



## THE ETIOLOGY OF ACUTE RENAL FAILURE IN THE IRANIAN CHILDREN: A SYSTEMATIC REVIEW AND META ANALYSIS

Ali Alidadi

Assistant Professor of Nephrology, Department of Nephrology, Zahedan University of Medical Sciences, Zahedan, Iran

Conflicts of Interest: Nil

Corresponding author: Ali Alidadi

### ABSTRACT

One of the important reasons for the hospitalization of children in intensive care units is to control and support various organ functions; including the function of the kidneys as highly susceptible organs. Acute kidney failure is not a disease but a complex syndrome in which, besides the kidneys, most body's organs are affected. The aim of this study was to evaluate The Etiology of Acute Renal Failure in the Iranian children.

**Methods:** The methods used in this systematic review were based on the Checklist (PRISMA) Guidelines. subgroups were analyzed to determine the heterogeneity by participants' age, year of publication, and Province. Finally, a meta-analysis was performed using STATA14 statistical software.

**Results:** According to the random effect model, the total prevalence of glomerular diseases in 766 acute renal failure patients was 24% (21-27% at a 95% confidence interval,  $I^2 = 96.7%$ ), the total prevalence of Congenital diseases in 568 acute renal failure patients was 36% (32-39% at a 95% confidence interval,  $I^2 = 98.8%$ ) and the total prevalence of Neurogenic bladder in 253 acute renal failure patients was 17% (13-22% at a 95% confidence interval,  $I^2 = 96.3%$ ).

**Conclusion:** Early diagnosis of Acute Renal Failure in children slows the progression of the disease and delays the final stage of failure, also considering that hemodialysis and kidney transplantation facilities are often available only for children weighing more than 12-10 kg, diagnosing the early and mysterious symptoms of chronic kidney failure (to prevent the progression of kidney failure as the child grows older, as well as to identify genetic diseases in the family and to prevent the birth of more unhealthy children) is of high significance.

**Key words:** Acute Renal Failure, Scorpion sting, Pediatric intensive care units, Prevalence

### INTRODUCTION

One of the important reasons for the hospitalization of children in intensive care units is to control and support various organ functions; including the function of the kidneys as highly susceptible organs (1). Acute kidney failure is not a disease but a complex syndrome in which, besides the kidneys, most body's organs are affected (2). By definition, acute kidney failure is a sudden decrease in kidney function that is manifested by a decrease in glomerular filtration, a decrease in urine volume, and an increase in blood urea and creatinine levels (3). Early diagnosis of this complication is very important for the patient's clinical treatment (4). Therefore, different rating systems have been suggested for the diagnosis of this disease (5). Despite the numerous benefits of breast milk, due to the lack of national plans to monitor breastfeeding adequacy in the first few days of life, some infants are admitted to treatment centers each year with clinical and laboratory symptoms of dehydration and renal failure (6). Acute kidney injury (AKI) leads to deterioration and sudden decrease in kidney function and kidney failure

excreting waste nitrogen products and regulating homeostasis, water, and electrolytes, and acidosis (7). Today, the term "acute kidney failure" has been largely replaced by "acute renal injury" (8). It is a syndrome that manifests itself as a rapid decline in renal blood flow, a decrease in glomerular filtration rate, a decrease in renal excretion, and an accumulation of nitrogen excretory products. In recent years, it has been shown that the relative increase in serum creatinine increases mortality (9).

### Methods

#### Inclusion criteria (eligibility criteria):

The methods used in this systematic review were based on the Checklist (PRISMA) Guidelines. In this research, cross-sectional, case-control, and cohort studies were included and case studies, letters to editors, case reports, clinical trials, study protocols, systematic reviews were excluded.

**Participants:** All studies of the prevalence of acute renal failure were studied.

**Findings:** The main purpose of this study was to determine the prevalence of acute renal failure in

patients undergoing heart surgery and the findings were reported.

**Sampling Methods and Sample Size:** All observational studies were included in the systematic review regardless of their design. The minimum sample size was 25 patients or more.

### Search Strategy:

The searches were conducted by two independent researchers and the aim was to find the relevant studies published from 1/1/2009 to 30/5/2019. The researchers searched for published studies in the English language in MEDLINE via PubMed, EMBASE via Ovid, the Cochrane Library and Trip database. For studies published in other languages, National Database (Magiran and SID, KoreaMed and LILACS), and for unpublished studies, OpenGrey ([www.opengrey.eu/](http://www.opengrey.eu/)), World Health Organization Clinical Trials Registry ([who.int/ictrp](http://who.int/ictrp)), and ongoing studies were searched. To ensure that the studies are adequate, the reference lists of the retrieved studies were also searched and studied. Systematic review articles were searched using MeSH and open terms in accordance with publication standards. After the MEDLINE strategy was finalized, the results were compared to search for other databases, as well as PROSPERO was searched for recent or ongoing systematic reviews. The keywords used in the search strategy are: Acute kidney injury, acute renal failure, creatinine

### Study Selection and Data Extraction

The two researchers independently analyzed the titles and abstracts of the articles according to eligibility criteria. After excluding additional studies, the full text of each study was evaluated on the basis of eligibility criteria and the information about the authors was collected as needed. The general information (the first author, province in which the study was conducted and year of publication), study information (the sampling technique, diagnostic criteria, data collection method, research conditions, the sample size, and risk of bias) and output scale (the prevalence of acute renal failure) were collected.

### Quality Assessment:

The extended scale of Hoy et al. was used to evaluate the quality of method and the risk of bias in each observational study. This 10-item scale assesses the quality of studies according to their external validity (items 1 to 4 evaluate the target population, sampling frame, and minimum selection bias) and internal validity (items 5 to 9

evaluate the data collection, problem statement, research scale and data collection tool, while item 10 evaluates the data analysis bias). The risk of bias was measured by two researchers independently and disagreements were resolved by consensus.

### Data Collection :

All eligible studies were included in the data collection after a systematic review and the data were integrated using the cumulative chart. The random effect model was evaluated based on the overall prevalence of the disease among the participants. The heterogeneity of the initial studies was assessed using the  $I^2$  test. In addition, subgroups were analyzed to determine the heterogeneity by participants' age, year of publication, and province. Finally, a meta-analysis was performed using STATA14 statistical software.

### Results:

#### Study Selection:

A total of 507 articles were extracted through preliminary searches in various databases. Of the 507 essential studies identified by the analysis of titles and abstracts, 483 ones were eliminated because of irrelevant titles. Of the 24 existing studies, 19 ones were excluded. Of the remaining studies, 5 met the study inclusion criteria. (Fig. 1)

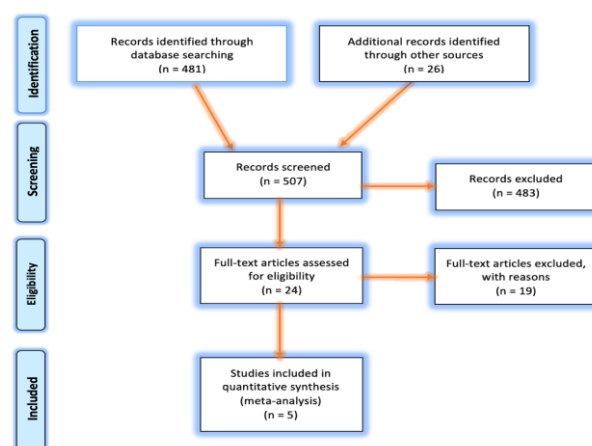


Figure 1: PRISMA flow diagram

#### Research Properties

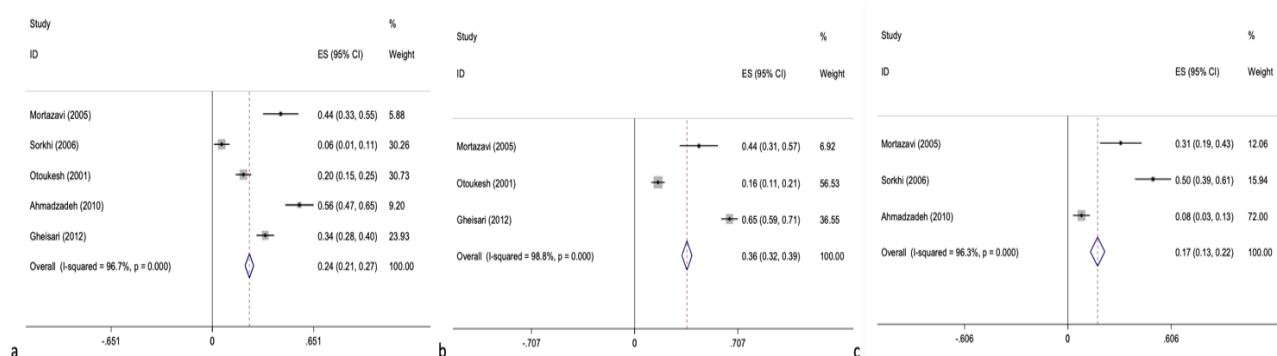
A total of 766 Acute Renal Failure patients and a total of 5 studies from 5 provinces that met the inclusion criteria were evaluated. Simple sampling was used to select the sample (n = 21). All the studies, were retrospective. Studies were from Tabriz ,Babol, Tehran Ahvaz and Isfahan. In most studies the risk of bias was low. Data were originally collected from medical records. The hospital was the main study site. (Table 1)

**Table 1: characteristics of the included studies**

| Author        | Publication year | Province | Mean of age | Male to female | Number of patients | Congenital diseases | glomerular diseases | Reflux nephropathy | Neurogenic bladder | Death |
|---------------|------------------|----------|-------------|----------------|--------------------|---------------------|---------------------|--------------------|--------------------|-------|
| Mortazavi 17  | 2005             | Tabriz   | 5.8         | 3/1            | 55                 | 44%                 | 25%                 | 18%                | 31%                | -     |
| Sorkhi 18     | 2006             | Babol    | 10.33±4.4   | 55/30          | 85                 | ----                | 6%                  | -----              | 50%                | 27%   |
| Otokesh 19    | 2001             | Tehran   | -----       | -----          | 245                | 16.3%               | 20%                 | 32%                | -                  | -     |
| Ahmadzadeh 20 | 2010             | Ahvaz    | 6.8         | 77/36          | 113                | -                   | 56%                 | ---                | 8%                 | -     |
| Gheisari 21   | 2012             | Isfahan  | 11.01±0.39  | 54/46          | 268                | 65%                 | 34%                 | -                  | -                  | 18.4% |

### The meta-analysis of the Prevalence of Acute Renal Failure in the Iranian children:

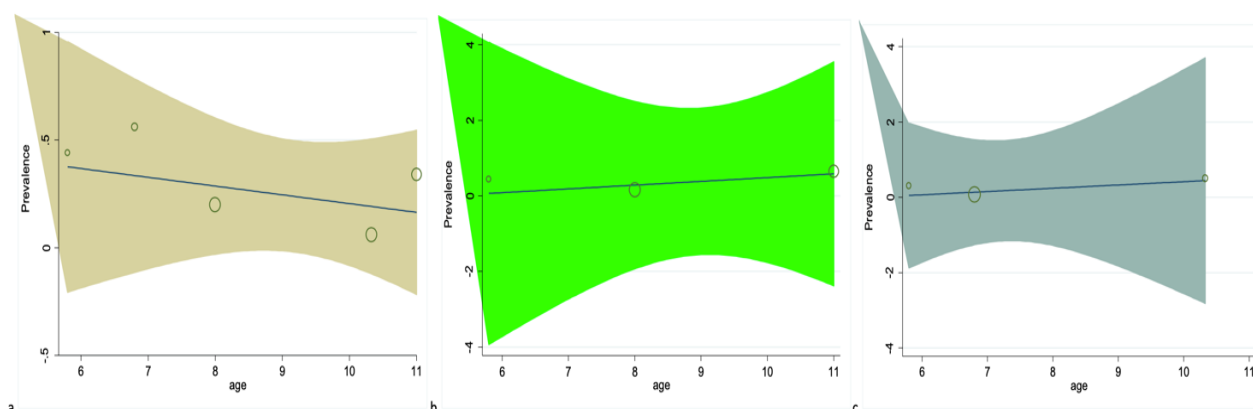
According to the random effect model, the total prevalence of glomerular diseases in 766 acute renal failure patients was 24% (21-27% at a 95% confidence interval,  $I^2 = 96.7%$ ), the total prevalence of Congenital diseases in 568 acute renal failure patients was 36% (32-39% at a 95% confidence interval,  $I^2 = 98.8%$ ) and the total prevalence of Neurogenic bladder in 253 acute renal failure patients was 17% (13-22% at a 95% confidence interval,  $I^2 = 96.3%$ ). (Fig. 2a-b-c, Table 2)

**Figure 2: The Etiology of Acute Renal Failure in the Iranian children**

### Meta Regression Results

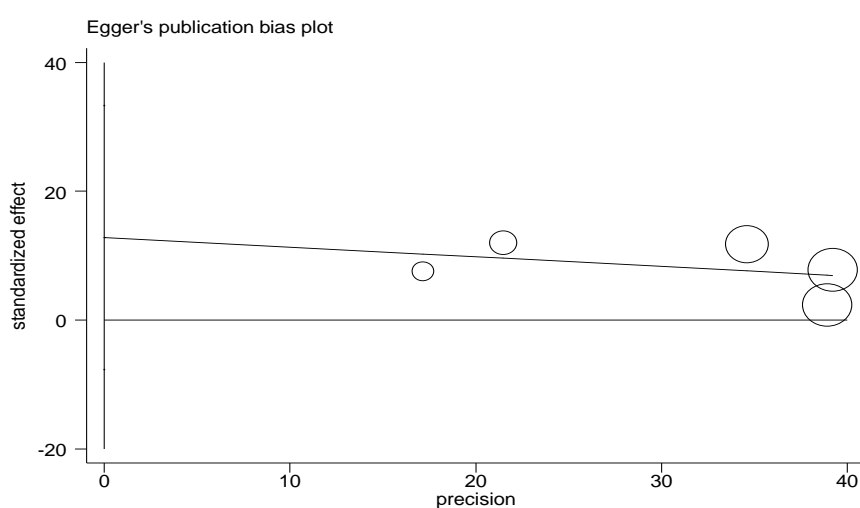
**The results of meta-regression between participants' age and the prevalence of Congenital diseases, glomerular diseases and Neurogenic bladder in acute renal failure patient:**

The regression of the study was evaluated by the relationship between the prevalence of Congenital diseases, glomerular diseases and Neurogenic bladder and participants' age. There was no significant linear trend in the univariate meta-regression to explain the effect size of participants' age. (Fig. 3a-b-c)

**Figure 3: The results of meta-regression between participants' age and the prevalence of glomerular diseases (a), Congenital diseases (b) and Neurogenic bladder (c) in acute renal failure patient**

### Publication Bias of Articles

The funnel plot in Fig. 4 does not show a publication bias and it is symmetric. The circle size indicates the size of the studies (the larger circles indicate more samples and the smaller circles indicate fewer samples). (Fig. 4)



**Figure 4: Publication Bias of Articles**

### Discussion:

According to the random effect model, the total prevalence of glomerular diseases in 766 acute renal failure patients was 24% (21-27% at a 95% confidence interval,  $I^2 = 96.7%$ ), the total prevalence of Congenital diseases in 568 acute renal failure patients was 36% (32-39% at a 95% confidence interval,  $I^2 = 98.8%$ ) and the total prevalence of Neurogenic bladder in 253 acute renal failure patients was 17% (13-22% at a 95% confidence interval,  $I^2 = 96.3%$ ). Acute Renal Failure (ARF) is the loss of a significant number of nephrons (10). Although acute Renal Failure is infrequent in children compared to adults, it is one of the leading causes of death and disability in children (11). About 5-10 children per year develop chronic kidney failure, and the majority of them die before hemodialysis and kidney transplantation (12). Although dialysis (hemodialysis or peritoneal dialysis) and kidney transplantation are widely used for these patients, the quality of life in children without kidneys and their families will be very different from other people (13). The causes of chronic kidney failure differ from one region to another depending on genetic and environmental factors, so determining these causes is of high importance (14). However, despite the early diagnosis, acute Renal Failure undergoes its normal development course but early diagnosis and follow-up measure can prevent the disease from progressing toward chronic kidney failure (15). Unfortunately, there are no accurate statistics in the country about the causes of acute Renal Failure, especially in children, and it is important to determine the cause and prognosis of these patients (16). Although kidney failure may increase

the mortality of children by 5-20%, it has been reported that if this complication occurs in intensive care units infant mortality is estimated to increase by 25-50% (17). The acute Renal Failure is often associated with the age in which kidney failure occurs. In children under 5 years of age, kidney disorders are more common, including congenital obstructions (18). Besides, causes such as glomerulonephritis are more common at higher ages. The symptoms of acute Renal Failure in the early stages are very mild and mysterious, and they mostly appear after the destruction of most nephrons (19). Because early diagnosis of chronic kidney failure in children slows the progression of the disease and delays the final stage of failure, also considering that hemodialysis and kidney transplantation facilities are often available only for children weighing more than 12-10 kg, diagnosing the early and mysterious symptoms of acute Renal Failure (to prevent the progression of kidney failure as the child grows older, as well as to identify genetic diseases in the family and to prevent the birth of more unhealthy children) is of high significance.

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