increased or little change in hydronephrosis, while children with grade IV hydronephrosis may cause progressive damage to renal function, and should be operated in time. In this study, grade I and grade II mild to moderate hydronephrosis accounted for 93.9% of the total hydronephrosis cases, and 64.7% returned to normal or the degree of hydronephrosis decreased during follow-up. One case of grade III hydronephrosis returned to normal, and one case of hydronephrosis was aggravated due to repeated urinary system infection, and renal function was decreased. The surgery was performed with amputated pyeloureteroplasty. One case of grade IV hydronephrosis was relieved during follow-up. It can be seen that hydronephrosis in neonates is mostly mild to moderate hydronephrosis, and most of them can recover to normal or reduce within one year after birth, but regular follow-up should be carried out to timely find pathological hydronephrosis caused by obstruction or reflux. At present, the gold standard for the diagnosis of vesicoureteral reflux is micturition cystourethrography. However, given that children with

low reflux grade may be self-healing without any intervention, a balance should be found between cases requiring immediate inspection and intervention and avoiding excessive diagnosis and treatment. In 2011, the American Academy of Pediatrics recommended that only urography should be used for the first evaluation of febrile urinary tract infection, and urination cystourethrography should be used only when the urinary system infection or ureterectasis is repeated, and ultrasound finds kidney abnormalities. Therefore, attention should be paid to the discovery and follow-up of neonatal hydronephrosis. For moderate and severe hydronephrosis that continues to not alleviate or gradually worsens, or urinary tract infection occurs, Imaging examinations such as radiography and radionuclide scanning should be carried out in time to assess the cause of hydronephrosis and renal function, and surgical treatment should be carried out as early as possible when necessary [2425].

In addition to hydronephrosis, 82 children with CAKUT found in this study also included 6 cases of duplicate kidney, 2 cases of multiple renal cysts, 2 cases of renal cystic dysplasia, 1 case of medullary sponge kidney, 3 cases of small kidney, 1 case of solitary kidney, and 1 case of horseshoe kidney. If early screening is not carried out for such CAKUT malformations, once clinical symptoms such as proteinuria, hypertension, anemia, etc. occur, they are often accompanied by renal insufficiency or even renal failure, Therefore, ultrasound screening is helpful for early diagnosis, early strengthening of renal function protection, careful use of nephrotoxic drugs, close follow-up of renal function and renal ultrasound changes, and consideration of surgical treatment when necessary to maximize the improvement of residual renal function, which has a positive role in improving the prognosis.

Among the high risk factors for the occurrence of CAKUT, the abnormality of fetal urinary system ultrasound in the third trimester of pregnancy is the primary high risk factor, accounting for 53.9%. Therefore, prenatal ultrasound diagnosis of fetal urinary system abnormalities is very important, which provides diagnostic basis for fetal prognosis judgment and early clinical measures, and also has important clinical value for eugenics. This study found that cesarean section, premature delivery, full-term small sample infants, neonatal asphyxia, etc. are also high-risk factors of CAKUT. Considering that there may be congenital deficiency factors with premature delivery and full-term small sample infants, some of the asphyxiated children have been in utero for a certain time and degree of hypoxia, which affects their development, but the correlation between these factors and CAKUT is not very clear, and further clinical research with a larger sample is needed.

Although prenatal ultrasound screening for CAKUT has been very common, it has not yet formed a routine in neonatal ultrasound screening for CAKUT, and research data on the incidence of CAKUT and follow-up outcomes are still limited. Foreign research data shows that [26], even if the same batch of newborns, the diagnostic rate of the CAKUT of postpartum ultrasound is 1.6 : 1 (61 : 38)higher than that of prenatal ultrasound screening. Tsuchiya et al, About 1.8% of newborns were detected to have CAKUT. Therefore, in addition to strengthening prenatal ultrasound screening for fetal CAKUT, it is also very necessary to routinely conduct urinary system ultrasound screening and follow-up in postpartum newborns. The treatment and management of CAKUT should run through pregnancy, neonatal period and even childhood. Based on fetal medicine, it should be combined with the participation of obstetrics, pediatric nephrology, pediatric urology, pediatric surgery and neonatology to provide a more effective program for the diagnosis and intervention of CAKUT in the near and long term.

The main management strategies of CAKUT should include: (1)establishing detailed prenatal counseling, and reducing the birth of severe congenital urinary system malformations through the inquiry of parents' medical history and gene examination; (2)Early diagnosis, intervention and treatment of the malformations that have occurred; (3)Try to slow down the development of CAKUT to chronic

kidney disease [28]. Some regions in Japan have carried out ultrasonic screening of the urinary system for infants at the age of one month and formed a set of screening standards, which has proved that such early screening is effective and has great social benefits [29]. At present, some regions in China have carried out ultrasonic screening of urinary system malformations in high-risk infants, and the three-level referral system of ultrasonic screening is gradually improving [30]. However, due to the large population and the large number of newborns in China, the cost-benefit problem needs to be considered for routine ultrasonic screening of urinary system in all newborns. At present, more research data related to ultrasonic screening of urinary system need to be supported.

This study found that the incidence of neonatal CAKUT was relatively high, accounting for 3.1% of the screened newborns. The most common CAKUT was hydronephrosis, which was mainly grade I and II mild to moderate. The left side of men was prone to occur, and most of the prognosis was good. Hydronephrosis gradually reduced or disappeared, but children with hydronephrosis above grade III might further aggravate, and irreversible renal function damage occurred. Other types of CAKUT include duplicate kidney, multiple renal cysts, renal cystic dysplasia, medullary sponge kidney, small kidney, solitary kidney, horseshoe kidney, etc. The abnormality of fetal urinary system ultrasound in the third trimester of pregnancy is the primary high risk factor of CAKUT. At the same time, the neonates with normal B ultrasound in maternal pregnancy also do not rule out CAKUT. Therefore, the ultrasound screening of the urinary system for neonates, especially the high-risk neonates with abnormal fetal urinary system ultrasound in maternal pregnancy, has important clinical significance for the early detection of CAKUT. All screened children with CAKUT should be followed up regularly to actively control and prevent infection, use nephrotoxic drugs cautiously, protect renal function, and perform early surgical intervention when necessary to maximize the prognosis.

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