Prevalence of recurrent urinary tract infection in children with congenital anomalies of the kidney and urinary tract (CAKUT)

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Abstract. Prevalence of congenital abnormalities varies from 3.5% up to 43% in pediatrics. This wide interval is due to limited numbers of research. Limitation of data on recurrent urinary tract infection in CAKUT infants as well as symptoms which resemble other diseases makes it quite a challenge. A study of the prospective cohort was established to analyze the prevalence of recurrent UTI among CAKUT in children at Neonatal and Nephrology Paediatric Department of H.Adam Malik Hospital from 2016 to 2017. Urinalysis and urine culture were used to assess the presence of UTI. The result showed that the prevalence of UTI in CAKUT patients reached 64% in which 52% is the obstructive type and 12% non-obstructive type. Pelvic ureteric junction obstruction is the most common cause. Children with known urinary tract problems such as CAKUT are very prone to developing recurrent UTI. Due to a low survival rate of children with ESKD, new strategies are needed to prevent CAKUT, preserve renal function, and reduce associated cardiovascular morbidity. Meanwhile, children with CAKUT requires a multi-disciplinary and longer follow up.

1. Introduction
Congenital anomalies of the kidney and urinary tract (CAKUT) are the spectrum of malformations that occur in the kidney, ureter, bladder, and urethra[1]. They represent a highly heterogeneous group, with a few being incompatible with life while minor abnormalities can be asymptomatic for long periods of time. Congenital abnormalities of the kidney and urinary tract have a high prevalence (3.5-43% in pediatric population)[2] and the most frequent cause (34-59%) of chronic kidney disease (CKD) in children[3].

Causes of CKD by CAKUT is reduced nephron numbers at birth and reduced acquired nephron loss[4]. Causes of CKD due to acquired nephron loss in childhood are most often. It came from urinary tract obstruction and infection (UTI). The high risk of UTI and obstructive uropathy against permanent kidney damage, leading to the management of these patients is the initiation of antibiotics and the elimination of obstruction. Therefore, it needs to make early diagnosis and initial therapy to minimize kidney damage, prevent or slow the onset of end-stage renal disease (ESRD) and provide supportive care for the prevention of ESRD complications.

Data on the prevalence of recurrent UTI in children with CAKUT is still limited. It is due to the lack of data about recurrent UTI in CAKUT infants and children because the symptoms of this disease
resemble another disease such as fever, vomiting, seizures and growth disorder. Therefore, this study aimed to analyze the prevalence of recurrent UTI from CAKUT in children.

2. Research Methods
This research is an analytic research with prospective cohort design, where the entire samples of research will be in following-up with the diagnosis of CAKUT group urinary tract malformation. The study was conducted in outpatient/inpatient clinics at Neonatal and Nephrology Paediatric Department of H.Adam Malik Hospital from 2016 to 2017.

The samples were all patients diagnosed with urinary tract malformations of the CAKUT diagnostic group including defects of the renal parenchyma documented by renal ultrasonography, voiding cystourethrogram (VCUG) and renal scan. The renal sonography was performed as soon as possible after diagnosis. VCUG was done at least one week after antibiotic therapy. The inclusion criteria were CAKUT children between 1 to 14 years old. Exclusion criteria were cases of pyelonephritis caused by another origin of CAKUT and urolithiasis.

Urinalysis and urine culture were used to assess the presence of UTI. The presence of UTI is the presence of significant bacteria with symptoms and sign of infection. The positive of urine culture was established as more than $10^5$/ml colony bacterial colonies in a specimen collected with a clean-catch urinary, more than $10^4$/ml from intermittent catheterization and any number of colonies from a suprapubic bladder aspiration. While for the sample research is part of the population who meet the criteria for inclusion, who went to H. Adam Malik hospital. All subjects will be asked for approval from parents after explanation.

The unpaired categorical analysis was used to estimate sample size. Total sampling was used to described sampling method. The data will be as frequency or percentage as appropriate.

3. Results
The study found that from a retrospective cohort study there were 31 children with CAKUT, consisting of 25 obstructive type children and six non-obstructive type children. When compared to all new cases in the nephrology of pediatric division of H.Adam Malik hospital for a year was 192 patients, so the prevalence of CAKUT a year was 16% with most cases being PUJO cases. Table 1 below describes the frequency of CAKUT abnormalities found during the study period.

| Renal diagnosis | Frequency (n) |
|-----------------|--------------|
| **Obstructive type** |             |
| PUV             | 7            |
| PUJO            | 11           |
| VUJO            | 7            |
| **Non-obstructive type** |     |
| Reflux          | 3            |
| Neurogenic      | 2            |
| Hypoplasia      | 1            |

PUV = Posterior Urethral Valve  
PUJO = Pelvic Ureteric Junction Obstruction  
VUJO = Vesica Ureteric Junction Obstruction

Table 2 below describes the subject characteristics data. Patients with male gender were 24 persons with mean glomerular filtration rate above 50 ml/minute/1.73 m$^2$.

| Variable | Obstructive type n= 25 | Non obstructive type n=6 |
|----------|------------------------|--------------------------|
| Age ± SD (years) | 8.9 ± 4.42 | 9.92 ± 2.42 |
Male gender (n)       20       4
Time suffered from CKD since early entry (years)       4.2       3.9
Mean basal GFR       52.8       55.4
Proteinuria (mg/mg)       0.25       0.28
Surgical cases (n)       10       3
Conservative cases (n)       15       3

The prevalence of UTI in CAKUT patients reached 64% consisting of 52% obstructive type and 12% non-obstructive type. This is in Table 3, where the PUJO situation is more frequent UTI.

|                  | UTI (+) | UTI (-) |
|------------------|---------|---------|
| PUV              | 5       | 2       |
| PUJO             | 7       | 4       |
| VUJO             | 4       | 3       |
| Reflux           | 3       | 0       |
| Neurogenic       | 1       | 1       |
| Hypoplasia       | 0       | 1       |
| **Total**        | **20**  | **11**  |

Table 3. Diagnosis associated with the occurrence of CAKUT.

One hundred and ten bacteria were isolated from 20 patients with 110 episodes of UTI. Microorganisms were causing UTI is from Table 4.

Table 4. Microorganisms causing urinary tract infection in CAKUT.

| Organism          | Total numbers (n=110) |
|-------------------|-----------------------|
| *Eschericia coli* (E.coli) | 48                    |
| *Klebsiella*      | 26                    |
| *Pseudomonas*     | 24                    |
| *Enterobacter*    | 12                    |

Table 5. Antibiotic sensitivity patterns.

| Organism          | Total numbers | AM   | MEM  | GM   | Cefo  | TMP  | AMOX |
|-------------------|---------------|------|------|------|-------|------|------|
| *Eschericia coli* | 48            | 48   | 45   | 48   | 42    | 41   | 45   |
| *Klebsiella*      | 26            | 24   | 21   | 21   | 20    | 18   | 19   |
| *Pseudomonas*     | 24            | 24   | 20   | 20   | 12    | 2    | 12   |
| *Enterobacter*    | 12            | 12   | 11   | 11   | 9     | 11   | 10   |

AM= Amikacin
MEM= Meropenem
GM= gentamycin
Cefo= Cefotaxime
TMP= Trimethoprim
AMOX= Amoxicillin
4. Discussion

Children with known urinary tract problems such as CAKUT are very prone to developing recurrent UTI. Previous studies on the prevalence of UTI in CAKUT patients ranged from 25-59\%\cite{5}. The prevalence of UTI in this study reached 64\%. It may be due to the average age of the CAKUT patients found to be detected at a relatively older age (except for PUV), and the CAKUT abnormality may persist until adolescence.

Urinary tract infection is responsible for approximately 20\% of ESRD in children. In young infants, three-fifths of all UTI is considered to be a risk factor for acquired renal damage and scarring. As a consequence, there is a belief that aggressive diagnostic workup is necessary to detect urinary tract malformation and VUR. Untreated high-grade VUR results in renal scarring, so any newborn with UTI, regardless of sex, should be presumed to have urinary obstruction or reflux and should have image studies to rule out these conditions. Further prophylactic management, either medical or surgical, is necessary to reduce the formation of renal scars and to preserve renal function\cite{6}.

Additional workup should be performed to confirm that culture-specific antibiotics are being used, that adequate drainage exists, and that the antibiotics reach all sites of bacterial infection\cite{7}. In our research, there was 110 episode of UTI with the amikacin antibiotic is most sensitive to the organism.

Surgical correction was performed in 13 patients and this was associated with UTI risk. The criteria for this action are recurrent UTI in children under one year, children with high and bilateral reflux levels, a worsening hydronephrosis condition (greater than 3 cm) accompanied by pain symptoms. Except for the PUV case, an early correction should be made\cite{6}. Most cases (18 cases) have not undergone surgery. The management of this group is conservative and tries to prevent kidney damage to terminal renal failure. The presence of recurrent UTI is one of the conditions that can aggravate kidney function, so the treatment is necessary for the patient to avoid dialysis.

Given that the survival rate of children with ESKD is about 30 times lower than that of healthy children\cite{8}, new strategies are needed to prevent CAKUT, preserve renal function, and reduce associated cardiovascular morbidity. In children with CAKUT requires long-term follow up multi-disciplinary cooperation. It led to more emphasis on teamwork than on professional work. Likewise in the prevention of UTI in CAKUT patients requires multi-disciplinary work including nephrologist, urologist, microbiologist and medical rehabilitation.
5. Conclusion
The prevalence of recurrent UTI in CAKUT patients was 64%. The average age of the CAKUT patients found to be detected at a relatively older age and the CAKUT abnormality may persist until adolescence. The presence of recurrent UTI is one of the conditions that can aggravate kidney function, so the recurrent UTI treatment is absolutely necessary for the patient to avoid dialysis.

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