

## Acute kidney injury in pediatric patients: experience of a single center during an 11-year period

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**Key words:** child; acute kidney injury; multiple organ dysfunction syndrome; etiology; outcome.

**Summary.** The aim of our study was to determine the causes of acute kidney injury (AKI) in children, to compare outcomes between two periods – 1998–2003 and 2004–2008 – and to evaluate the influence of new methods of renal replacement therapy on mortality.

**Material and methods.** A retrospective analysis of medical record data of all children treated for AKI at the Clinic of Children Diseases, Hospital of Kaunas University of Medicine, during the period of 1998–2008 was made. Both periods were compared regarding various variables.

**Results.** Of the 179 children with AKI, 75 (41.9%) were treated during 1998–2003 and 104 (58.1%) during 2004–2008. Primary glomerular disease and sepsis were the leading causes of AKI in both the periods. AKI without involvement of other organs was diagnosed for 106 (59.2%) children: for 42 (56.0%) children in the first period and 64 (61.5%) in the second. A total of 124 (69.3%) children were treated in a pediatric intensive care unit. Multiple organ dysfunction syndrome with AKI was diagnosed for 33 (44%) patients in the first period and for 40 (38.5%) in the second. A significant decrease in mortality among patients with multiple organ dysfunction syndrome during the second period was observed (78.8% vs. 37.5%).

**Conclusions.** More than half of patients had secondary acute kidney injury of nonrenal origin. More than two-thirds (69.3%) of patients with AKI were treated in the pediatric intensive care unit. Multiple organ dysfunction syndrome was diagnosed for 40.8% of children with AKI. Renal replacement therapy was indicated for one-third of patients with AKI. A 2.5-fold decrease in mortality was observed in the second period as compared to the first one.

### Introduction

Acute kidney injury (AKI) is a reversible, poly-etiological clinical syndrome, which is characterized by an increase in the concentration of creatinine and nitrogenous waste products in blood and by the inability of the kidney to regulate fluid and electrolyte homeostasis (1, 2). AKI was previously known as acute renal failure, but after extensive pathophysiological studies, it has been revealed that ischemic and hypoxic processes take place in the kidneys much earlier than an increase in creatinine level appears (1). There are many causes of AKI. It is known that the prognosis of AKI depends on the etiology of the injury. Unfortunately, there are no uniform standardized criteria that would define AKI clearly (1, 2). The results of retrospective studies presented in literature are controversial. From 2% to 5% of children treated in a pediatric intensive care unit (PICU) and from 8% to 24% of infants in neonatal

departments suffer from AKI (3, 4). Mortality among children with AKI varies from 8 to 89% (3–5). Such variation in mortality can be explained by the use of different criteria defining AKI. One-third of patients with AKI need renal replacement therapy (RRT) (5, 6). The choice of RRT procedure depends on the etiology of the disease, age of the patient, fluid overload, the presence of multiple organ dysfunction syndrome (MODS). The use of continuous renal replacement therapy (CRRT) procedures for pediatric patients 20 years ago made the treatment of AKI for unstable patients possible. It reduced the mortality rate in pediatric patients with MODS. Some authors indicate that early start of CRRT (during the first days in PICU) results in better outcome (7). AKI due to primary kidney disease usually has better outcome. The decrease in mortality rate during the last decade due to better medical support before entering the PICU, better fluid overload control, and effective treatment

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of metabolic disorders was documented for patients with AKI due to extrarenal diseases (6). The prognosis of the recovery is highly dependent on the cause of AKI. The latest studies have shown that AKI in complex with other organ dysfunctions determines the occurrence of chronic renal disease (8). The aim of our study was to determine the causes of acute kidney injury in children, to compare outcomes between two periods – 1998–2003 and 2004–2008 – and to evaluate the influence of new methods of renal replacement therapy on mortality.

### Material and methods

A retrospective analysis of medical record data of all children treated for AKI at the Clinic of Children Diseases, Hospital of Kaunas University of Medicine, during the period of 1998–2008 was made. All children were diagnosed with AKI based on the following criteria: oliguria (diuresis, <1 mL/kg/h) and anuria (diuresis, <0.5 mL/kg/h) which lasted more than 6 hours, rise of serum creatinine by 26.4  $\mu\text{mol/L}$  or increase to  $\geq 150$ –200% from baseline (9). Both periods (period I, 1998–2003, and period II, 2004–2008) were compared regarding various variables. Age, sex, primary disease that caused AKI, indications for RRT (PD was performed for children aged from 1 month to 1 year, CRRT – for children with unstable hemodynamics, HD – for the rest of patients), methods of RRT used, outcomes, and possible risk factors causing death were evaluated. Comparing the mortality within both periods, the patients were divided into two groups. One group consisted of children who had AKI (because of primary renal disease or other causes) without injury of other organs. Children of the second group had multiple organ dysfunction including AKI. Children with chronic renal failure were excluded from the study.

Statistical data analysis was performed using Fisher's exact test. The significance level of 0.05 was chosen.

### Results

Of the 179 children with AKI, 75 (41.9%) were treated during 1998–2003 (period I) and 104 (58.1%) during 2004–2008 (period II). The age ranged from 1 month to 18 years (Table 1). There were 102 (57%) boys and 77 (43%) girls. However, there was no significant gender difference comparing two periods ( $P > 0.05$ ). Due to serious condition, 124 (69.3%) children were treated in the PICU. Primary glomerular disease and sepsis were the most common cause of AKI in both the periods, while other causes distributed similarly. Fig. shows the outcomes of patients with AKI with/without multiorgan dysfunction syndrome MODS. AKI without involvement of other organs was diagnosed for 106 (59.2%) children: for 42 (56.0%) children in the first period and 64 (61.5%) in the second. Renal disease was the cause of isolated AKI in 50 (47.2%) children. Multiple organ dysfunction syndrome with AKI was diagnosed for 33 (44.0%) patients from the first period and for 40 (38.5%) from the second period. Sixty-eight (93.2%) children had MODS that was not of renal origin. Sepsis was the most common cause of MODS in both the groups: 10 (30.3%) and 18 (45.0%), respectively.

Table 1. Distribution of patients according to age

Age	Period 1	Period 2	Total
1 month to 1 year	25	20	45
1–2 years	7	16	23
3–6 years	7	7	14
7–15 years	36	45	81
16–18 years	0	16	16

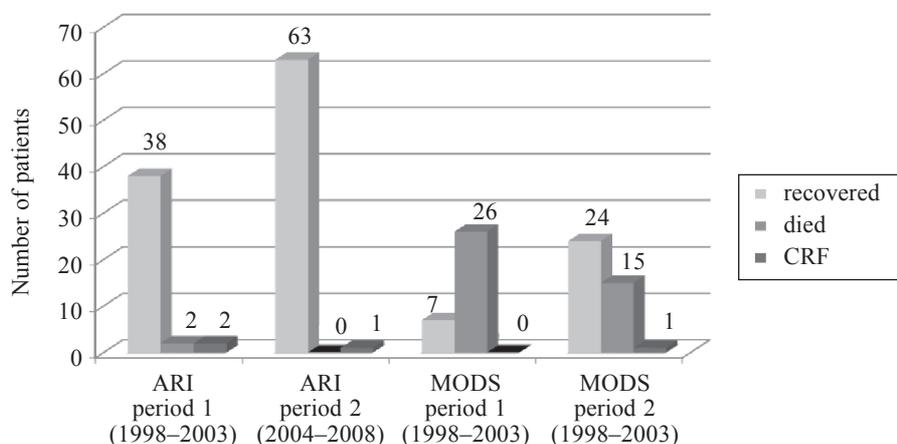


Fig. Outcomes of patients with acute renal injury (AKI) with/without multiorgan dysfunction syndrome (MODS)

RRT was administered for 21 (28.0%) children in the first period and for 31 (29.8%) in the second. During the first period, peritoneal dialysis (PD) and hemodialysis (HD) were performed, while continuous renal replacement therapy (CRRT) was included in the second period. Within the first period, 23.8% of children underwent PD and 76.2% of children HD. During the second period, HD, PD, and CRRT were performed in 25.8%, 61.3%, and 12.9% of children, respectively. The highest mortality was observed among children aged from 1 month to 1 year ( $n=17$ , 37.8%) and 7–16 years ( $n=20$ , 24.7%). The overall mortality among patients with MODS during the period of 1998–2008 was 56.2%; however, a significant decrease in the mortality among patients with MODS during the second period was seen: 26 (78.8%) vs. 15 (37.5%) ( $P=0.0007$ ). Within the first period mortality rate among children treated with HD – 43.8% ( $n=7$ ), PD – 20.0% ( $n=1$ ). During the second period mortality rate was as follows: HD – 15.8% ( $n=3$ ), PD – 12.5% ( $n=1$ ), CRRT – 75.0% ( $n=3$ ). The influence of CRRT on mortality rate among children who needed RRT between two periods was not significant. Full recovery after the disease was documented in 45 (60%) children in the first period and 87 (83.7%) in the second period ( $P=0.0007$ ). Chronic renal failure after AKI remained in 4 patients during both periods.

### Discussion

AKI must be considered as a syndrome not a disease, which can manifest not only during kidney diseases, but diseases of other organs as well (1, 5). According to the 20-year experience of American colleagues, such patients must be transferred to hospitals with pediatric nephrology and intensive care units in order to get a high-quality supportive therapy and timely RRT (10). The majority ( $n=124$ , 69.3%) of children of our clinic were treated in PICU unit as well.

In our study, acute glomerulonephritis ( $n=49$ , 27.4%), sepsis ( $n=39$ , 21.8%), hemolytic-uremic syndrome ( $n=15$ , 8.4%), polytrauma ( $n=8$ , 4.5%) were the most common causes of ARI. Authors from other European countries reported similar causes of AKI: sepsis was the cause of AKI in 17.4% of cases and hemolytic-uremic syndrome in 9.6% of cases. However, cardiac surgery was indicated as the leading cause of AKI (42.6%) (6). Pediatric cardiac surgeries are rarely carried out in our center; therefore, we had no cases of AKI cause by cardiac surgeries. Flynn et

al. reported kidney diseases and sepsis to be the most common causes of AKI after surgery (4). During the period of 2004–2008, we documented a marked increase in the proportion of patients with sepsis-induced AKI (from 14.6% to 26.9%). This might be conditioned by the fact that patients with suspected sepsis were referred to our center because of high-quality support, including early start of RRT. Sepsis was the most common cause of MODS during both periods (30.3% and 45%).

Many authors, while analyzing long-term experience, point out that incidence of so-called secondary AKI caused by cardiac surgery, polytrauma, bone marrow and stem cell transplantation and their complications has been increasing during the last decade (1). Nonrenal causes of AKI were predominant in our study as well. Secondary AKI develops as a life-threatening complication, which leads to an 11-fold higher mortality rate (4). In such cases, it is very important to pay attention to treatment regimen before a patient is transferred to the PICU (4). Many authors indicate that only 2–5% of PICU patients have AKI; however, mortality rate in this group of patients (8–89%) remains very high (3–5). The overall mortality rate of patients with AKI in our clinic was 24%. The majority of patients who experienced bad outcome had MODS (Table 2).

It was shown that mortality rate of patients with MODS depends on the number of organs affected (11). We observed a significant decrease in mortality among children in this group (from 78.8% to 37.5%;  $P=0.0007$ ). There was no difference in the frequency of RRT procedures comparing both the periods, and, on the average, it was 29.1%. Other authors reported similar findings and concluded that about one-third of patients who developed AKI needed RRT (5, 6, 10, 12, 13). The method of RRT is chosen considering the age, hemodynamic stability, and clinical situation

Table 2. Causes of acute renal injury

Cause	Period 1	Period 2	<i>P</i>
Glomerulonephritis	22 (29.3%)	27 (26.0%)	>0.05
Sepsis	11 (14.7%)	28 (26.9%)	>0.05
Hemolytic-uremic syndrome	7 (9.3%)	8 (7.7%)	>0.05
Intestinal infection	6 (8.0%)	4 (3.9%)	>0.05
Trauma	3 (4.0%)	5 (4.8%)	>0.05
Interstitial nephritis	0 (0%)	6 (5.8%)	0.03
Congenital cardiac disease	3 (4.0%)	2 (1.9%)	>0.05
Complicated viral infection	2 (2.7%)	2 (1.9%)	>0.05
Leptospirosis	0 (0%)	2 (1.9%)	>0.05
Other	21 (28.0%)	20 (19.2%)	>0.05
Total	75 (100%)	104 (100%)	

of the patient. Warady and Bunchman summarized the results of 123 pediatric nephrology centers (116 in North America and 7 in Europe) and concluded that PD was the first-choice RRT modality in 64% of 0–2-year-old children, while in the group of children aged 12 years and more, the frequency of PD decreased to 20% (12). Many authors advice wider application of CRRT among pediatric patients with MODS (2, 6). Some authors pointed out that better outcomes were observed in patients in whom CRRT was started earlier because usually MODS develops more quickly in children than adults, and after 72 hours following the admission to the PICU, the maximum number of organs are affected (7, 8, 14). It is stated that the use of CRRT, which has increased during the last 5 years two times, is superior to PD and HD in the treatment of children with AKI (6, 8, 12). The study by Lowrie reported an experience with renal replacement therapy in children with MOD and showed that the frequency of PD, HD, and CRRT was 30%, 20%, and 50%, respectively (15).

In the second period of our study, a decrease in mortality from 78.8% to 37.5% among children with MODS was documented. However, there was no significant impact of CRRT on mortality among children who needed RRT. We hypothesize that the impact of CRRT was not significant because of small sample size in both the groups. However, not all centers offer CRRT services because special facilities

and well-trained pediatric nephrology medical staff are limited (12). Early referral of critically ill patients to the clinic and introduction of new methods of RRT have led to better outcomes: during the second period, more patients were cured than during the first one (87 [83.7%] vs. 45 [60%];  $P=0.0004$ ). Depending on the etiology of the disease, up to 11% of patients can develop chronic renal insufficiency (1). In our clinic, 4 cases of chronic renal insufficiency were determined at discharge during both the periods. After implementation of new RRT technologies, we succeeded to decrease mortality rate. Recently, the aim is set at diagnosing AKI at early stage, introduction of new biomarkers in clinical practice, and prevention of children from AKI.

### Conclusions

1. More than half of patients had secondary acute kidney injury of nonrenal origin.
2. More than two-thirds of patients with acute kidney injury were treated in the pediatric intensive care unit.
3. Multiple organ dysfunction syndrome was diagnosed for 40.8% of children with acute kidney injury.
4. Renal replacement therapy was indicated for one-third of patients with acute kidney injury.
5. A 2.5-fold decrease in mortality was observed in the second period as compared to the first one.

## Vaikų ūminis inkstų pažeidimas. Vieno centro 11 metų patirtis

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**Raktažodžiai:** vaikai, ūminis inkstų pažeidimas, dauginis organų nepakankamumas, etiologija, baigtys.

**Santrauka.** *Tyrimo tikslas.* Išanalizuoti vaikų ūminio inkstų pažeidimo priežastis ir baigtis, įvertinti naujų pakaitinės inkstų terapijos metodų įtaką mirštamumui, duomenis palyginti suskirstant juos į du laikotarpius 1998–2003 m. ir 2004–2008 m.

*Tyrimo medžiaga ir metodai.* Retrospektyviai išanalizuoti visų vaikų, kurie dėl ūminio inkstų pažeidimo buvo gydyti Kauno medicinos universiteto klinikų Vaikų ligų klinikoje 1998–2008 m., ligos istorijų duomenis.

*Rezultatai.* 179 vaikams nustatytas ūminis inkstų pažeidimas. Ligonių skaičius nagrinėtais laikotarpiais pasiskirstė atitinkamai – 75 (41,9 proc.) ir 104 (58,1 proc.). Dažniausia ūminio inkstų pažeidimo priežastis abiem nagrinėtais laikotarpiais buvo pirminė inkstų liga ir sepsis. Tik ūminis inkstų pažeidimas nustatytas 106 (59,2 proc.) vaikams, atitinkamai – per pirmąjį laikotarpį 42 (56,0 proc.), per antrąjį – 64 (61,5 proc.). Dėl sunkios būklės 124 (69,3 proc.) ligoniai buvo gydyti vaikų intensyviosios terapijos skyriuje. Dauginis organų nepakankamumas su ūminiu inkstų pažeidimu nustatytas panašiam ligonių skaičiui per abu tyrimų laikotarpius – 33 (44,0 proc.) ir 40 (38,5 proc.) ligonių. Statistiškai patikimai ( $p<0,0007$ ) šios grupės ligonių mirštamumas sumažėjo per antrąjį laikotarpį (nuo 78,8 iki 37,5 proc.).

*Išvados.* Daugiau kaip pusė ligonių nustatytas neinkštinės kilmės ūminis inkstų pažeidimas. Daugiau kaip du trečdaliai (69,3 proc.) vaikų gydyti vaikų intensyvosios terapijos skyriuje. Dauginis organų nepakankamumas nustatytas 40,8 proc. vaikų, sirgusių ūminiu inkstų pažeidimu. Trečdaliui vaikų, kuriems buvo nustatytas ūminis inkstų pažeidimas, taikyta pakaitinė inkstų terapija. Vaikų, sirgusių ūminiu inkstų pažeidimu, bendrasis mirštamumas per antrąjį laikotarpį sumažėjo 2,5 karto, o sirgusiųjų dauginiu organų nepakankamumu – daugiau kaip du kartus.

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