https://doi.org/10.32394/pe.76.19

Abbas Moghimbeigi[1], Amir Adibi[2], Seyed Mohammad Reza Azimi Meibodi[3], Zahra Abdan[4], Diana Sarokhani[5],Moloud Fakhri[6], Ali Hasanpour Dehkordi[7,*]*

PREVALENCE OF RENAL SCARRING CAUSED BY URINARY TRACT INFECTIONS IN CHILDREN: A SYSTEMATIC REVIEW AND META-ANALYSIS

[1]Department of Biostatistics and Epidemiology, School of Health & Health, Safety and Environment Research Center, Alborz University of Medical Sciences, Karaj, Iran.
[2]Department of Child and Adolescent Psychiatry, Ilam University of Medical Sciences, Ilam, Iran
[3]Department of Otorhinolaryngology, Yazd Branch, Islamic Azad University of Medical Sciences, Yazd, Iran
[4]Clinical Research Development Center, Imam Reza Hospital, Kermanshah University of Medical Sciences, Kermanshah, Iran
[5]School of Health & Health, Safety and Environment Research Center, Alborz University of Medical Sciences, Karaj, Iran.
[6]Traditional and Complementary Medicine Research Center, Addiction Institute, Mazandaran University of Medical Sciences, Sari, Iran
[7]Community-Oriented Nursing Midwifery Research Center, Nursing and Midwifery School, Shahrekord University of Medical Sciences, Shahrekord, Iran
[*]Corresponding Authors

ABSTRACT

PURPOSE. SOURCES OF INFORMATION. Urinary tract infection (UTI) is the second most common infection in children, the most important complication of which is renal scarring. The aim of present study was to evaluate the prevalence of renal scarring after UTI in children through systematic review and meta-analysis.
METHODS. The international databases of Science Direct, PubMed, Scopus, and Web of Science and the Google Scholar search engine were searched using standard keywords. The sources found were from 2010 to 2020 and the search stage was updated until 2021.02.16. Data were analyzed using STATA-14 software and the significance level was considered at $P<0.05$.
RESULTS. In 29 studies with a sample size of 9,986 children, the prevalence of renal scarring in children was estimated at 35% (95% CI: 29-41). Also, the prevalence of renal scarring was in girls 61% (95% CI: 40-81) and in boys 34% (95% CI: 11-57). The prevalence of unilateral renal scarring in children was 56% (95% CI: 48-65) and bilateral renal scarring was 31% (95% CI: 14-48). In addition, the prevalence of scar was 54% in children with reflux and 12% in children without vesicoureteral reflux.
CONCLUSIONS. More than one third of people under the age of 18 after UTI have renal scarring. The prevalence of this complication in girls is about 2 times higher than that in boys and in people with reflux, it is about 4 times higher than people who do not have urinary reflux. Also, about half of people under the age of 18 suffer from unilateral renal scarring and about one third of them suffer from bilateral renal scarring.

Keywords: *renal scarring, kidney scarring, urinary tract infection, urinary reflux, children*

INTRODUCTION

Based on international organizations' data, $17-29 billion is spent annually on the treatment and recovery of nosocomial infections, of which 39% is related to the cost of urinary tract infections (UTI) (1). Urinary tract infection is one of the most common infections among children (2). UTI in children is associated with complications, the most important of which is permanent renal scarring. Renal scarring refers to a range of abnormal radiographic findings in the kidney that are associated with focal or extensive areas of irreversible parenchymal damage to the kidneys. Scar occurs because of an inflammatory reaction caused by infection between the host and bacterial markers (3, 4). Permanent renal scarring after urinary tract infection has been observed in 15% to 60% of affected children (5, 6).

Diagnostic methods used to assess the urinary tract include renal ultrasound (RUS), voiding cystourethrogram (VCUG) and nuclear cystogram (NCG) (7), and mTc-Dimercaptosuccinic acid (DMSA) scintigraphy is the current gold standard for diagnosing renal scarring. This method has a higher sensitivity (sensitivity between 80 and 100%) for scar detection when compared to other imaging techniques such as intravenous urography, ultrasound, computed tomography, and magnetic resonance imaging (8).

Several studies with very diverse statistics have been published in the world on the prevalence of renal scarring in children and general and accurate statistics are not available in this regard, so this study aims to investigate the prevalence of renal scarring in children (under 18 years) using meta-analysis method. The present study is a systematic and meta-analysis review study that examines the prevalence of renal scarring in children aged below 18 years.

METHODS

Protocol study. In this study, the PRISMA protocol (9), which used is for systematic review and meta-analysis studies, was used.

Study population. Participants in the study were children under the age of 18 without gender or race restrictions.

Study implications:

Primary outcome. The main outcome of this meta-analysis was to estimate the prevalence of renal scarring in children (under 18 years of age) in the world.

Secondary outcomes of this meta-analysis include the prevalence of renal scarring in children (under 18 years of age) separately for studied countries, gender, type of renal scarring (unilateral OR bilateral), presence or absence of urinary reflux.

Search strategy. In this meta-analysis, Science Direct, PubMed, Scopus, and Web of Science electronic databases and the Google Scholar search engine, the keywords of "renal scarring", "kidney scarring", "urinary tract infection", "urinary reflux", and "children" and the MeSH equivalent were searched. Their combinations were also searched using the "AND" and "OR" conjunctions in the above-mentioned databases. In the search stage, a time limit was applied but no language limit. The found sources were from 2010 to 2020 and the search was updated until 2021.02.16. In addition, a reference list of all initial studies entered at the end of the PRISMA flowchart was reviewed for manual search.

Inclusion and exclusion criteria. The meta-analysis included studies that examined the prevalence of renal scarring in children under 18 years of age. For this purpose, studies with non-random sample selection, case report studies, non-reporting of information required for data analysis such as number of samples or prevalence of renal scarring, low quality studies based on The Newcastle-Ottawa Scale (NOS) checklist (10), and studies reported renal scarring in individuals over 18 years of age were excluded from systematic review and meta-analysis process.

Qualitative assessment of studies. After identifying the initial studies, two independent authors evaluated the studies qualitatively using the Newcastle Ottawa Scale checklist, and the cut-off point of this checklist was considered at score 4. If there is disagreement among researchers about the qualitative evaluation of studies, the third researcher eliminated this disagreement. In this checklist, 3 sub-sets including: group selection (4 questions), group comparability (1 question) and exposure or outcome (2 questions), are examined. This tool is a reliable tool with a long history of reliability (11).

A star system is used to evaluate the quality of the study, so that for the highest quality studies, a maximum of one star is allocated for each case, except for the case related to comparison, where two stars can be allocated. Based on this checklist, articles are rated from zero (lowest quality) to ten (highest quality) and studies with a total score of less than 4 are recognized as low quality studies and are excluded. However, in this meta-analysis, we did not find a study with a score less than 4 (10).

Extracting the data. The two researchers independently extracted data from studies to minimize bias in reporting and data collection. The researchers entered the extracted data into a designed checklist. This checklist included name of author, type of study, age group, sample size, year of publication, country of study, prevalence of renal scarring, diagnostic method, number of girls and boys, prevalence of renal scarring in girls and boys, and prevalence of unilateral and bilateral renal scarring.

Statistical analysis. The studies were combined according to the number of samples and the variance of each study. To evaluate the heterogeneity of the studies, Q Cochrane test and I^2 index were used. There are three classifications in the I^2 index (less than 25%= low heterogeneity, between 25% and 75%= moderate heterogeneity, and more than 75%= severe heterogeneity). Since the fixed effects model is used for low heterogeneity and the random effects model is used for high heterogeneity, in the present study, the random effects model was used.

Meta-regression was used to investigate the relationship between the prevalence of renal scarring in children with year of publication. Data analysis

was performed with STATA-14 software and the significance level of the tests was considered at P<0.05.

RESULTS

Study selection process. First, with a search of the above databases, 300 articles were found. By reviewing the study title, 121 duplicate studies were excluded. The remaining 179 abstracts were reviewed and among them, 115 articles were excluded according to the exclusion criteria. Out of the remaining 64 articles, another 35 articles were excluded due to incomplete information or lack of full text, and finally the remaining 29 articles entered the quality evaluation stage, all of which had good quality and entered the meta-analysis process (Figure 1).

Out the 29 articles reviewed, with a sample size of 9,986, 28 studies reported the prevalence of renal scarring in children by number of patients. Only one study reported the prevalence of renal scarring in children based on the number of kidneys.

In the mentioned study, published by Koçyiğit A et al. in 2014 in Turkey, 32% of 77 kidneys with VUR (49 patients studied) had renal scarring following a urinary tract infection (12). Also, the diagnostic method used in most of the studies was DMSA scan and the age limit of children was under 18 years. In the current meta-analysis, the lowest prevalence of renal scarring in the study conducted by Al-Kaabi A et al. (13) in Qatar was 0.03% and the highest prevalence of renal scarring in the study conducted by Yiee JH et al. (14) was 90% in the United States. The characteristics of the studies eligible for the systematic review and meta-analysis stage are presented in Table 1.

With exclusion of the Al-Kaabi A et al. (13) and Yiee JH et al.(14) studies, which were considered outlier data, the overall prevalence of renal scarring in children (<18 years) was 35% (CI 95%: 29-41) (Figure 2).

Prevalence of renal scarring in children (<18 years) among subgroup including girls and boys was 61% (CI 95%: 40-81), and 34 % (CI 95%: 11-57) respectively. In the analysis based on the type of renal scarring, the prevalence of unilateral renal scarring in children was 56% (95% CI: 48-65) and the prevalence of bilateral renal scarring was 31% (95% CI: 14-48). In an analysis conducted based on the countries, except for Iran, Ireland, the United States, the United Kingdom, Turkey, and Taiwan, only one study was available, so we did not list them in Table 2.

Finally, we observed that the prevalence of renal scarring in children in the United States, UK, Iran, Egypt, South Korea, Thailand and Japan is higher

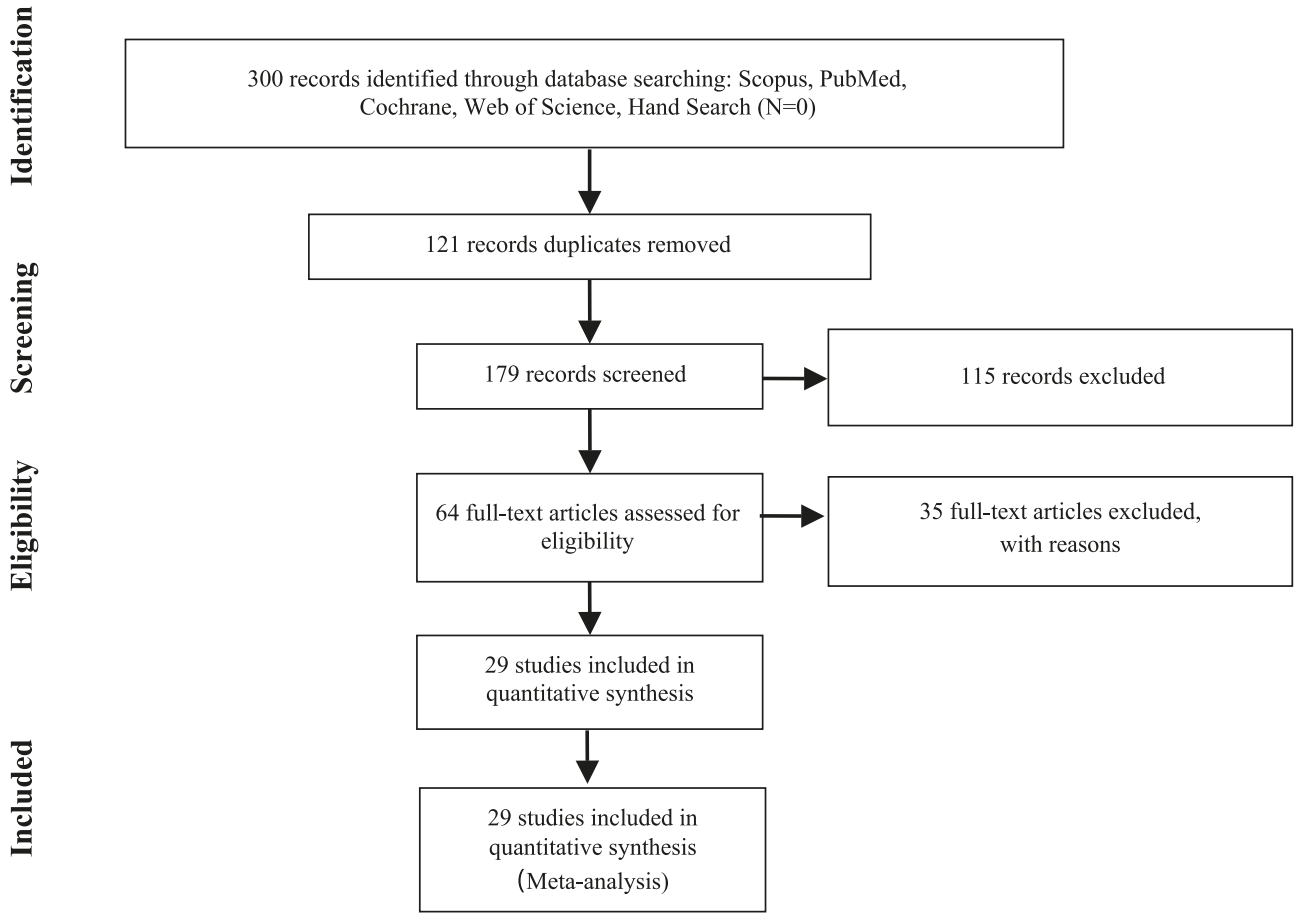

Figure 1. PRISMA flow diagram study.

Table 1. Characteristics of articles entered into the meta-analysis process.

Authors name	Year of publication	Country	Diagnostic method of renal scarring	Diagnostic method of Urinary reflux	Age range (Year)	Clinical presentation	Sample Size	Number of girls	Number of boys	Prevalence of renal scarring (%)
Finkelstein JB(15)	2020	USA	DMSA scan		<14		144	116	28	66
Akhavan Sepahi M(16)	2020	Iran	DMSA scan	VCUG	<1		140	---	---	32.1
Finkelstein J(17)	2019	USA	DMSA scan		<14		745	---	---	53
Bandari B(18)	2019	India	---		<5	dysuria, increased frequency of micturition, urgency with or without fever	40	22	18	35
Jayaweera JA(19)	2018	Sri Lanka	DMSA scan		0-12	fever lasting longer than 48 h, as well as with poor feeding, vomiting, and diarrhea	70	---	---	31
Sims-Williams HJ(20)	2018	UK	---		10-14		68	---	---	64
Pokrajac D(21)	2018	Bosnia and Herzegovina	DMSA scan , 6-8 months	VCUG	<1		66	54	12	27
Hung TW(22)	2016	Taiwan	DMSA scan		<2	Febrile	310	115	195	27
Mattoo TK(23)	2016	USA	DMSA scan	VCUG	0-6		599	551	48	10
Hsu CC(24)	2016	Taiwan	DMSA scan		<2		388	133	255	28.6
Yılmaz S(25)	2016	Turkey	DMSA scan		<18		300	231	69	19.4
Kitao T(26)	2015	Japan	DMSA scan		<1		49	14	35	65.3

Hussein A(27)	2015	Egypt	DMSA scan		<18		104	---	---	44.2
Tolunay O(28)	2015	Turkey	DMSA scan		7.68		30	24	6	3.3
Narchi H(29)	2015	United Arab Emirates	---	VCUG	0-2		43	---	---	37
Berdichevski EH(30)	2013	Brazil	DMSA scan		<2		157	---	---	5.1
Amornchai-charoensuk Y(31)	2013	Thailand	---		<18		34	15	19	38.2
Mir S(32)	2013	Turkey	DMSA scan	VCUG	0-15		90	60	30	48.9
Hunziker M(33)	2012	Ireland	DMSA scan, 4-6 month	VCUG	0-6		300	---	---	23.1
Lee YJ(34)	2012	Korea	DMSA scan, 6 month	VCUG	<1		213	61	152	17.4
Ehsanipour F(35)	2012	Iran	DMSA scan, 4-6 month	VCUG	0-13		80	62	18	55
Erdogan H(36)	2012	Turkey	DMSA scan		1-18		78	53	25	48.7
Al-Kaabi A(13)	2012	Qatar	DMSA scan		6-12		3645	1994	1651	0.0003
Hunziker M(37)	2012	Irland	DMSA scan		<13		1765	1221	554	21.8
Oh MM(38)	2012	South Korea	DMSA scan, 6 month	VCUG	<1		129	---	---	46.5
Singh C(39)	2011	UK	DMSA scan		1.5-16.3		22	---	---	72
Yiee JH(14)	2010	USA	DMSA scan, least 6 months		5-9		29	14	15	90
Barros AC(40)	2010	Portugal	DMSA scan		<18		348	---	---	13.3

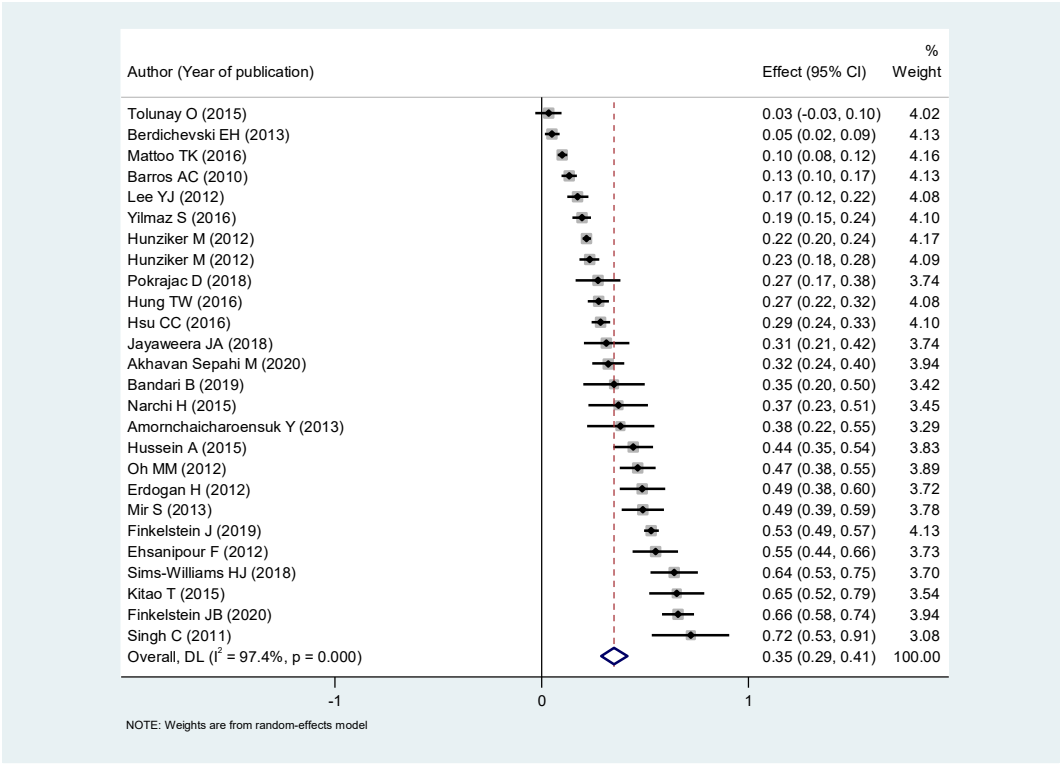

Figure 2. Forest plots of prevalence of renal scarring in children for random effects meta-analyses. (Squares represent effect estimates of individual studies with their 95% confidence intervals of prevalence of renal scarring with size of squares proportional to the weight assigned to the study in the meta-analysis. The diamond represents the overall result and 95% confidence interval of the random-effects meta-analysis

Table 2. Prevalence of renal scarring in children and 95% confidence interval in the studied subgroups

Subgroups		Number of study	Prevalence (%)	95% confidence intervals		I^2(%)	P-value (The significance level of the tests)
				Low	Up		
Prevalence of renal scarring by Sex	Total	27	35	29	41	97.4	<0.0001
	Girls	8	61	40	81	98.3	<0.0001
	Boys	7	34	11	57	96	<0.0001
Prevalence of renal scarring by type of scar	Unilateral	2	56	48	65	0	0.478
	Bilateral	3	31	14	48	82.5	0.003
Prevalence of reflux		8	36	17	56	98.9	<0.0001
Prevalence of renal scarring	with reflux	3	54	34	74	94.6	<0.0001
	without reflux	3	12	6	19	74.1	0.021
Prevalence of renal scarring by Countries	Turkey	4	30	10	49	96.3	<0.0001
	USA	4	54	22	87	99.5	<0.0001
	Ireland	2	22	20	24	0	0.620
	Taiwan	2	28	25	31	0	0.725
	Iran	2	43	21	66	91.1	0.001
	UK	2	66	56	76	0	0.475

than the global prevalence of renal scarring in children (37%). Also, the prevalence of renal scarring in children in Qatar, Turkey, Brazil, Portugal, North Korea, Ireland, Bosnia and Herzegovina, Taiwan, Sri Lanka and India is lower than the global prevalence of renal scarring in children (37%) (Table 2).

As you can see in Table 2, the heterogeneity between the studies is very high (i^2=97.4%). Many factors contribute to this heterogeneity. Including: 1) In some categories, children are divided into 3 groups, less than 6 years old, between 6 and 12 years old, 12 to 18 years old. Naturally, the prevalence of kidney scars is higher at younger ages. 2) Time between urinary tract infection and performed DMSA examination, 3) Gender of children.

Figure 3 shows that the prevalence of renal scarring in children in the worldwide is increasing from 2010 to 2020, although this relationship is not statistically significant (P=0.427).

DISCUSSION

According to the results of this meta-analysis, one in three children after UTI suffers from some degree of kidney scarring, and the prevalence of pediatric renal scarring in girls was about twice that of boys. It can be concluded that female gender was a risk factor for renal scarring. In the analysis based on the type of renal scarring, it was demonstrated, that the prevalence of unilateral renal scarring in children was 56% and bilateral renal scarring was 31%, the prevalence of unilateral renal scarring was significantly higher than the prevalence of bilateral scarring. Also, the prevalence of renal scarring in children with reflux (54%) was about 4 times higher than in children without reflux (12%).

In a study conducted by Benador et al. on children under 16 years of age, 55% of abnormal scans were observed in children under one year of age, 86% were observed in children between 1 and 5 years of age, and 69% were observed in children over 5 years of age. After 2 months of repeated DMSA scans, 40% of children aged below one year, 79% of children aged between 1 and 5 years, and 64% of children aged more than 5 years had renal scarring (41). This study showed that the prevalence of urinary tract infections at a younger age, and thus, the prevalence of renal scarring, is higher, which may be due to issues such as enuresis, diaper use, non-circumcision of boys, and changing children's diapers late.

The results of meta-analysis of Najafi et al. in 2019 showed that the prevalence of renal scarring in Iranian children is 31% (14% in girls and 23% in boys), the prevalence of renal scarring is 47% and 12% in children with urinary reflux and in children without urinary reflux respectively (42). In this study, as in the

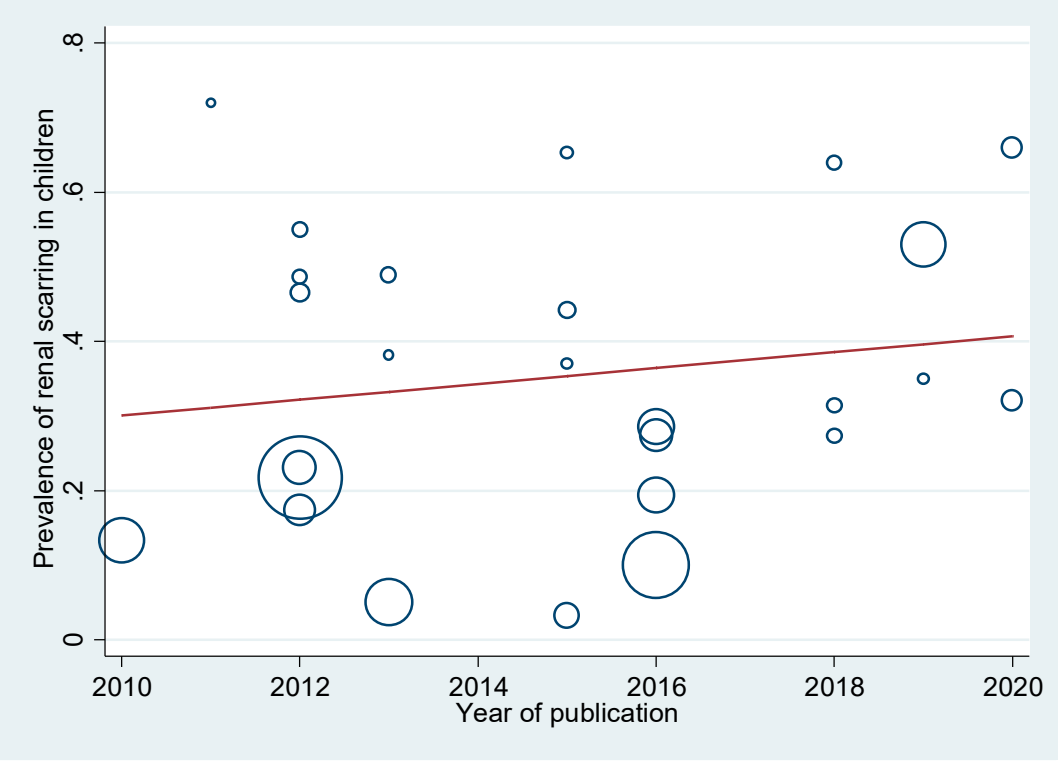

Figure 3. Meta-regression of the relationship between the prevalence of renal scarring in children and the year of publication of the study

current meta-analysis, one-third of the children after UTI had kidney scars. In fact, the results of our study confirm the results of the meta-analysis of Najafi et al. In the meta-analysis conducted by Sheikh et al., the prevalence of renal scarring was 15.5% and 4.1% of children had some degree of urinary reflux. The prevalence of renal scarring was 16.3% in girls and 14.2% in boys. Also, the prevalence of renal scarring in children with reflux was higher than in children without reflux (43). The prevalence of kidney scars in Sheikh's study is half the prevalence reported in the study of Najafi et al. Therefore, a general meta-analysis study is needed to report the prevalence of renal scarring in children worldwide, regardless of age or geographical limitations. Of course, previous meta-analyzes had similarities. For example, in these two meta-analyses, the prevalence of renal scarring was higher in girls compared to boys and it was higher in children with reflux than in children without reflux, which is consistent with the results of the present meta-analysis.

In a meta-analysis conducted in 2013, 22 studies met the requirements for entering the meta-analysis. The researchers looked at the relative prevalence and risk of urinary tract infections in different age groups. The relative risk was 9.91 for those aged 0 to 1, 6.56 for those aged 1 to 16, and 3.41 for those over 16. They reported that 32.1% of uncircumcised boys compared with 8.8% of circumcised individuals experience a urinary tract infection during their lifetime. Thus, lack of circumcision increases the risk of urinary tract infection in boys (44). In a systematic review study conducted by Sheikh et al. in 2010, 1,533 articles were found in the search strategy phase and finally 33 articles entered the meta-analysis process. Among children with early-stage urinary tract infections, 57% of the cases were associated with acute pyelonephritis and 15% of children had evidence of renal scarring on the follow-up DMSA scans. Children with bilateral reflux were significantly more likely to develop pyelonephritis RR=1.5 and kidney scars RR=2.6. So urinary reflux is also a risk factor for kidney scarring (6). In a 2003 meta-analysis study, 12 valid studies were found. It was analyzed how effectively the finding VUR on micturition cystography (MCU) in children hospitalized with UTIs predicted kidney parenchymal disease by 99mTc-DMSA. Seven studies included data from 537 children and results of 59% of 99mTc-DMSA scans were positive. Seven studies with data on 1,062 kidneys were included and the results of 36% of 99mTc-DMSA scans were positive. A meta-analysis showed that a positive MCU increased the risk of kidney injury in hospitalized UTI patients by about 20% (45).

Research limitations. Unavailability of the full text of some studies (despite contacting the corresponding with them) caused us to lose the results of those studies. The lack of uniform distribution of studies among different countries and continents made statistics of some countries be unavailable. Since the age of children in the studies was reported as age range and these ranges overlapped with each other, we could not present the prevalence of renal scarring in children separately based on age, as an important factor.

CONCLUSIONS

In the analyzed studies, more than a third of people under the age of 18 have renal scarring after UTI. The prevalence of this complication in girls is about 2 times higher than in boys and in children with vesicoureteral reflux is about 4 times higher than in children without vesicoureteral reflux. Also, about half of children under the age of 18 suffer from unilateral renal scarring and about one-third of them suffer from bilateral renal scarring. The diagnostic methods used may influence the frequency of detecting complications after UTI.

Acknowledgments:
The authors wish to thank all the researchers whose studies were used in this meta-analysis. The authors also thank the Alborz University of Medical Sciences for their financial support.

REFERENCES

1. Arabestani M, Mahmoudi H, Alikhani M, et al. Evaluation prevalence agents of urinary tract infection and antibiotic resistance in patients admitted to hospitals in Hamadan University Of Medical Sciences 1391-92. [Persian]. Pajouhan Sci J 2014;12(3):20-7.
2. Selekman R, Allen I, Copp H. Determinants of practice patterns in pediatric UTI management. J Pediatr Urol 2016 Oct;12(5):308.e1-e6.
3. Infection SoUT. Reaffirmation of AAP Clinical Practice Guideline: The Diagnosis and Management of the Initial Urinary Tract Infection in Febrile Infants and Young Children 2-24 Months of Age. Pediatrics 2016;138(6):e20163026.
4. Korbel L, Howell M, Spencer J. The clinical diagnosis and management of urinary tract infections in children and adolescents. Paediatr Int Child Health 2017;37(4):273-9.
5. Faust W, Diaz M, Pohl H. Incidence of post-pyelonephritic renal scarring: a meta-analysis of the dimercapto-succinic acid literature. J Urol 2009;181(1):290-8.
6. Sheikh N, Ewing A, Bhatnagar S, et al. Risk of renal scarring in children with a first urinary

tract infection: a systematic review. Pediatrics 2010;126(6):1084-91.
7. Sepahi MA, Toloii F, Jang SA, et al. The Prevalence of Renal Scars Among Infants Under One Year Old With a First UTI With or Without VUR in Qom, Iran, 2017. Iranian J Kidney Dis 2020;14(4):308.
8. Roebuck DJ, Howard RG, Metreweli C. How sensitive is ultrasound in the detection of renal scars? Br J Radiol 1999;72:345-8.
9. Moher D, Shamseer L, Clarke M, et al. Preferred reporting items for systematic review and metaanalysis protocols (PRISMA-P) 2015 statement. Syst Rev J 2015;4(1):1e9.
10. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. Eur J Epidemiol 2010;25(9):603e5.
11. Luchini C, Stubbs B, Solmi M, et al. Assessing the quality of studies in meta-analyses: advantages and limitations of the Newcastle Ottawa Scale. World J Meta Anal 2017;5(4):80.
12. Koçyiğit A, Yüksel S, Bayram R, et al. Efficacy of magnetic resonance urography in detecting renal scars in children with vesicoureteral reflux. Pediatr Nephrol 2014;29(7):1215-20.
13. Al-Kaabi A, Almaslamani T, Toaimah F, et al. Urinary screening for renal disease among apparently healthy school children in Qatar. J Trop Pediatr 2012;58(1):81-4.
14. Yiee J, DiSandro M, Wang M, et al. Does severity of renal scarring on DMSA scan predict abnormalities in creatinine clearance? Urology 2010;76(1):204-8.
15. Finkelstein J, Rague J, Chow J, et al. Accuracy of Ultrasound in Identifying Renal Scarring as Compared to DMSA Scan. Urology 2020;138:134-7.
16. Akhavansepahi M, Toloii F, Jang S, et al. The Prevalence of Renal Scars Among Infants Under One Year Old With a First UTI With or Without VUR in Qom, Iran, 2017. Iranian J Kidney Dis 2020;14(4):308-11.
17. Finkelstein J, Rague J, Varda B, et al. MP64-14 RENAL SCARRING IS ASSOCIATED WITH ADVERSE RENAL OUTCOMES DURING LONGITUDINAL ASSESSMENT. J Urol 2019r;201(Supplement 4):e946-7.
18. Bandari B, Sindgikar S, Kumar S, et al. Renal scarring following urinary tract infections in children. Sudan J Paediatr. 2019;19(1):25–30.
19. Jayaweera J, Reyes M. Antimicrobial misuse in pediatric urinary tract infections: recurrences and renal scarring. Ann Clin Microbiol Antimicrob 2018;17(1):27.
20. Sims-Williams H, Sims-Williams H, Mbabazi Kabachelor E, et al. Renal outcomes in children with operated spina bifida in Uganda. Int J Nephrol 2018;2018:6278616.
21. Pokrajac D, Sefic-Pasic I, Begic A. Vesicoureteral reflux and renal scarring in infants after the first febrile urinary tract infection. Med Arch. 2018;74(4):272–5.
22. Hung T, Tsai J, Liao P, et al. Role of renal ultrasonography in predicting vesicoureteral reflux and renal scarring in children hospitalized with a first febrile urinary tract infection. Pediatrics & Neonatology. 2016;57(2):113-9.
23. Mattoo T, Chesney R, Greenfield S, et al. Renal scarring in the randomized intervention for children with vesicoureteral reflux (RIVUR) trial. Clin J Am Soc Nephrol. 2016;11(1):54-61.
24. Hsu C, Tsai J, Ku M, et al. Antimicrobial Resistance and Diagnostic Imaging in Infants Younger Than 2 Months Old Hospitalized With a First Febrile Urinary Tract Infection. Pediatr Infect Dis J 2016;35(8):840-5.
25. Yılmaz S, Özçakar Z, Şükür E, et al. Vesicoureteral reflux and renal scarring risk in children after the first febrile urinary tract infection. Nephron 2016;132(3):175-80.
26. Kitao T, Kimata T, Yamanouchi S, et al. Urinary biomarkers for screening for renal scarring in children with febrile urinary tract infection: pilot study. J Urol 2015;194(3):766-71.
27. Hussein A, Elderwy A, Askar E, et al. Impact of common functional polymorphisms in renin angiotensin system genes on the risk of renal parenchymal scarring following childhood urinary tract infection. J Pediatr Urol 2015;11(3):152.e1-.e7.
28. Tolunay O, Buyan N, Tan M, et al. Urodynamic disorders and renal scarring in pediatric patients with nonmonosymptomatic nocturnal enuresis. Turk J Med Sci. 2015;45(2):320-4.
29. Narchi H, Marah M, Khan A, et al. Renal tract abnormalities missed in a historical cohort of young children with UTI if the NICE and AAP imaging guidelines were applied. J Pediatr Urol 2015;11(5):252.e1-e7.
30. Berdichevski E, Mattos S, Bezerra S, et al. Prevalência de pielonefrite aguda e incidência de cicatriz renal em crianças menores de dois anos de idade com infecção do trato urinário avaliadas por cintilografia renal com 99mTc-DMSA: a experiência de um hospital universitário. Radiologia Brasileira. 2013;46(1):30-4.
31. Amornchaicharoensuk Y, Parklug P. Prevalence and Risks Factors of Renal Scarring in Pediatric Patients with Urinary Tract Infection and Vesicoureteral Reflux. Vajira Medical Journal: J Urban Med 2013;57(2):81-8.
32. Mir S, Ertan P, Ozkayin N. Risk factors for renal scarring in children with primary vesicoureteral

reflux disease. Saudi J Kidney Dis Transpl. 2013;24(1):54-9.
33. Hunziker M, Puri P. Familial vesicoureteral reflux and reflux related morbidity in relatives of index patients with high grade vesicoureteral reflux. The Journal of urology. 2012;188(4S):1463-6.
34. Lee Y, Lee J, Park Y. Risk factors for renal scar formation in infants with first episode of acute pyelonephritis: a prospective clinical study. J Urol 2012;187(3):1032-6.
35. Ehsanipour F, Gharouni M, Rafati A, et al. Risk factors of renal scars in children with acute pyelonephritis. Braz J Infect Dis. 2012;16(1):15-8.
36. Erdogan H, Mir S, Berdeli A, et al. Renal scarring and osteopontin gene C/T polymorphism in children with primary vesicoureteral reflux. Indian pediatrics. 2012;49(4):311-3.
37. Hunziker M, Kutasy B, D'Asta F, et al. Urinary tract anomalies associated with high grade primary vesicoureteral reflux. Pediatr Surg Int. 2012;28(2):201-4.
38. Oh M, Kim J, Park M, et al. The impact of therapeutic delay time on acute scintigraphic lesion and ultimate scar formation in children with first febrile UTI. Eur J Pediatr. 2012;171(3):565-70.
39. Singh C, Shah S, Fernando R, et al. Detection of renal scars by transplant renal ultrasounds and DMSA scans after urinary tract infections in paediatric renal transplant recipients. Archives of Disease in Childhood. 2011;96(Suppl 1):A71-2.
40. Barros A, Oliveira E, Rodrigues L, et al. Infecções Urinárias na Criança: 5 anos de Dados clínicos e microbiológicos. Arquivos de Medicina. 2010;24(6):247-52.
41. Benador D, Benador N, Slosman D, et al. Are younger children at highest risk of renal sequelae after pyelonephritis? Lancet 1997;349(9044):17-9.
42. Najafi F, Sarokhani D, Hasanpour-Dehkordi A. The prevalence of kidney scarring due to urinary tract infection in Iranian children: a systematic review and meta-analysis. J Pediatr Urol 2019;15(4):300-8.
43. Sheikh N, Craig J, Rovers M, et al. Identification of children and adolescents at risk for renal scarring after a first urinary tract infection: a meta-analysis with individual patient data. JAMA pediatrics. 2014;168(10):893-900.
44. Morris BJ, Wiswell TE. Circumcision and lifetime risk of urinary tract infection: a systematic review and meta-analysis. The Journal of urology. 2013;189(6):2118-24.
45. Gordon I, Barkovics M, Pindoria S, et al. Primary vesicoureteric reflux as a predictor of renal damage in children hospitalized with urinary tract infection: a systematic review and meta-analysis. J Am Soc Nephrol 2003;14(739-744):3.

Received: 21.10.2021
Accepted for publication: 14.08.2022

Address for correspondence:
Moloud Fakhri
e-mail: mmfir@yahoo.com
&
Ali Hasanpour-Dehkordi
e-mail: alihassanpourdehkordi@gmail.com