The Correlation of Congenital Anomalies of The Kidney and Urinary Tract with Renal Function in Children

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Abstract

Background: Congenital Anomalies Kidney and Urinary Tract (CAKUT) are the leading cause of kidney failure in children and cause of 30-40% end-stage renal disease with obstructive uropathy as the main cause. CAKUT obstructive type are: *vesico uretric junction obstruction* (VUJO), *pelvic uretric junction obstruction* (PUJO), *posterior uretral valve* (PUV) and non-obstructive type are reflux, neurogenic and hypoplasia. The aim of this study is to describe the effect of CAKUT on renal function in child.

Methods: Retrospective study from medical records of children with CAKUT at Dr. Soetomo General Hospital, Surabaya, Indonesia from January 2013 - March 2018. The characteristic of sex, age range, type of CAKUT and glomerulus filtration (GFR) value were recorded from medical record. Data processing using descriptive analysis with SPSS.

Result: A total of 94 Children on CAKUT abnormalities, both boys and girl's presentation equal 50%. Median age 3.0 (minimum-maximum 1.0-15.0) year. The most common CAKUT type in male were VUJO 17 (36.2%) and in female neurogenic type 19 (40.4%). Median initial glomerular filtration rate 2.7 ml/ min/1.73 m^2. Analysis of correlation between CAKUT and renal function p=0.072 (R^2=0,03). From 94 children of CAKUT, only 12 (12.8%) patients have undergo surgical intervention.

Conclusion: CAKUT with dominant obstructive type was more common in male and non-obstructive type in female pediatric patient. There was no significance correlation of GFR between obstructive and non-obstructive type.

Keywords: *Kidney, Urinary tract, Children, CAKUT, GFR*

Introduction

Congenital Anomaly of Kidney and Urinary Track (CAKUT) has a broad clinical spectrum and phenotype with clinical manifestations of obstruction and non-obstruction through different mechanisms [1]. CAKUT is a disease that is mostly found in children with a prevalence of 16.3 per million children with an incidence of CAKUT of 3-6 per 1000 live births. [2,3]. One third of these diseases will develop into end-stage renal disease (ESRD) [1]. It is important to determine the estimation of kidney function for each patient with CAKUT in order to minimize the occurrence of kidney damage and suppress the complications of kidney failure by periodic evaluation of renal function and adequate therapy [4]. Kidney function is assessed by calculating the estimated glomerular filtration rate, which depends on how many nephrons are still functioning normally. Currently, CAKUT therapy is largely conservative and maintains kidney function. This study aims to analyze the relationship between CAKUT and a decrease in the Glomerular Filtration Rate (GFR) in children.

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Methods

This study was an observational analytic study with a cross sectional study design to determine the effect of CAKUT and kidney function in children.

Subject Criteria

The subjects of the study were 94 pediatric patients experiencing symptoms of kidney and urinary tract disorders in the Pediatric Nephrology Clinic, Dr. Soetomo General Hospital, Surabaya in the period January 2013 - March 2018 using total sampling. All subjects who met the selection criteria (inclusion and exclusion) were included in the study. The inclusion criteria in this study included: age 1 month to 18 years, Fulfilling the diagnosis of CAKUT, there are results of renal function tests to determine the glomerular filtration rate. The exclusion criteria in this study were incomplete medical document data. Data from ultrasound results and kidney function tests were taken from the patient's medical records.

GFR calculation based on serum creatinine, age, body size, sex was calculated according to the formula [5]. CAKUT criteria were congenital abnormalities of the kidney and urinary tract, both structural and functional, which could occur in the kidneys, calix system, bladder, or urethra, as evidenced by urological ultrasound results [6].

Data Analysis

To test the correlation of CAKUT on both obstructive and non-obstructive kidney function, the simple liner regression test was used. Simple liner regression test is a test for correlation with categorical variables, if $p < 0.05$, a relationship between CAKUT and glomerular filtration rate was obtained.

Result

The results of this study indicate the characteristics of CAKUT patients as a whole, the sex and type of CAKUT have the same percentage, 50% each group. The most age is less than 5 years. The types of CAKUT in this study were divided into obstruction and non-obstruction types, the most subject type of CAKUT was the vesico uretro junction obstruction (VUJO) type followed by the pelvic uretro junction obstruction (PUJO) and the Posterior Uretral Valve (PUV) type, for the non-obstruction type respectively neurogenic followed by hypoplasia and reflux last (Table 1).

Table 1. Basic characteristics of subject

Variable				n (%)
Age (year), median (min-max)				5,0 (1,0-18,0)
Age at baseline (years), median (minimum-maximum)				3,0 (1,0-15,0)
Age (year), n (%)				
< 5 years old				41(43,6)
5-10 years old				36(38,3)
> 10 years old				17(18,1)
Sex, n (%)				
Male				47(50.0)
Female				47(50.0)
Type of CAKUT, n (%)				
Obstruction (n,%)	VUJO	PUV	PUJO	48(51,0)
				26(27,7)
				1 (1,1)
Non-obstruction (n, %)	Neurogenic			21(22,3)
	Hypoplasia			46(48.0)
	Reflux			28(29.8)
Therapy, n (%)				13(13,8)
Operative				5(5,3)
Conservative				12(12,8) 82(87,2)

The median GFR value in the obstruction CAKUT group was lower than that in the non-obstructed group. GFR values in CAKUT overall median were 102 (Minimum 2.7 - Maximum 269.0) ml / minute / 1.73 m2 (Table 2).

Table 2. Characteristics of GFR values in CAKUT

CAKUT	Median (Min-Max) (ml / menit / 1,73 m2)
Obstruction	98 (6.0 – 209.0)
Non-obstruction	103 (2.70 – 269.0)

In this study, based on the Kolmogorov-Smirnov test, it was obtained p <0.05, which indicates that the data distribution was normal. The simple linear regression test results obtained R2 = 0.035 and p = 0.072. p value was stated to be significant if p <0.05 so there was no relationship between glomerular filtration rate and obstruction and non-obstruction.

Discussion

The types of CAKUT in this study were divided into obstruction and non-obstruction types, where the obstruction type was divided into vesicoureteral junction obstruction (VUJO), pelvic-ureteric junction obstruction (PUJO), posterior urethral valve (PUV) and non-obstruction type divided into reflux, neurogenic and hypoplasia. The most obstruction group was VUJO type with 26 (27.7%), followed by PUJO type with 21 (22.3%) and PUV 1 type (1.1%). CAKUT was the most neurogenic type of non-obstruction group with 28 (29.8%), followed by hypoplasia 13 (13.8%) and reflux 5 (5.3%).

In contrast to the study from Soliman et al., 2015 showed PUV was the most common disorder found (36.4%), followed by VUR (19.6%), then PUJO (18.7%) [7]. Another study reported PUJO (62.7%) and VUR (16.6%). In a recent study from Radhakrishna et al., 2019, it was shown that although the majority of CAKUT has evidence of antenatal hydronephrosis, CAKUT sufferers begin to show symptoms of delayed presentation of various CAKUT, especially PUV and PUJO [8].

Characteristics of the GFR value in CAKUT each obstruction group median was 98 (Minimum 6.0 - Maximum 209.0 ml / minute / 1.73 m2) and the non-obstruction median group was 103 (Minimum 2.70 - Maximum 269.0 ml / minute / 1.73 m2). In this study, there was no significant difference in GFR values in each CAKUT group. In this study, it was found that there was no relationship between obstruction and non-obstruction of GFR (p = 0.072). CAKUT in children with stage 2 and 3 CKD has a high incidence of terminal renal failure over 5 years. Kidney anatomy abnormalities are more common than lower urinary tract disorders and often cause terminal renal failure [9]. The longer a patient suffers from CAKUT, the more likely it is to suffer from various diseases [10].

A study from Radakhrisna et al., 2019 in 81 children with CAKUT, there were 27% of children with hypertension, this group had a lower GFR value than the non-hypertensive group, but this result was not statistically significant, suggesting that the etiology of hypertension is multifactorial and not. depending on the level of renin plasm [8]. The number of functional nephrons formed at 32 to 34 weeks of pregnancy determines kidney function. Nephrogenesis stops after 34 weeks of gestation. The growth of the renal tubules and the expansion of the glomerular cross-sectional area increases the functional capacity of the kidney. The increase in glomerular base surface area after birth contributes to an increase in the glomerular filtration rate during infancy, childhood and adolescence. Reduced nephron count was associated with adult-onset hypertension. In severe dysplasia, it indicates renal insufficiency, whereas in renal dysgenesis disorders, it occurs at the level of tubule number, cross-sectional area, and renal cell maturation. Abnormal tubular differentiation such as kidney dysplasia limits the capacity of the kidneys to concentrate urine, absorb sodium and secrete potassium so that electrolyte imbalance will occur [6].

In this study, the research sample and kidney function, in this case the GFR data, were only taken once when the patient first came to the pediatric nephrology clinic, so that the average sample still had good kidney

function. This study did not assess the frequency of incidence of UTI, hypertension and proteinuria which can complicate children with ACE and have an effect on glomerular filtration rate. There is a strong relationship between CAKUT and chronic kidney disease, where the incidence of recurrent UTIs in the presence of functional morphological anomalies can lead to CKD. This was not done because of limited research time.

The benefit of this research was to know kidney function through glomerular filtration rate to determine the degree of severity or decrease in kidney function in CAKUT patients then kidney function evaluation and optimal therapy are given to minimize the occurrence of kidney damage and avoid complications of kidney failure

Conclusion

CAKUT with dominant obstructive type was more common in male and non-obstructive type in female pediatric patient. There was no significance correlation of GFR between obstructive and non-obstructive type.

Conflict of Interest : None declared.

Source of Funding : The authors received no specific grants from any funding agency in the public, commercial, or not-for-profit sectors.

Ethical Clearance : Approved by the Health Research Ethics Committee of the Dr. Soetomo General Hospital, Surabaya No. 0225/KEPK/IV/2018

References

1. Hiraoka M. Medical management of congenital anomalies of the kidney and urinary tract. Pediatrics international : official journal of the Japan Pediatric Society. 2003;45(5):624–33.
2. Fletcher J, Mcdonald S. Prevalence of genetic renal disease in children. 2013;251–6.
3. Yosypiv I V. Congenital Anomalies of The Kidney and Urinary Tract: A Genetic Disorder? International Journal of Nephrology. 2012;2012:1–11.
4. Sanna-Cherchi S, Ravani P, Corbani V, Parodi S, Haupt R, Piaggio G, et al. Renal outcome in patients with congenital anomalies of the kidney and urinary tract. Kidney International. 2009;76(5):528–33.
5. Pardede SO, Chunnaedy S. Penyakit Ginjal Kronik pada Anak. Sari Pediatri. 2009;11(3):199–203.
6. Sahay M. Congenital anomalies of kidney and urinary tract (CAKUT). Clinical Queries: Nephrology. 2013 Oct;2(4):156–65.
7. Soliman NA, Ali RI, Ghobrial EE, Habib EI, Ziada AM. Pattern of clinical presentation of congenital anomalies of the kidney and urinary tract among infants and children: Clinical phenotypes of CAKUT. Nephrology. 2015 Jun;20(6):413–8.
8. Radhakrishna V, Kumaravel S, Priyamvada PS, Hanumanthappa N, Jindal B, Govindarajan K, et al. Clinico-Biochemical Profile of Children with Congenital Anomalies of the Kidney and Urinary Tract: A Cross-Sectional Study. Kidney Diseases. 2019;5(1):51–7.
9. Rodriguez MM. Congenital Anomalies of the Kidney and the Urinary Tract (CAKUT). Fetal and Pediatric Pathology. 2014 Oct;33(5–6):293–320.
10. Renkema KY, Winyard PJ, Skovorodkin IN, Levtchenko E, Hindryckx A, Jeanpierre C, et al. Novel perspectives for investigating congenital anomalies of the kidney and urinary tract (CAKUT). Nephrology Dialysis Transplantation. 2011 Dec 1;26(12):3843–51.