

Original Article:

Evaluation of Abnormal Radiological Findings in Children Under Five Years With Acute Pyelonephritis: A Retrospective Cohort Study



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Citation Parvaresh S, Soltani Nejad N, Shafie'ei M. Evaluation of Abnormal Radiological Findings in Children Under Five Years With Acute Pyelonephritis: A Retrospective Cohort Study. Journal of Pediatric Nephrology. 2022; 10(1):23-31. <https://doi.org/10.22037/jpn.v10i1.36606>

doi <https://doi.org/10.22037/jpn.v10i1.36606>



Article info:

Received: Oct 2021

Accepted: Nov 2021

Published: Jan 2022

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ABSTRACT

Background and Aim: Urinary tract infection is one of the most common infections in childhood. The disease should not be overlooked because it has long-term complications such as renal scarring and failure. We aimed to determine the relationships between radiological findings in children under five years with acute pyelonephritis and its long-term complications.

Methods: In this retrospective study, we reviewed the medical records of all children hospitalized with acute pyelonephritis in a two-year period. We studied, extracted, and analyzed the imaging and demographic data of the patients.

Results: Out of 210 available cases, 54 children with acute culture-positive pyelonephritis were included. All the included cases had undergone ultrasound, Radionuclide Cystogram (RNC), Voiding Cystourethrography (VCUG) (for urinary reflux), and late DMSA (Dimercaptosuccinic Acid) scintigraphy. We found that 46.2% had Vesicoureteral Reflux (VUR), and 57.4% had an abnormal ultrasound, with hydronephrosis being the most common finding (74.1%). We also found a significant correlation between ultrasound and VUR ($P=0.002$). About 37% also had abnormal DMSA scintigraphy. However, in those with normal ultrasound results, 20% suffered from VUR, with one being severe. Seven cases also had abnormal DMSA scintigraphy.

Conclusion: We demonstrated that a normal urinary ultrasound does not rule out the possibility of VUR or the risk of progression to renal parenchymal dysfunction and scarring. Therefore, we suggest further utilizing the available radiologic techniques to diagnose and minimize subsequent renal complications in the disease promptly.

Keywords: Pyelonephritis, Urinary tract infections, Kidney diseases, Vesicoureteral reflux, Ultrasonography, Technetium Tc 99m dimercaptosuccinic acid, Radionuclide imaging

Introduction

Urinary tract infections are among the most critical diseases in childhood. These common diseases of the genitourinary system in children affect 3%-5% of girls and 1% of boys [1]. Pyelonephritis and asymptomatic bacteriuria are the main types of urinary tract infections diagnosed via positive urinary culture.

Acute pyelonephritis, an upper urinary tract infection, involves renal parenchyma and presents with several symptoms, including flank or generalized abdominal pain, fever, malaise, nausea, vomiting, or even diarrhea, along with many nonspecific symptoms [2, 3]. If not appropriately cared for, acute pyelonephritis can lead to irreversible renal damage, arterial hypertension, and even renal failure [4]. It is difficult to differentiate between pyelonephritis and other urinary tract infections by clinical evaluation. Therefore, the need for laboratory and radiologic techniques arises [4].

In addition, in cases with Vesicoureteral Reflux (i.e., the backtracking of urine to ureters and kidneys; VUR), there is a further predisposition to urinary infections, mainly due to the easy accessibility of the pathogenic bacteria to the viscus. Even though the diagnosis of VUR is primarily based on the radiologic findings of Radionuclide Cystogram (RNC) and Voiding Cystourethrography (VCUG), it can also be detected in routine examinations of pyelonephritis. The safety-wise level of irradiation in RNC is lower than VCUG [2]. However, more anatomical information can be detected via the VCUG [2].

Overall, the purpose of imaging studies in children with urinary tract infections is to identify anatomical abnormalities that predispose the individual to infection and assess the functions of the kidneys and whether there is a risk of, or an active involvement of, the mentioned organs [2]. For that matter, the bottom-up (either or both of the renal ultrasound and VCUG) and the top-down (Dimercaptosuccinic Acid [DMSA] RNC) methods are the two accepted approaches based on the clinician's judgment [5]. Furthermore, among children with febrile urinary tract infections, approximately 50% have a positive DMSA scintigraphy, and about 50% later develop renal scars in areas of current acute pyelonephritis. However, it is also recommended that if the scan returns positive for abnormal findings, a VCUG should also be performed [2].

There are two available guidelines on the performance of diagnostic radiologic interventions: the American Academy of Pediatrics (AAP) and the National Institute for Health and Care Excellence (NICE). AAP recommends an ultrasound of the kidneys, ureters, and bladder for all children with a first-time urinary tract infection between 2 and 24 months of age. Then, if ultrasound results indicate abnormalities, such as the evidence of hydronephrosis, scarring, reflux, or recurrent infection, VCUG and DMSA are recommended as the interventions in line. However, further routine examinations are not recommended in cases where ultrasound is normal. Moreover, these guidelines only apply to children with the age mentioned. So, the decision about older children is left to their respective physicians to whether or not to perform radiologic imaging [6]. NICE, as mentioned, has also Published ed guidelines for diagnosing and managing imaging following a urinary tract infection. Based on the guidelines, first-hand ultrasound sonography is recommended in those under six months. However, VCUG is performed only in children under three years who have atypical features (cultures positive with pathogens other than *E. coli* or those with recurrent infections) or abnormal urinary tract infections on ultrasound. DMSA scintigraphy is only performed on children up to 3 years with a history of recurrent or atypical infection, 4 to 6 months after the initial infection [3]. Furthermore, for those over six months, performing ultrasound is recommended only in cases of atypical positive urine culture (i.e., non-*E. coli*) and recurrent infections [3, 5].

In recent years, overwhelming evidence has been gathered, indicating that a significant number of children with urinary tract infections are not identified under the two mentioned guidelines. Therefore, the Pediatric Urology Association has called for further studies on this subject [2].

Regarding this issue and the importance of correct and timely diagnosis of complications from pyelonephritis, finding an appropriate approach for the utility of radiological examinations is of considerable importance. Subsequently, we conducted this study on children younger than five years, as they are more vulnerable to infections and subsequent scarring.

Materials and Methods

In our care center, as an accepted and implemented protocol, ultrasound sonography of the urinary tracts is performed in all cases of acute pyelonephritis. Then, during admission, shortly after the urine culture is negative, VCUG or RNC is performed. Ultimately, a late DMSA

scintigraphy is performed as a follow-up for renal scarring 4 to 6 months after the completion of therapy due to the natural incidence course of the scarring phenomena.

Study design

In this retrospective analytical cohort study, we aimed to determine radiological findings in children under five years who had been diagnosed with acute pyelonephritis in our care center. After obtaining informed consent, we included all the eligible cases in two years up until the start of the study.

Ethical approval

The local Ethics Committee approved our study. Our work also complied with the principles laid down in the Declaration of Helsinki.

Inclusion and exclusion criteria

Our inclusion criteria were aged less than five years, a definite diagnosis of pyelonephritis based on positive urinary culture (collected either midstream, in those with urinary continence, or via a catheter, in those with urinary incontinence), and the availability of records of all radiologic technique results (sonography; VCUG in male cases and RNC in female cases; DMSA). Also, all patients should have been followed up for six months after discharge to evaluate the patient's treatment outcome. We excluded those with incomplete demographic information, previous history of urinary abnormalities, history of immunodeficiencies such as any malignancy, long-term steroid use, no urine culture results, and no radiological technique results in patients' records.

Data collection

After determining our study's group of included cases, we collected their demographic and laboratory urinary data. The data included the age and sex of the individuals and the overall presence of white and red blood cells, indicating pyuria or hematuria, bacteria, and nitrate, indicating the presence of nitrifying bacteria. The other extracted information was the presence of a family history of VUR, personal history of VUR or urinary tract infections, overall clinical manifestations, presence of abnormal findings on the ultrasound examinations and if present, the finding that was reported, results of the late DMSA scintigraphy, and lastly current presence of VUR and renal scarring.

Ultimately, we divided the included individuals into two groups based on the abnormal findings on the ul-

trasound examinations. We evaluated the risk of developing renal scarring between the two groups while also looking for the factors possibly affecting the individual's predisposition to the outcome.

Statistical analysis

Ultimately, the extracted data were analyzed by the latest (the 26th) edition of the IBM SPSS software. The frequency and percentage of distribution indices were used to describe qualitative variables. In addition, quantitative variables were described using mean and standard deviation. The Chi-square statistic was used to compare the two groups' demographic data and intended outcomes.

Results

Of 210 eligible cases, 54 with acute pyelonephritis were included in our study. The demographic and laboratory data of the included cases are presented in [Table 1](#), with most cases being female and aged from 6 to 36 months. Moreover, most cases also had no history of urinary tract infections. Furthermore, laboratory analysis of the blood samples also demonstrated Mean±SD values of 13.99±5.47, 40.04±35.7, and 37.87±3.50 for White Blood Cell (WBC), Erythrocyte Sedimentation Rate (ESR: mm/hr), and C-Reactive Protein (CRP: mg/L), respectively. In addition, 7 patients (13%) required readmission after follow-up.

Furthermore, when accounting for the cases' clinical manifestations, we found that an overwhelming number of cases suffered, in order of frequency, from fever, nausea and vomiting, irritability, abdominal or flank pain, and dysuria. Some cases also complained of poor feeding urinary frequency, foul odor, poor weight gain, and even in one case, seizures ([Table 1](#)). The urine cultures of 53(98.1%) cases returned positive with *E. coli*, while one 1(1.9%) returned positive with enterococci.

Ultrasound examinations revealed that the most common finding was hydronephrosis (23 cases). Of the abnormal ultrasounds, 15 (48.4%) had experienced their first urinary tract infection. However, among those with normal ultrasounds, 20% (5 cases) had VUR, and 35% had abnormal DMSA scintigraphy ([Tables 2 and 3](#)).

Based on the results presented in [Table 4](#), we found no significant correlation between the frequency of clinical manifestations and an abnormal DMSA. Furthermore, there was no significant association between the results of the DMSA scintigraphy and laboratory results, age, and gender, even though most of the abnormal findings

Table 1. The demographic data and clinical manifestations of the studied samples

Variables		No. (%)
Age	Younger than six months	7(13.0)
	Between 6 months and 3 years	33(61.1)
	Between 3 and 5 years	14(25.9)
Sex	Female	48(88.9)
	Male	6(11.1)
Family history of urinary reflux	Positive	3(5.6)
	Negative	51(94.4)
Prior personal history of urinary infections	Positive	23(42.6)
	Negative	31(57.4)
Personal history of urinary reflux	Positive	4(7.4)
	Negative	50(92.6)
Clinical manifestations	Fever	53(98.1)
	Gastroenteritis	3(5.6)
	Nausea and vomiting	13(24.1)
	Dysuria	7(13.0)
	Irritability	13(24.1)
	Poor-feeding	2(3.7)
	Urinary frequency	2(3.7)
	Abdominal pain	9(16.7)
	Poor weight gain/failure to thrive	2(3.7)
	Flank pain	3(5.6)
	Seizures	1(1.9)
	Foul urine odor	1(1.9)
	Nocturia	1(1.9)

in the DMSA scintigraphy were observed in those aged between 6 months and 3 years. Moreover, there were no significant correlations between the possibility of abnormal findings on DMSA scintigraphy and ultrasound examinations.

Of those with VUR, 52% (13 cases) experienced a first-time urinary tract infection. When determining whether the presence of VUR had any correlation with the age of the individuals or their clinical manifestations, the results were not statistically significant. However, significant

correlations were noted between the presence of VUR and the results reported from ultrasound sonography, with 20 of 25 cases with VUR also demonstrating abnormalities in their ultrasound examinations compared to 11 of the 29 whose ultrasound examinations reported normal findings (Table 4).

Ultimately, when evaluating the available data for the correlations between the incidence of scarring, the age, gender, frequency of manifestations, laboratory data,

Table 2. Ultrasound findings in the studied samples

Right-Sided		No. (%)
Hydronephrosis	Positive	23(42.6)
	Negative	31(57.4)
Hydroureteronephrosis	Positive	3(5.6)
	Negative	51(94.4)
Increased bladder thickness	Positive	3(5.6)
	Negative	51(94.4)
Anatomical abnormalities	Positive	2(3.7)
	Negative	52(96.3)

and the ultrasound findings of the individuals, we found no statistical significance (Table 4).

Discussion

Acute pyelonephritis is one of the most common and concerning infections in childhood, with many complications without early diagnosis and improper or inadequate care [2].

Although ultrasound was performed in the acute phase of infection in several studies [7-9], and we could demonstrate a significant correlation between abnormal ultrasound results and the presence of VUR, it had a small role in the diagnosis of our cases. In our study, 20% of cases with the diagnosis of VUR had normal ultrasounds. In addition, out of our 5 cases of reflux with normal ultrasounds, one had severe VUR. In the study by Juliano et al. [10], 25% of cases with the first incident of pyelonephritis who had a normal ultrasound suffered

from VUR, which is consistent with the results of our study. Furthermore, in another study, severe grades of VUR were seen in children with normal ultrasounds who had no history of urinary tract infections [11].

About 52% of our first-time urinary tract infections cases had an ongoing VUR, with the highest incidence in those aged six months and above. Therefore, if NCIE protocols were considered, many cases of VUR would be missed. As concerning as it may seem, in a study on Kuwaiti children, almost half of those with ongoing VUR developed renal scarring, further emphasizing the early detection of VUR [12].

Seven of the cases with normal ultrasounds had abnormal DMSA scintigraphy results. Furthermore, scarring was reported in one case with an abnormal finding on the initial ultrasound examination (hydronephrosis), even though this case had no history of urinary tract infection or personal or family history of VUR. Scarring was also

Table 3. The correlation between ultrasound findings and the history of urinary tract infections, personal and family history of VUR

Variable		No. (%)		P
		Normal Ultrasound	Abnormal Ultrasound	
History of urinary tract infections	Positive	7(30.4)	16(51.6)	0.120
	Negative	16(69.6)	15(48.4)	
History of urinary reflux	Positive	0(0)	4(12.9)	0.073
	Negative	23(100)	27(87.1)	
Family history of urinary reflux	Positive	1(3.4)	2(6.5)	0.729
	Negative	22(95.7)	29(93.5)	

Table 4. Correlation between radiological, clinical, and laboratory findings in study group

Variable	DMSA Scintigraph, No. (%)		P	VUR, No. (%)		P	Scarring, No. (%)		P	
	Normal	Abnormal		Negative	Positive		Yes	No		
Age	28 days to 6 months of age	3(8.8)	4(20)	0.357	4(13.8)	3(12)	0.086	7(13.2)	0(0)	0.233
	Six months to 3 years of age	23(67.6)	10(50)		21(72.4)	12(48)		33(62.3)	0(0)	
	3 to 5 years of age	8(23.5)	6(30)		4(13.8)	10(40)		13(24.5)	1(100)	
Sex	Female	30(88.2)	18(90)	0.842	26(89.7)	22(88)	0.847	47(88.7)	1(100)	0.721
	Male	4(11.8)	2(10)		3(10.3)	3(12)		6(11.3)	0(0)	
Clinical manifestations	Fever	3(97.1)	20(100)	0.439	28(96.6)	25(100)	0.349	52(98.1)	1(100)	0.89
	Gastroenteritis	2(5.9)	1(5)	0.891	1(3.4)	2(8)	0.467	3(5.7)	0(0)	0.807
	Nausea and vomiting	9(26.5)	4(20)	0.591	7(24.1)	6(24)	0.991	13(24.5)	0(0)	0.57
	Dysuria	5(14.7)	2(10)	0.619	2(6.9)	2(20.5)	0.153	6(11.3)	1(100)	0.009
	Irritability	8(23.5)	5(25)	0.903	9(31)	4(16)	0.198	13(24.5)	0(0)	0.57
	Poor-feeding	0(0)	2(10)	0.06	0(0)	2(8)	0.121	2(3.8)	0(0)	0.843
	Frequency	1(2.9)	1(5)	0.699	1(3.4)	1(4)	0.915	1(1.9)	1(100)	0.001
	Abdominal pain	6(17.6)	3(15)	0.801	5(17.2)	4(16)	0.903	9(17)	0(0)	0.652
	Failure to gain weight	2(5.9)	0(0)	0.715	1(4)	3(4)	0.835	2(3.8)	0(0)	0.76
	Flank pain	3(8.8)	0(0)	0.529	2(8)	1(3.4)	0.604	3(5.7)	0(0)	0.649
	Seizures	0(0)	1(5)	0.289	0(0)	1(3.4)	0.715	1(1.9)	0(0)	0.935
	Foul urine odor	1(2.9)	0(0)	0.935	0(0)	1(3.4)	0.715	1(1.9)	0(0)	0.935
	Nocturia	1(2.9)	0(0)	0.935	0(0)	1(3.4)	0.715	1(1.9)	0(0)	0.935

Variable	DMSA Scintigraph, No. (%)		P	VUR, No. (%)		P	Scarring, No. (%)		P	
	Normal	Abnormal		Negative	Positive		Yes	No		
Lab data	Pyuria	32(94.1)	18(90)	0.577	27(93.1)	23(92)	0.877	49(92.5)	1(100)	0.775
	Bacteriuria	19(55.9)	12(60)	0.768	21(72.4)	10(40)	0.016	31(58.5)	0(0)	0.241
	Nitrite	5(14.7)	4(20)	0.614	7(24.1)	2(8)	0.113	9(17)	0(0)	0.652
	Hematuria	7(20.6)	2(10)	0.313	6(20.7)	3(12)	0.393	19(17)	0(0)	0.652
Ultrasound findings	Normal	16(47.1)	7(35)	0.387	18(62.1)	5(20)	0.002	23(43.4)	0(0)	0.385
	Abnormal	18(52.9)	13(65)		11(37.9)	20(80)		30(56.6)	1(100)	
History of multiple admissions	Positive	3(8.8)	4(20)	0.238	4(13.8)	3(12)	0.845	7(31.2)	0(0)	0.697
	Negative	31(91.2)	16(80)		25(86.2)	88(22)		46(86.8)	1(100)	
History of urinary infection	Positive	18(52.9)	5(25)	0.45	11(37.9)	12(48)	0.456			
	Negative	16(47.1)	15(75)		18(62.1)	13(52)				
History of urinary reflux	Positive	3(8.8)	1(5)	0.604	0(0)	4(16)	0.025			
	Negative	31(91.2)	19(95)		29(100)	21(84)				
Family history of urinary reflux	Positive	2(5.9)	1(5)	0.891	1(3.4)	2(8)	0.467			
	Negative	32(94.1)	19(95)		28(96.6)	23(92)				

reported in 23 patients with normal findings in their initial ultrasound examinations, indicating that if only one radiological diagnostic method were performed, many future renal scarring cases would be missed. In a study by Zaki et al. on acute pyelonephritis, 38% of patients with abnormalities in acute phase DMSA scintigraphy later developed scarring based on their late DMSA scintigraphy findings [12]. In two studies by Hitzel et al., the predictive value of ultrasound, as well as early and late DMSA scintigraphy, were evaluated. In the first study, 51% of acute pyelonephritis cases developed scarring on

follow-up examinations [13]. In the second study, out of 26 patients with abnormal imaging findings during the acute phase of pyelonephritis, 46% showed less than desirable improvement, developing scars in the long run [14]. In another study by Montini et al., 15% of cases with acute pyelonephritis developed renal scarring on their late DMSA 12-month follow-up scans, showing poor predictability values of both ultrasound and cystography [15]. One study by Temiz et al. also demonstrated the degree of inaccuracy of sonography in detecting renal scarring, with 35% of cases with normal sonographies

suffering from scarring on their DMSA scintigraphy [16]. The findings of the above studies further confirm our concerns. Furthermore, a meta-analysis concluded that a single protocol is not required for all care centers. However, based on the same study, the protocols should be constantly updated [17].

Conclusion

Since ultrasound was abnormal in approximately half of our cases, we recommend performing an ultrasound of the urinary tract in all pediatric patients with acute pyelonephritis. Additionally, the strong correlation between ultrasound abnormalities and VUR increases the importance of utilizing this method. Furthermore, since two-thirds of our cases had abnormal VCUGs or RNCs, we can recommend performing VCUG in these cases, too, though in its timely manner. Moreover, as presented, performing late DMSA scintigraphy would determine the presence of renal scarring, prevent any misdiagnoses, and provide the clinician and the patient with information regarding the necessary precautions. These remarks emphasize that none of the three mentioned radiologic procedures should be hastily disregarded, as each can provide invaluable information.

Lastly, we have to make clear that even though preventing complications regarding the misdiagnoses or late diagnoses of acute pyelonephritis is essential, minimizing the need for unnecessary diagnostic procedures (which exposes the child to radiation and could have a significant financial burden) and maximizing their benefits are also of utter importance. However, we cannot provide a definite conclusion regarding the issues mentioned, as our study suffered from limitations, including its retrospective nature and relatively small sample size. Therefore, in our opinion, prospective longitudinal studies with larger sample sizes should be conducted. Then, in the long run, as the evidence piles up, our result could be systematically reviewed and meta-analyzed to decide what direction would be better in appropriately managing acute pyelonephritis in children.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Ethics Committee of the Kerman University of Medical Sciences.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

All authors declared no conflict of interest.

Acknowledgments

Authors express their gratitude and thankfulness from Afzalipour Hospital staff for their help and cooperation.

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