

Original Research Article

Radiological Characteristic in Children with Urinary Tract Infection in Hasan Sadikin General Hospital Bandung

ABSTRACT

Neglected urinary tract infection can be a potent contributor to chronic kidney disease later. The aim of this study is to describe the radiological findings in children with urinary tract infection (UTI). We retrospectively analyzed medical records of children with UTI in 2019 – 2021 period at Hasan Sadikin Hospital who performed radiological examination including kidney ultrasound, CT-scan, mictio cystourethrography (MSU), and MRI. Demographic and radiological characteristics of investigations were assessed. Of 74 patients with abnormalities, 45.9% found in 2019. There are 42 patients aged 1 – 3 years, 15 aged 2 – 5 years, and 3 aged 28 days to 1 year. Male patients dominated most of the cases (51.4%) with most of the patient undergo renal ultrasound (RUS) as much as 98.6% followed by MRI. Thickening of the bladder, hydronephrosis, and other abnormalities i.e., duplicating of ureter, vesico-ureteral reflux, and duplicating of collecting system were found in 54, 17, and 6 children respectively. UTI is more common in children aged 1 – 3 years, particularly in boys. Abnormalities finding profoundly in RUS examination. Thickening of the bladder is detected in more than half of the children followed by hydronephrosis and other abnormalities.

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INTRODUCTION

Urinary tract infection (UTI) is a bacterial infection that often occurs in children in both developed and developing countries.¹ UTI, especially recurrent ones, has a high rate of complications against kidney scarring, hypertensive crisis, and most often is chronic kidney disease (CKD).^{1,2} Data published by the US Renal Data System found that 3.5% of patients with chronic pyelonephritis had End-stage kidney disease (ESKD). Meanwhile, the prevalence of hypertension in UTI patients can vary greatly from 1.2% to 35%.³ The impact of this UTI will have a high economic impact. In 2011 Simmering et al. found that the economic burden arising from the treatment of UTI reached 43,596,140,000 rupiah. This economic burden has increased by 52% since 1998.⁴

The prevalence of urinary tract infections (UTIs) is influenced by factors such as gender, age, race, and circumcision status. UTIs are found in 8.4% of girls and 1.7% of boys by the age of seven. The incidence of UTIs peaks during three periods: infancy, toilet training, and the onset of sexual activity (in girls). Key risk factors for UTIs in children include being female, younger age, white race,

being an uncircumcised infant boy, the duration of fever, high-grade vesicoureteral reflux (VUR), a history of UTIs, congenital anomalies of the kidney and urinary tract (CAKUT), bowel and bladder dysfunction (BBD), spinal dysraphism, and the use of an indwelling bladder catheter. In older children and teenagers, additional risk factors include sexual activity, pregnancy, kidney stones, immune deficiencies, and diabetes. The prior use of antibiotics, especially penicillin or ampicillin, also raises the likelihood of developing a UTI⁵⁻⁷.

Recurrent UTIs are generally caused by complicated factors that involve anatomical or physiological disturbances. Comorbid diseases in complicated UTIs that cause disturbances in the flow of urine in the form of vesicourethral reflux or urinary vesica dysfunction cause the urinary tract to be more susceptible to bacterial infections.¹ A total of 248 patients who had episodic UTIs had comorbidities in the form of VUR, thickening of the urinary vesica wall, and decreased urinary vesica function.⁸ In determining the risk factors, comorbidities, or causes of UTI complications is certainly necessary radiological examination. In addition, radiological examination becomes important to determine the incidence of complications in patients and of course determine the importance of intervention or treatment needed.⁴ total of 75 infants of 224 children less than 3 months of age who developed bacteremia in the US were found to have abnormalities in the MSU results. In addition, 69 out of 75 babies had VUR.

In general, pharmacological therapy in some cases of complicated urinary tract infections such as VUR or urolithiasis has less effective results due to resistance.⁹ Patients who underwent open surgery had a 98% success rate in healing patients.² In addition, patients with calculi who performed lithotripsy had improved quality of life, decreased the incidence of complications, and improved healing.¹⁰ Therefore, surgical correction can have a good prognosis in patients with complicated UTIs, especially those with anatomical structural abnormalities.

Urinary tract infections are often considered trivial, even though UTIs can cause VUR and nephrolithiasis, hence the risk of recurrent UTI becomes higher than before. This increased risk of recurrent UTI will also raise the risk of pyelonephritis, thereby increasing the risk of kidney scarring. Once kidney scarring occurs, the risk of developing hypertension and CKD also increases. The two risk factors identified as having the highest recurrence rate over two years are VUR and BBD, with their combination resulting in an even greater risk⁶. The neglected abnormalities associated UTI complications in children have a prolonged impact even functionally, anatomically, or decreased quality of life. Hence, it is important to describe the radiological picture in children with UTI, so that it can provide information about the proportion of abnormalities in the structure of the kidneys and urinary tract in children with UTI. This can then be used as a reference on the importance of conducting radiological examinations in children with UTIs for screening for complicated UTIs.

Historically, most children diagnosed with a UTI underwent various radiological tests, such as ultrasound, voiding cystogram, scintigraphy, urography, CT scans, or MRI, to identify urinary malformations that could lead to lasting kidney damage. While it is established that a UTI can result in kidney scarring, it is often the case that parenchymal damage is either congenital or caused by significant obstruction¹¹. The guidelines for conducting an ultrasound of the urinary system (KUS) after a febrile urinary tract infection (UTI) vary. Some recommend performing a KUS in children younger than 2 years, while others limit it to those under 6 months or suggest it only when additional risk factors are present, such as UTIs caused by unusual pathogens or recurring UTIs¹¹. A voiding cystourethrogram (VCUG) is a diagnostic procedure that can identify vesicoureteral reflux (VUR), urethral valves, or bladder irregularities. This test is typically conducted in young children after a febrile urinary tract infection (UTI) if the ultrasound results are abnormal or if the infections occur repeatedly^{11,12}.

Renal imaging using a radionuclide dimercaptosuccinic acid (DMSA) scan can confirm pyelonephritis or identify renal scarring. For the former, the scan should be conducted within a week after a febrile urinary tract infection (UTI), while for the latter, it should be done 6 to 12 months later. The DMSA scan can also aid in diagnosing congenital renal hypodysplasia, which appears differently from acquired scarring. Guidelines on UTIs vary regarding the recommendation of a DMSA scan; some do not suggest it, whereas others recommend it for atypical infections or high-grade vesicoureteral reflux (VUR). A retrospective study indicates that deep learning (DL) could potentially distinguish between normal and abnormal kidneys in children using 99mTc-DMSA SPECT imaging^{11,13}.

Computed tomography (CT) offers high-resolution imaging of the urinary system. While sedation is generally unnecessary, intravenous contrast is typically required. A significant concern with CT is radiation exposure, so its application should be restricted to situations where it is crucial for confirming a diagnosis. Recently, a retrospective study assessed the effectiveness of non-contrast CT in diagnosing acute pyelonephritis in older adults; a future prospective study could be conducted in

children^{11,14}. Magnetic resonance studies (MRU) are generally not advised for children with UTIs because they require sedation. However, in the future, MRUs might become more accessible and affordable. In certain situations, MRU could be a preferable option since it does not involve radiation exposure^{11,15}. Urodynamic studies (UDSs) help in detecting bladder dysfunctions, which play a significant role in causing UTIs and renal scars in children with VUR¹⁶.

METHODS

The study subjects were children aged 0 to 18 years who were diagnosed with a UTI in Hasan Sadikin General Hospital (HSGH) between January 2019 and December 2021 and underwent radiologic examination. We enrolled the samples from the medical record. The inclusion criteria are: Children aged 0 to 18 years who are diagnosed with UTI via urinalysis; patients with structural and functional urinary tract abnormalities or the presence of foreign bodies in the urinary tract, and patients who undergo at least one of the following examinations: USG, MSU (miksio-cystourethrography), CT, or MRI are all eligible for the study. The data taken from medical records obtained included demographic data (sex and age) and radiological characteristics of the urinary tract, such as hydronephrosis, hydroureter, pyelonephritis, and thickening of the urinary bladder.

This is a descriptive, cross-sectional study performed by analyzing medical records of UTI patients. Microsoft® Excel 365 was used to analyze the data, which will be presented as tables and categorical data in numbers and percentages. Researchers have already obtained an ethical exemption letter from Universitas Padjajaran's Ethics Committee number 1133/UN6.KEP/EC/2022 and research permit letter from HSGH number LB.02.01/X.2.2.1/25250/2022.

RESULT AND DISCUSSION

From the total of 416, only 74 data points were collected, and the rest were excluded, because of the incomplete data.

Table 1 Case Distribution of Children with UTI in 2019-2021

Incidence year	n (%)
2019	34 (45.9)
2020	17 (23)
2021	23 (31.1)
Total	74 (100)

Table 1 shows that most patients with abnormalities of the urinary tract were diagnosed in 2019 (45.9%), followed by 2021 (31.1%), and 2020 (23%). There are 42 patients aged 1 – 3 years, 15 aged 2 – 5 years, and 3 aged 28 days to 1 year. From this information (table 1 and table 2), along with the increase in age, the incidence of UTI is gradually decreasing. Male patients dominated most of the cases (51.4%), while females made up 48.6%. Most of the patients undergo USG (98.6%), and 3 out of 74 patients go through MRI examination. None of the data came from MSU (miksio-cystourethrography) or renal CT-scan examination (Table 2).

Table 2 Demographic Data

Characteristics	n (%)
Age	
0-28 days	0
28 days-1 years	3 (4.1)
1-3 years	42 (56.8)
3-5 years	15 (20.3)
5-10 years	8 (10.8)
10-18 years	6 (8.1)
Sex	
Male	38 (51.4)
Female	36 (48.6)

Characteristics	n (%)
Type of radiological examination	
USG	73 (98.6)
Mikcio-cystourethrography (MSU)	0
Renal CT-scan	0
MRI	1 (1.4)
USG, ultrasonography; MSU, mictiocyctourethrography	

Table 3 shows that eight patients have two or more abnormalities. The abnormalities found in these patients are a combination of hydronephrosis, hydroureters, thickening of the bladder, and/or other diseases, i.e., duplicated bladders, vesicoureteral reflux, double collecting systems, and calculus obstruction. Acute pyelonephritis has not been found in all patients. Moreover, in children aged 3 – 5 years and 5 – 10 years, hydroureter, hydronephrosis, and nephrolithiasis were not found. Only bladder thickening was observed in patients aged 28 days to one year. Most cases found in the radiologic exam are thickening of the bladder (n = 54), hydronephrosis (n = 17), and others (n = 6). Ages 1 – 3 years old have the most frequent cases of thickening of the bladder and hydronephrosis, and ages 5 – 10 years old have the most frequent cases of other abnormalities. Based on sex, boys have a higher tendency of abnormalities than girls.

According to the radiological findings, the thickening of the bladder is higher in girls, and hydronephrosis is more common in boys. This is not consistent with previous studies which stated that UTIs are more common in girls. However, this may occur because HSGH is a referral hospital, so children referred with complicated UTIs happen to be mostly boys. Data on the distribution of UTIs in children at primary and secondary health centers need to be studied.

Table 3 Patients Characteristics

Variable	Hydronephrosis (n)	Hydroureter (n)	Acute Pyelonephritis (n)	Nephrolithiasis (n)	Thickening of Bladder (n)	Other
Age						
0-28 days	0	0	0	0	0	0
28 days-1 years	0	0	0	0	3	0
1-3 years	10	1	0	1	33	1
3-5 years	3	0	0		11	2
5-10 years	1	0	0	0	5	3
10-18 years	3	2	0	1	2	0
Total	17	3	0	2	54	6
Sex						
Male	9	3	0	1	27	3
Female	7	0	0	1	28	3
Total	16	3	0	2	55	6

Two similar studies have been found, one of them in low-birth-weight patients. The sex demographic findings in this study correspond to those found at Songklanagarind Hospital in Southern Thailand.¹⁷ It has been shown that men are more likely to experience abnormality (68.4%), whereas this study discovered 51.4%.¹⁸ In another study, the number of UTIs occurring in men is getting higher (76%). This is because the study's mean age was infants (27.7 ± 2.9 weeks), and the prevalence of UTI is highest in men during the first year of life.^{3,19}

Children aged 1 – 3 years tend to have more UTIs (56.8) than children above 3 years old. Our findings are consistent with previous research that explains why UTI is most common in children under the age of two, particularly boys.¹⁷ Meanwhile, in Iraq, there are slightly different rates of UTI in children aged 6–10 years (47%).²⁰ This difference might be a result of the population study in Iraq that is being conducted in a city.²⁰ Furthermore, the methods used in those studies calculated the prevalence of UTI in all children at risk.²⁰ As a result, the findings are based on children diagnosed with UTI in a large population that includes healthy patients. Children under the age of 5 have a higher tendency towards congenital anomalies of the kidney and urinary tract (CAKUT). Monitoring the growth and development of children at this age is very important as a primary prevention effort for CKD. The potential for CKD can be seen from weight and height not increasing, which in this case is related to UTIs with symptoms that are difficult to be detected by the parents. Early detection of UTIs will impact early management, thereby preventing kidney scarring associated with UTIs.

The majority of UTI cases occur in 2019, then decrease significantly in 2020, becoming 17 cases (23%). The year 2020 coincides with the peak of the COVID-19 pandemic in Indonesia and most countries. The COVID-19 pandemic has an impact on both the psychology and health of patients and their parents. This pandemic has made patients afraid to check their health, either in clinic or hospital settings. A shift in patient behavior could contribute to an increase in the number of undiagnosed cases. Another factor, such as improved hygiene among many people, may reduce the prevalence of UTI in the pandemic.²¹ Our findings are consistent with a study in Finnish which incidence of cystitis and pyelonephritis decreased by 12% and 16%, respectively during the COVID-19 pandemic.²¹

The amount of abnormality in patients mostly through kidney ultrasound (98.6%) and MRI (1.4%). The least invasive supportive examination after urinalysis is renal ultrasound (RUS), followed by a computed tomography (CT) scan and magnetic resonance imaging (MRI). CT scans and MRIs, however, have the drawback that the child must remain still during the scan. In addition, to produce informative images, the use of contrast agents is required, which are administered intravenously. This is, of course, very unpleasant for children. The next important but uncomfortable examination for children is MSU (micti cystography). The cause of this discomfort is the insertion of a urinary catheter, which is needed to introduce contrast material into the urethra.

In accordance with the article of Ransom et al. which also do renal ultrasonography (RUS) in 78% after UTI.²² In another, case in Songklanagarind Hospital has a little different between MSU and RUS.¹⁸ In Songklanagarind Hospital mostly patient has abnormality as vesicoureteral reflux (VUR). Based on guideline of National Institute for Health and Clinical Excellence (NICE) in Uwaezuoke et al. recommended children with atypical febrile UTI undergo RUS.²³ NICE also suggested children aged under 3 years should not undergo MSU.^{23,24} That study was conducted where RUS is not popular yet compared to RUS. Hence, the slightly differences caused by more patients is undergo MSU so a greater number of VUR patient is detected. The use of RUS is very necessary, especially for children who experience UTIs during infancy or have recurrent UTIs. The RUS can detect the presence of urinary tract obstruction in a less invasive manner. Obstructions in the right, left, or bilateral ureters are often initially identified by the presence of pelvocaliectasis on RUS. If unilateral pelvocaliectasis is found, there is a high likelihood that the obstruction is in the right ureter; conversely, if left pelvocaliectasis is present, the obstruction is likely in the left urinary tract. If bilateral pelvocaliectasis is observed, there is a high possibility of a posterior urethral valve (in boys) or vesicoureteral reflux (in both genders).

VUR has been the most commonly found abnormality at Songklanagarind Hospital in the last decade, followed by hydronephrosis and other conditions such as ureter duplication.¹⁸ Unlike at HSGH, the abnormalities most commonly found are not only VUR, but also posterior urethral valve, double collecting system, and pelviureteral junction obstruction. However, since there was no option to code these diagnoses in the electronic medical record, the only choice available was hydronephrosis. This results in the present study showing that most of the anatomical abnormalities found were hydronephrosis.

Regular flushing of the urinary tract serves as the main defense against urinary tract infections (UTIs). Strains of uropathogenic *E. coli* (UPEC) exhibit extraintestinal virulence due to specific

antigens and genes that enhance their pathogenicity. Important virulence factors for UPEC include P-fimbriae, toxins, protectins, and siderophores. The ability of UPEC to attach to the uroepithelium is facilitated by fimbriae on their surface, which bind to the host epithelium in a lock-and-key manner. This attachment interferes with the normal process of urine flow and bladder emptying ⁵.

It is thought that constipation can lead to the compression of the bladder and bladder neck, which results in increased pressure for bladder storage and a higher volume of urine remaining after voiding. Furthermore, a swollen colon or fecal contamination can serve as a significant reservoir for pathogens within the colon ⁶.

Engaging in sexual activity, becoming pregnant, having infrequent urination habits, a history of bladder infections, vesicoureteral reflux (VUR), anatomical irregularities, kidney stones, and the presence of foreign objects can elevate the likelihood of developing cystitis in teenagers ⁶.

Examination of interventions was performed while fever as chief complaint, which might be a sign of an acute period of UTI.¹⁸ As a result, an invasive exam, such as the VCUG, can be easily performed to gain a more thorough or comprehensive understanding of the abnormality. This is consistent with the findings of that study, which identified more VUR as abnormal. Otherwise, bladder thickening is more common than other abnormalities in this study. Variations of this may be the result of the patients' late diagnosis. It may cause either patient unawareness or, at the time of the study, MSU as a bottom-up approach where MSU obtained if RUS were abnormal, considered bladder thickening due to prolonged inflammation. The abnormality of hydronephrosis is more likely to be found with a modest difference in the study where the majority of the sample is infants.³

In Indonesia, various factors contributed to the treatment of UTI where patients has less compliance. In addition, many people in Indonesia still live below the poverty line and have low awareness of personal and community hygiene, which leads to a high occurrence of gastrointestinal infections, increasing the risk of recurrent UTIs. Gastrointestinal infections often occur due to the community's very low awareness of their environment, as well as poor healthy living behaviors for themselves and their families. This factor increased the number of microbial resistances in UTI patients. As a result, many patients have prolonged inflammation or it may worsen, similar to a recurring UTI. Thickening of the bladder is one impact of prolonged inflammation that's shown in this study, and more patients have it. Hydronephrosis follows our findings right after the thickening of the bladder. Hydronephrosis if left untreated will destroy kidney parenchym.²⁵ For this type of patient, invasive management is usually required. Medical treatments such as catheterization, stent usage, or lithotripsy may be used depending on the patient's condition.²⁵ Hydronephrosis in children is mostly obstructive, therefore there is a tendency for urine stasis, which leads to a high risk of bacteriuria and bacterial colonization in the bladder.

Research has shown that urinary tract infections (UTIs) can lead to kidney scarring. Approximately 15% of children with vesicoureteral reflux (VUR) exhibit renal scars, a condition known as reflux nephropathy (RN). The scarring associated with VUR can be either congenital or a consequence of acute pyelonephritis. Distinguishing between congenital and acquired RN is challenging: congenital RN typically features large scars and is more prevalent in boys, while acquired RN is characterized by smaller scars, often located in the upper kidney poles, and is more common in girls. The exact process causing kidney scarring is not well understood and likely involves multiple factors. It is suggested that localized infections trigger the release of inflammatory mediators such as cytokines, chemokines, bacterial toxins/peptides, and complement proteins, leading to scarring. An overly active innate immune response during UTIs may result in permanent kidney damage. The mechanisms behind kidney fibrosis are complex, with genetic and epigenetic factors playing a regulatory role. Myofibroblasts, when activated, are believed to be the primary contributors to fibrosis. Experimental studies indicate that dysregulated macrophage-dependent inflammatory responses can exacerbate kidney damage and fibrosis. Several risk factors for renal scarring in children with UTIs have been identified, including bacterial virulence factors, intra-renal reflux, recurrent febrile UTIs, delays in treatment, high VUR grades, and bladder and bowel dysfunctions (BBDs). The rarity of renal scars in adults with UTIs implies a genetic predisposition to kidney damage. Children aged two and older are significantly more likely to develop kidney scarring compared to younger children. As children age, intra-calyceal pressure increases; in the presence of VUR, papillary damage may occur in young children with intra-renal reflux, even without a UTI. The formation of new scars in young

adults has not been confirmed, except in transplant patients. Additionally, previous research has indicated a high incidence of hypertension and reduced renal function in patients with a history of UTIs over a period of 5 to 20 years ¹¹. It is not possible to identify the types of uropathogens during the study. The data collected does not reveal which uropathogens are responsible for the infections. Consequently, we are unable to compare abnormalities caused by uropathogens with findings from other studies, most of which are attributed to E. Coli ¹¹.

Although UTIs are among the most common infections in children and a large number of scientific papers are continuously published, more studies are needed. Further knowledge of the mechanism involved in the aggression of bacteria to the urinary tract and kidney may stimulate new therapies. Bladder dysfunctions have a critical role and should be properly investigated. The role of urobiome and other factors involved in the natural defense against virulent bacteria deserve further investigation. It is crucial to understand the pathogenesis of scars in the kidney and detect risk factors leading to permanent kidney damage and consequent high blood pressure, eclampsia, and the possible loss of renal function. Permanent kidney damage is rarely observed in adults after a UTI, indicating a possible congenital predisposition. Future studies should concentrate on the genetic predisposition of kidney damage in children with UTIs. Urine cultures are still needed for the diagnosis of a UTI, but urine collection should be collected in a simpler way in small children, and quicker results should be offered; a quick chemical analysis of urine is possible with new technologies, which should be tested in children. Imaging studies should be limited to those giving crucial information for treatment, and more bladder function investigations should be carried out since bladder and bowel dysfunctions are associated with UTIs. Antibiotic treatment is mandatory in febrile UTIs, and several drugs are available, while chemoprophylaxis should be restricted to a minority of patients who are at risk of recurrent UTIs or kidney damage; however, the use of immunomodulators and probiotics may be an alternative. Surgery has been largely performed in the past; its role is now limited to very few cases. Several guidelines have been produced and updated, but we recommend preparing simple guidelines for general practitioners and pediatricians with limited resources ¹¹.

This study has many limitations, including its descriptive design, setting in only a single center, and being conducted at a tertiary referral hospital, which may result in numerous biases. Recommendations for future research on the radiological characteristics of children with CKD are to conduct it in a multicenter study, not only at referral centers, but also in primary and secondary healthcare settings. This study also does not demonstrate cause and effect, so to obtain better data, the data obtained from this study could be continued in a cohort study to observe the tendency of recurrent UTIs in various radiological presentations of children with complicated UTIs.

CONCLUSION

In general, UTI is more common in children aged 1 – 3 years, particularly in boys. Abnormalities were predominantly found on in RUS examination. Thickening of the bladder is detected in more than half of the children followed by hydronephrosis and other abnormalities. The suggestion for further research is to connect the variable of thickening of the bladder wall with urodynamic study performance, as an effort to identify risk factors for recurrent UTI.

AUTHOR'S CONTRIBUTION STATEMENT

The contribution of each authors are: AW and PEB wrote entire original draft; RRS contributed to methodology design and data analysis; AW provided data for discussion and data analysis; PEB: data analysis and manuscript editing, AW: manuscript editing and data analysis.

CONFLICTS OF INTEREST

No author of this paper has a conflict of interest, including specific financial interests, relationships, and/or affiliations relevant to the subject matter or materials included in this manuscript.

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