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Prevalence of Renal Scarring in Children with Urinary Tract Infection: A systematic review and meta-analysis

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Abstract

Introduction: Since diagnosis of the scar is an important step in examining patients with UTI, the present study was conducted to determine the prevalence of post-UTI renal scar among Iranian children.

Methods: The methods used in the present systematic review were developed in accordance with the instructions in the PRISMA checklist. Hoy et al tools were used to evaluate the quality of the methodology and the risk of bias in each individual observational study. Meta-analysis was conducted using STATA 14.

Results: Six studies conducted on 587 children were included in the meta-analysis, the overall Prevalence of Renal Scarring in 587 Iranian children was 30.5 % (95% CI: 27.2, 33.9; $I^2 = 84.3\%$).

Conclusion: since the development of scar is a known complication of urinary tract infection and since hypertension and ulcerative kidney disease are late complications of the development of scar, prevention, early diagnosis, appropriate treatment and adequate follow up in children with Urinary Tract Infection is essential.

Keywords: Renal Scarring, Children, Urinary Tract Infection

Introduction

Urinary tract infection (UTI) is the most common bacterial infection during infancy and childhood (1). This new infection is caused mainly by intestinal bacteria. UTI is caused by *E. coli*, followed by *Klebsiella* and *Proteus* in girls in 75-90% of cases (2). In boys more than one year old, UTI is a protozoan with an outbreak such as *Escherichia coli* (3). The incidence of UTI in boys and girls younger than 6 years has been reported to be 1.8% and 6.6% in order (4). Regardless of age, children who suffer from urinary tract infection are likely to develop acute pyelonephritis and kidney scarring, unless Dimercaptosuccinic acid scan (DMSA) turns out to be normal, in which case the risk of scarring due to subsequent infections is low (5). The development of renal scar and nephropathy reflux depends on the degree of reflux, and children with high grade reflux who develop urinary tract infection are at increased

risk of pyelonephritis and renal scarring (6). Scar covers a range of disorders observed in the imaging of the kidneys, which is actually associated with irregularities of parenchymal damage in focal or diffuse areas (7). Renal scar is detectable by ultrasound, Dimercaptosuccinic acid scan and Intravenous pyelogram (IVP) scan (8). Acute pyelonephritis often does not leave kidney scarring or permanent damage to the kidney parenchyma in adults; however, it can cause scarring and disrupt the kidney function permanently in children through impaired kidney growth (9). Since the development of renal scar is associated with future complications, one has to find a way to prevent scarring and altering the quality of life of patients (10). Since diagnosis of the scar is an important step in examining patients with UTI, the present study was conducted to determine the prevalence of post-UTI renal scar among Iranian children.

Materials and Methods

The methods used in the present systematic review were developed in accordance with the instructions in the PRISMA checklist (11). Cross-sectional, case-control, and cohort studies were included in the present research; case series, letter to editors, case reports, clinical trials, study protocols, systematic review and narrative review are not included.

Searching strategy

The searches were conducted in English and Persian by two independent scholars in international databases (PubMed, Web of Science, Scopus and Google Scholar) and domestic ones (SID, Magiran) to find relevant studies with a time span from the very onset of the database until September 2018 (without time limit). The keywords used in the searching strategy included "prevalence" Renal Scarring, Children, Urinary Tract Infection and "Iran" which were combined with Boolean operators, AND, OR and NOT.

Study selection and data extraction

Two researchers reviewed the titles and abstracts independently, taking into account the eligibility

criteria. After removing repeat studies, the full text of the studies was evaluated based on eligibility criteria and, if needed, the required information was obtained from the authors.

Quality assessment

Hoy et al tools were used to evaluate the quality of the methodology and the risk of bias in each individual observational study (12). Meta-analysis was conducted using STATA 14.

Results

Study selection

The initial searching process yielded a total number of 355 articles from various sources. 144 studies turned out to be non-repetitive, out of which 211 studies were excluded due to unrelated titles during title and review process. 6 out of 22 studies met eligibility criteria. 16 other studies were removed for different reasons, 3 were reviews, 3 were letters to editor, and 10 did not have the minimum required to be included the study.

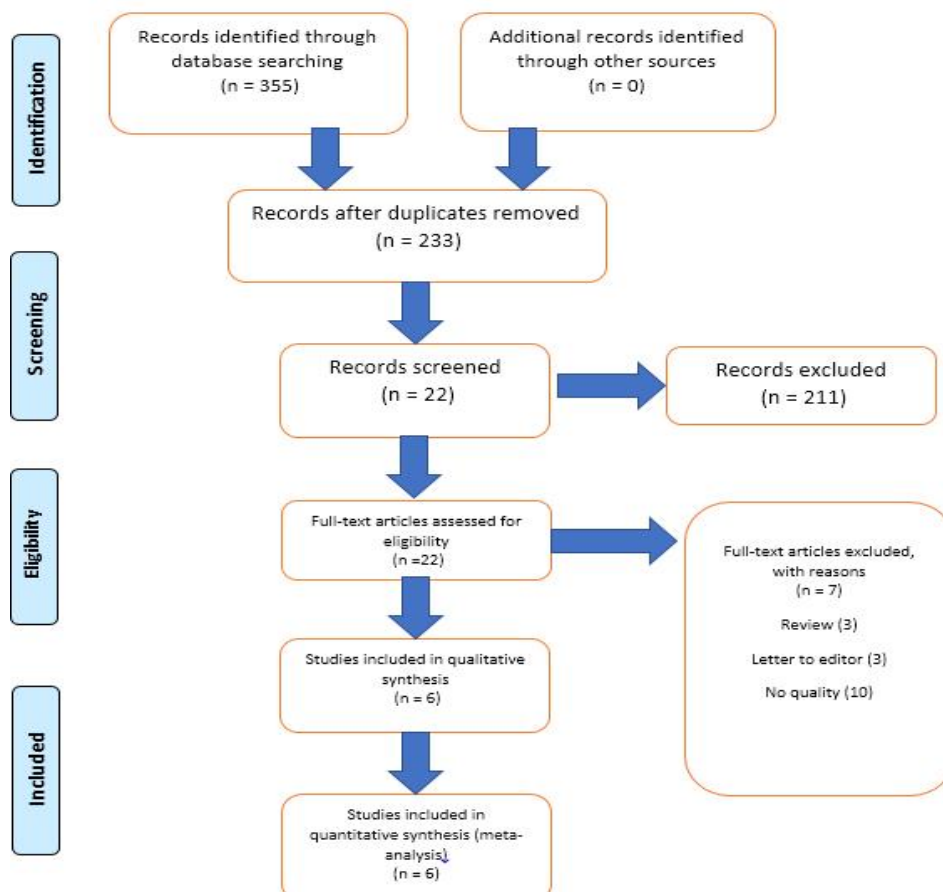


Fig 1. PRISMA flow diagram

Study Specifications

Studies had been conducted on 587 patients. The age range of the subjects was between 1 and 14 years old. 16 out of 18 studies had provided cross-sectional data. 18 studies, which underwent the review process, were obtained from four provinces, Tehran, Mashhad, Mazandaran and Kermanshah. The most common sampling methods turned out to be simple sampling, purpose-based, census-based, and simple random sequences. More than 50% of studies turned out to

have minor risk of bias. The most common site at which studies had been conducted was hospital (n = 6) (Table 1).

Prevalence of Renal Scarring in Children with Urinary Tract Infection

Six studies conducted on 587 children were included in the meta-analysis, the overall Prevalence of Renal Scarring in 587 Iranian children was 30.5 % (95% CI: 27.2, 33.9; I² = 84.3%).

Table 1. Studies included in the systematic review and Prevalence of Renal Scarring in Children with Urinary Tract Infection

ID	First Author	Year	Province	Sample size	ES	95% CI for ES		% Weight	Risk of bias
						Low	Up		
1	Beiraghdar ⁽²²⁾	2012	Tehran	176	0.267	0.202	0.332	26.55	Low
2	Ghotbi ⁽¹⁷⁾	2002	Tehran	36	0.132	0.021	0.243	9.25	Moderate
3	Ghanesh ⁽²¹⁾	2011	Mashhad	50	0.440	0.303	0.577	5.99	Low
4	Jafari ⁽²⁰⁾	2017	Mazandaran	208	0.340	0.276	0.404	27.36	Low
5	Seyedzade ⁽¹⁹⁾	2000	Kermanshah	133	0.250	0.177	0.323	20.93	Moderate
6	Sorkhi ⁽¹⁸⁾	2005	Mazandaran	84	0.510	0.403	0.617	9.91	low
	Pooled ES	----	-----	587	0.305	0.272	0.339	100	-----

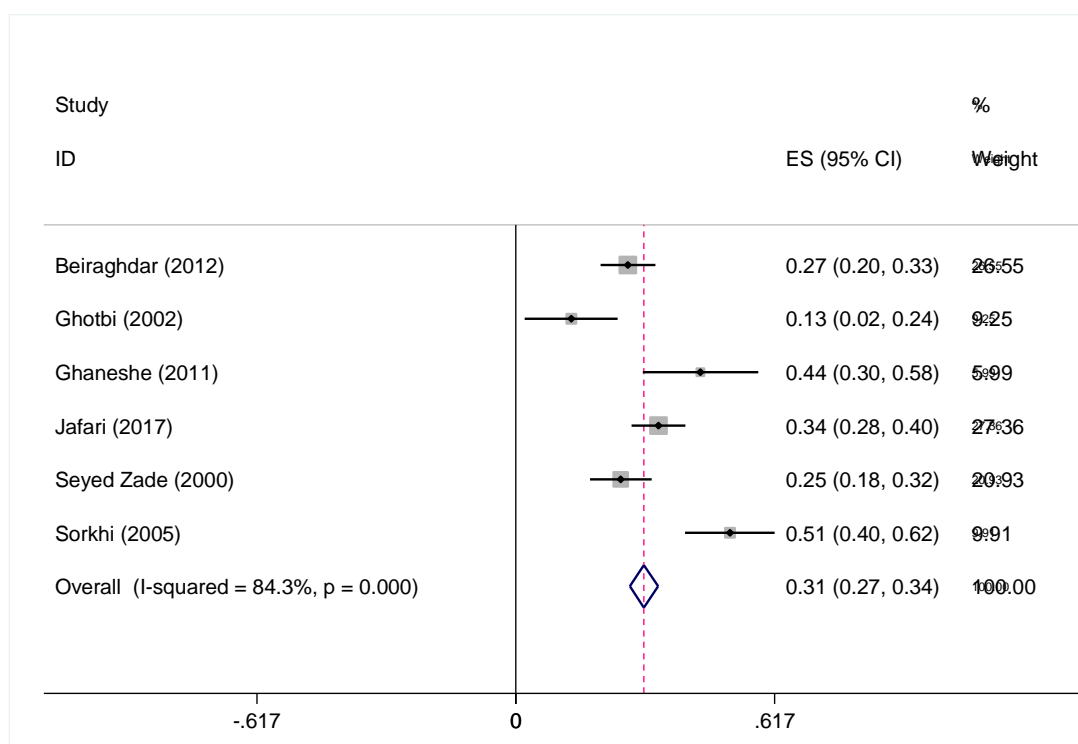


Fig. 2 : The Prevalence of Renal Scarring in Children with Urinary Tract

Infection and its 95% interval for the studied cases according to the year and the city where the study was conducted based on the model of the random effects model. The midpoint of each section of the line

estimates the % value and the length of the lines showing the 95% confidence interval in each study. The oval sign shows Prevalence of Renal Scarring in Children with Urinary Tract Infection for all studies.

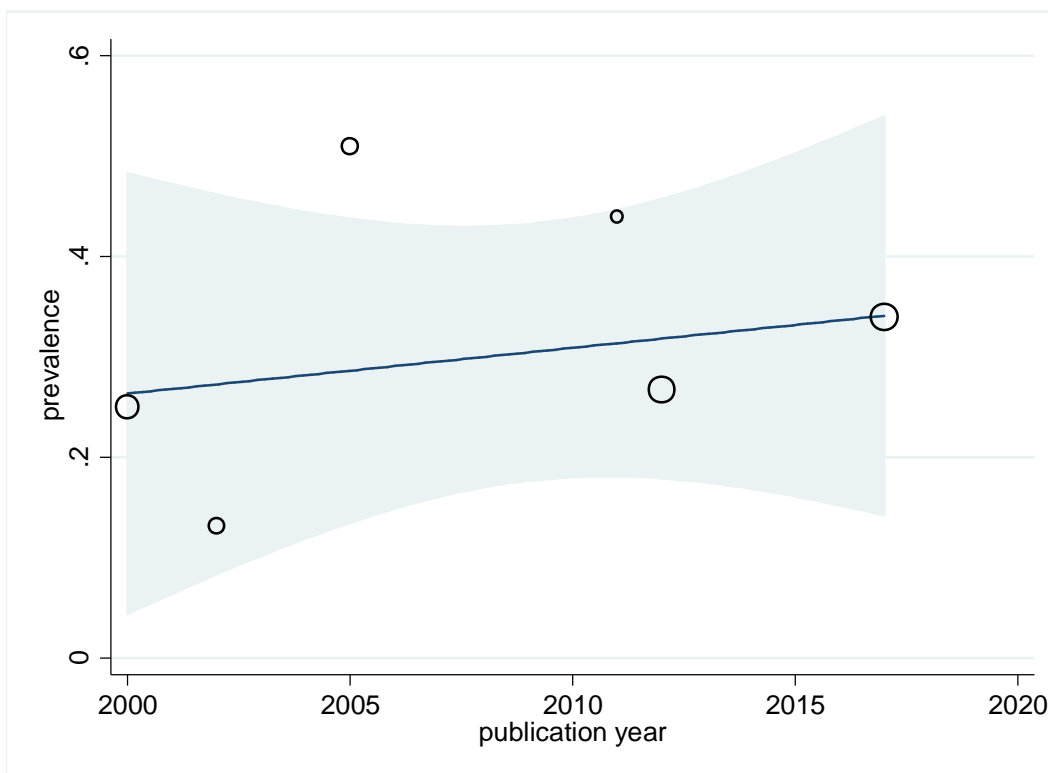


FIG. 3. Meta-regression between publication year and Prevalence of Renal Scarring in Children with Urinary Tract Infection

Discussion

Six studies conducted on 587 children were included in the meta-analysis, the overall Prevalence of Renal Scarring in 587 Iranian children was 30.5 % (95% CI: 27.2, 33.9; $I^2 = 84.3\%$). Scar is the result of an inflammatory reaction caused by infection between the host and bacterial agents. DMSA is nowadays a gold standard for detecting parenchymal kidney cysts (13-17). Several studies have shown that urinary reflux is a risk factor for causing scar and permanent kidney damage (23). For example, the results of Gordon et al meta-analysis conducted on all studies performed in 1966-2002 showed that positive 5VCUG for urinary reflux causes a 20% increase in risk of renal impairment in patients who have been admitted for urinary tract infections (24). In a retrospective study conducted on 58 children suffering from UTI aged 2 months to 11 years old, Masodo et al showed that fever and being female are risk factors for developing renal scars, especially in the presence of dilated urinary tract (grade III and IV and V); however Wang

et al (2008) stated that urinary reflux is more prevalent among boys. Therefore, providing solid proof in regard with the role of sex in the development of kidney scar requires further studies (25). Therefore, in order to control and decrease the incidence of kidney scars following urinary tract infections and prevent hypertension or chronic renal failure, it is essential to minimize various risk factors such as preventing the recurrence of infection using prophylaxis antibiotics, appropriate treatment for ureteral bladder reflux, and removal of obstruction in the pathway of urinary system; it is, also, necessary to provide urination education in cases where anatomical defects are present in the bladder (15 and 16). Also, since the development of scar is a known complication of urinary tract infection and since hypertension and ulcerative kidney disease are late complications of the development of scar, prevention, early diagnosis, appropriate treatment and adequate follow up in children with Urinary Tract Infection is essential.

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