

Kenia Machado Souza Freire<sup>1</sup>,  
 Nilzete Liberato Bresolin<sup>2</sup>, Ana  
 Camila Flores Farah<sup>3</sup>, Francisca  
 Lígia Cirilo Carvalho<sup>3</sup>, José Eduardo  
 Coutinho Góes<sup>3</sup>

## Acute kidney injury in children: incidence and prognostic factors in critically ill patients

*Lesão renal aguda em crianças: incidência e fatores prognósticos em pacientes gravemente enfermos*

1. Pediatric Intensive Care Resident Physician of Hospital Infantil Joana de Gusmão – Florianópolis (SC), Brazil.
2. Assistant Professor of Pediatric Nephrology for the Universidade Federal de Santa Catarina - UFSC - Florianópolis (SC), Brazil; Physician of the Pediatric Intensive Care Unit of Hospital Infantil Joana de Gusmão - Florianópolis (SC), Brazil.
3. Physician of the Intensive Care Unit of Hospital Infantil Joana de Gusmão - Florianópolis (SC), Brazil.

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### Author for correspondence:

Kenia Machado Souza Freire  
 Rua Lourenço Vanucci, 47 - Jardim  
 Guarujá  
 Zip Code: 18050-606 – Sorocaba (SP),  
 Brazil.  
 Phone: +55 (15) 3221-1386  
 E-mail: keniafreire@yahoo.com.br

### ABSTRACT

**Objectives:** Acute kidney injury is characterized by sudden and generally reversible renal function impairment involving inability to maintain homeostasis. In pediatrics, the main causes of acute kidney injury are sepsis, use of nephrotoxic drugs and renal ischemia in critically ill patients. The incidence of acute kidney injury in these patients ranges from 20 to 30%, resulting in increased morbid-mortality, a 40 to 90% rate. This study aimed to evaluate the incidence of acute kidney injury in intensive care unit patients, to categorize the severity of the acute kidney injury according to the Pediatric Risk, Injury, Failure, Loss, End-Stage (pRIFLE), examine the relationship between the acute kidney injury and severity using the Pediatric Index of Mortality (PIM) and to analyze outcome predictors.

**Methods:** A prospective study of the patients admitted to the intensive care unit of Hospital Infantil Joana de

Gusmão - Florianópolis / SC – Brazil was conducted between July 2008 and January 2009. Were evaluated daily the urine output and serum creatinine, and the patients were categorized according to the pRIFLE criteria.

**Results:** During the follow-up period, 235 children were admitted. The incidence of acute kidney injury was 30.6%, and the maximal pRIFLE score during hospitalization was 12.1% for R, 12.1% for I and 6.4% for F. The mortality rate was 12.3%. The patients who developed acute kidney injury had a ten times bigger risk of death versus the not exposed patients.

**Conclusions:** Acute kidney injury is frequent in critically ill patients. Early diagnosis and prompt and appropriate therapy for each clinical aspect may change this condition's course and severity, and reduce the patients' morbidity and mortality.

**Keywords:** Child; kidney/injuries; Mortality; Critical illness

### INTRODUCTION

Acute kidney injury (AKI) is characterized by a sudden and generally reversible renal function impairment, involving inability to maintain the homeostasis, and may or not be accompanied by reduced diuresis.<sup>(1-5)</sup>

Usually, AKI may be categorized as pre-renal, related to reduced renal blood flow (RBF) for inappropriate cardiac output or intravascular volume; intrinsic renal disease, from an insult to the renal parenchyma including ischemic, vascular, tubular or glomerular disorders; and post-renal, due to urinary tract obstruction either in single kidney or both kidneys.<sup>(1,3,4,6)</sup>

During the childhood, the main AKI causes are sepsis, nephrotoxic drugs, and renal ischemia in critically ill patients.<sup>(1,6)</sup>

These patients, particularly those staying in intensive care units (ICUs), are exposed to a number of conditions which may result in renal impairment, thus significantly increasing the morbi-mortality rate.<sup>(5,7-10)</sup> Among the main causes we should mention: hypovolemia leading to hypoperfusion and consequent hypoxia; inflammatory and thrombotic events caused by sepsis; systemic inflammation from trauma, major surgeries, extracorporeal circulation; use of vasodilator drugs such as phosphodiesterase inhibitors, sedatives, epidural blockade; vasopressors; and use of nephrotoxic drugs as aminoglycosides, amphotericin B, radiological contrasts, and drugs interfering with the renal hemodynamics such as angiotensin converting enzyme inhibitors and angiotensin II receptor blockers.<sup>(2,4,11,12)</sup>

Sepsis, and specially the septic shock, is one of the main causes of AKI. AKI prevalence in sepsis ranges from 9% to 40%, involves poor prognosis, and is associated with a 70% mortality rate.<sup>(2,13,14)</sup>

Among critically ill renal impaired patients, about 6% may need renal replacement therapy (RRT), with a mortality rate increased by 50 to 80%, particularly associated with sepsis, septic shock, and multiple organ and systems dysfunction (MODS).<sup>(6,15,16)</sup>

Considering the close association between severely ill patients and AKI, the quantification of ICU patient's severity is mandatory. In pediatrics, the most used prognostic indicators are PRISM (Pediatric Risk Index Score for Mortality) and PIM (Pediatric Index of Mortality).<sup>(17,18)</sup>

The AKI diagnosis methods include: clinical evaluation of the urinary output and laboratory tests as urinalysis, blood urea nitrogen, and creatinine, however with low sensitivity and specificity.<sup>(19)</sup> Biomarkers for

early AKI detection are currently under investigation, among them neutrophil gelatinase associated lipocalin (NGAL), cystatin C, interleukin 18, and kidney injury molecule-1 (KIM-1).<sup>(20)</sup> Although these markers have good sensitivity and specificity, they are not routinely used due to their low availability and high costs.<sup>(19,20)</sup>

In this context, the Acute Dialysis Quality Initiative (ADQI), which involves the participation of nephrologists and intensivists, held in 2002 in the city of Vicenza the Second International Consensus Conference of the ADQI.<sup>(21)</sup> where adult AKI diagnosis criteria were proposed and decided, and detailed published in 2004 with the name RIFLE criteria. These are currently under scientific community evaluation.<sup>(22)</sup>

The RIFLE criteria define three grades of increasing AKI severity (R – Risk of renal dysfunction; I – Injury of the kidney; F – Failure of kidney function) and two outcome variables (L - Loss of kidney function and E - End-stage kidney disease). For the first three categories, the RIFLE criteria aimed to standardize AKI definition by patients' stratification according to serum creatinine and urinary output changes from baseline. Loss of kidney function and End-stage kidney disease define two categories based on the RRS time required after the initial insult.<sup>(21)</sup>

Recently, Akcan-Arikan et al. provided a pediatric patients-modified RIFLE version (pRIFLE), based on a 12 months single center study where 150 critically ill children were prospectively analyzed.<sup>(23)</sup> The proposed pRIFLE criteria are based on the estimated creatinine clearance (ECC) calculated by means of the Schwartz formula<sup>(24)</sup> or on the urinary output reduction, in a body weight per hour basis, as detailed on Table 1.

This study aimed to evaluate the incidence of AKI in ICU patients, and to categorize the AKI severity according to the new pRIFLE diagnosis criteria, quantify and analyze the AKI and PIM-evaluated severity, and to evaluate the associated prognostic factors.

**Table 1 – RIFLE criteria modified for children**

	Estimated creatinine clearance (ECC)	Urinary output
Risk of kidney injury	ECC reduction by 25%	< 0.5 mL/kg/h for 8 hours
Renal injury	ECC reduction by 50%	< 0.5 mL/kg/h for 16 hours
Renal function failure	ECC reduced by 75% or ECC < 35 mL/min/1.73m <sup>2</sup>	< 0.3 mL/kg/h for 2 hours or anuria for 12 hours
Loss of kidney function	Persistent renal function failure > 4 weeks	
End-stage renal disease	Persistent renal function failure > 3 months	

**Source:** Akcan-Arikan A, Zappitelli M, Loftis LL, Washburn KK, Jefferson LS, Goldstein SL. Modified RIFLE criteria in critically ill children with acute kidney injury. *Kidney Int.* 2007;71:1028-35. RIFLE - risk, injury, failure, loss, end-stage; ECC – estimated creatinine clearance.

## METHODS

A prospective study was conducted from July 2008 to January 2009 which included all patients admitted to the pediatric intensive care unit (PICU) of the Hospital Infantil Joana de Gusmão (HIJG) – Florianópolis (SC) - Brazil. This is an eight beds pediatric ICU, of tertiary degree of complexity, and receives both clinical and surgical patients.

This study was approved by the Institution's Ethics Committee (registration number 041/2008). This study was explained to the patients' parents or legal representatives, before they were asked to sign the Informed Consent Form.

The inclusion criteria were: patients older than 29 days and younger than 16 years, and time of stay above 24 hours. Patients with previous renal disease were excluded.

The included patients were followed during their stay in the PICU, and their data were collected daily according to the approved protocol. The patients were categorized according to their age, gender, mortality risk rate prognosis by admission (using the PIM II prognosis score)<sup>(18)</sup>; admission diagnosis, degree of kidney injury (pRIFLE) during the hospitalization, mechanic ventilation (MV) need, vasoactive drugs (VD) need, nephrotoxic drugs (ND) exposure, peritoneal dialysis (PD) need, time of stay in days (HD) and outcome (either discharge or death).

For kidney injury degree (pRIFLE)<sup>(23)</sup> categorization, were analyzed daily: urinary output and serum creatinine level, and the estimated creatinine clearance was calculated according to the Schwartz formula.<sup>(24)</sup> The patients admitted with missing baseline renal function data had the normal clearance value of 100 mL/1.73 m<sup>2</sup>/24 h considered as reference, as proposed by Akcan-Arikan et al.<sup>(23)</sup>

The data collected were statistically analyzed. The quantitative variables were expressed as means and standard deviations, lower, higher and median values. The categorical variables were described by their absolute (n) and relative (%) frequencies. The association between the different variables was analyzed by appropriate hypothesis testing (Pearson's Chi-square, exact Fisher's, Mann-Whitney's, and Kruskal-Wallis tests). The relative risks (RR) for patients' gender, different diagnosis, outcomes for either with or without acute renal failure were calculated, as well as their respective 95% Confidence Intervals (95%CI). P values ≤ 0.05 were considered significant.<sup>(25)</sup> The analysis were performed using the MS Excel and EpiInfo 6.04 softwares.

## RESULTS

During this six months period 245 children were admitted to the PICU, being ten of them excluded for chronic renal failure. Of the 235 children in this study, 48.9% were male (Table 2).

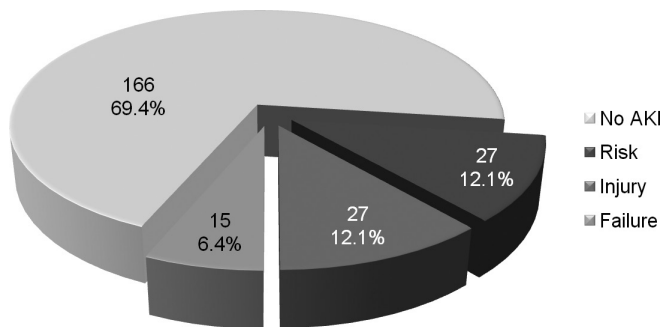
**Table 2 – Profile of patients admitted to the intensive care unit**

Variables	Kidney injury		Total	RR	95%CI	P value
	No N (%)	Yes N (%)				
Gender						
Male	80 (68.4)	37 (31.6)	117	1.00		
Female	86 (72.9)	32 (27.1)	118	0.86	0.58-1.28	0.4480
Diagnosis						
Resp.Fail.	32 (74.4)	11 (25.6)	43	0.83	0.44-1.54	0.5600
SIRS/sepsis	16 (39.0)	25 (61.0)	41	3.76	2.14-6.59	<0.0010
HT/Trauma	30 (88.2)	4 (11.8)	34	0.32	0.12-0.88	0.0150
General PS	48 (90.6)	5 (9.4)	53	0.25	0.10-0.60	<0.0010
Heart PS	12 (41.4)	17 (58.6)	29	3.41	1.72-6.75	<0.0010
Others	28 (80.0)	7 (20.0)	35	0.60	0.28-1.31	0.1870
Outcome						
Discharge	154 (74.8)	52 (25.2)	206	1.00		
Death	12 (41.4)	17 (58.6)	29	10.43	5.95-18.28	<0.0001
Total	166	69	235			

RR – relative risk; CI – confidence interval; Resp.Fail. – respiratory failure; SIRS – systemic inflammatory response syndrome; HT – head trauma; PS –post surgery. Pearson's Chi-square test.

Post-operative patients constituted 34.9% of the sample (Table 2). Patients admitted for primary heart, neurological or hematological disease were categorized under “other” diagnosis.

Of the 235 patients, 69 (30.6%) had some degree of AKI, being the maximal pRIFLE value during their hospitalization 12.1% for Risk (R), 12.1% for Injury (I) and 6.4% for Failure of the renal function (F) (Figure 1). Regarding the diagnosis, patients admitted due to Systemic Inflammatory Response Syndrome (SIRS)/Sepsis and heart surgery post-operative period had a three fold risk of developing AKI (RR 3.76 95%CI 2.14-6.59 and RR 3.41 95%CI 1.72-6.75, respectively), while patients admitted for respiratory failure and “other” had no statistically significant difference (Table 2).



AKI – acute kidney injury

**Figure 1 – Distribution of the patients admitted to the intensive care unit according to their maximal level of acute kidney injury during the time of stay.**

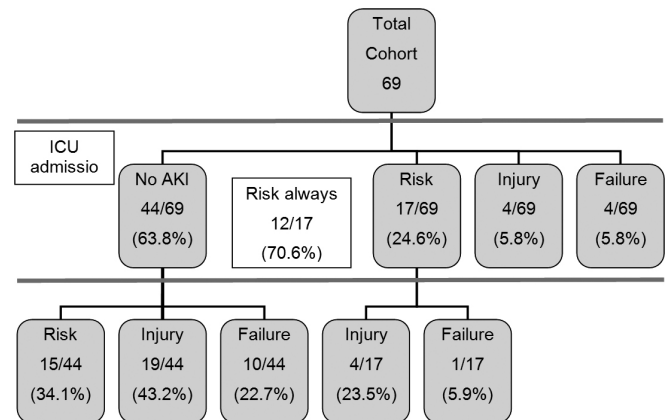
Twenty nine (12.3%) of the 235 admitted patients died, and those with AKI had a risk of death ten times bigger versus the non-exposed (RR 10.43 95%CI 5.95-18.28) (Table 2).

Of the 69 AKI patients, 37 (53.6%) were male. Infants were the predominant age range (44; 63.8%). The vast majority (46; 66.7%) stayed shorter than seven days. Only eight (11.6%) patients needed RRT. Seventeen patients (24.6%) died.

Among the AKI patients, the maximal pRIFLE score identified during the stay was 39.1% R, 39.1% I and 21.8% F (Table 1).

Figure 2 shows that by the ICU admission, 63.8% (44/69) of the patients had no AKI, which was diagnosed in variable degrees, being 34.1% (15/44) R, 43.2% (19/44) I, and 22.7% (10/44) F. Of the patients admitted with AKI R (17/69;

24.6%), 70.6% (12/17) remained in this level, 23.5% (4/17) progressed to I, and 5.9% (1/17) progressed to F. Differently, of the 5.8% (4/69) patients admitted with level I, no one had AKI level progression, as well as 5.8% (4/69) of the admitted with AKI level F.



ICU – intensive care unit; AKI – acute kidney injury.

**Figure 2 – Distribution of the patients admitted to the intensive care unit according to the maximal kidney injury progress during the time of stay.**

Of the patients with any level AKI, 53.6% were male, with an average age of 34 months, median 11 months, and standard deviation of 47%, and no statistically significant difference was identified for AKI (Table 3). The time of stay ranged from one day to 58 days, average 9 days, median 4 days, and standard deviation 11.7%. The patients were categorized according to the time of stay in  $\leq 7$  days and  $> 7$  days, as in the Akcan-Arikan et. al.<sup>(23)</sup> article. The patients who stayed longer (more than seven days), had more severe AKI (I and F) ( $p = 0.019$ ) (Table 3).

The patients' mortality rate was evaluated using the PIM II prognosis score. The mortality rate ranged between 0.1% and 100%, average 25%, median 2.9%, standard deviation 36.5%, and patients with higher PIM levels (above 10%) were observed to have more severe AKI ( $p = 0.026$ ) (Table 3).

Regarding the PICU admission diagnosis, those admitted for respiratory failure, SIRS/sepsis and after heart surgery had increased AKI severity ( $p = 0.047$ ) (Table 3).

Regarding mechanic ventilation or vasoactive drugs requirement, and exposure to nephrotoxic drugs, the

exposed patients had increased renal injury ( $p = 0.03$ ,  $0.001$  and  $0.002$ , respectively) (Table 3).

Patients requiring RRT also had more severe AKI ( $p = 0$ ) (Table 3). This is confirmed in figure 3, showing that 40% of the level F AKI patients

needed RRT.

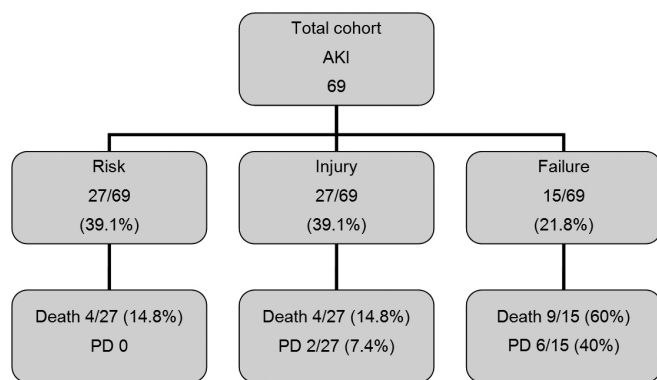
Regarding the outcome, the patients who died had more severe renal injury versus those who were discharged ( $p = 0.002$ ) (Table 3). In Figure 3 it is shown that 60% of the level F AKI patients died.

**Table 3 – Profile of patients admitted to the intensive care unit who developed acute kidney injury and their prognostic factors**

Kidney injury level	Risk N (%)	Injury N (%)	Failure N (%)	P value	Total
<b>Variables</b>					
Gender				0.554	
Male	15 (40.5)	16 (43.3)	6 (16.2)		37
Female	12 (37.5)	11 (34.4)	9 (28.1)		32
Age range				0.222	
Infant	16 (36.4)	21 (47.7)	7 (15.9)		44
Preschool	8 (50.0)	3 (18.7)	5 (31.3)		16
School/Adolescent	3 (33.3)	3 (33.3)	3 (33.3)		9
Time of Stay				0.019	
$\leq 7$	23 (50.0)	16 (34.8)	7 (15.2)		46
$>7$	4 (17.4)	11 (47.8)	8 (34.8)		23
PIM (%)					
$\leq 10$	18 (47.4)	15 (39.5)	5 (13.1)		38
$> 10$	8 (32.0)	7 (28.0)	10 (40.0)		25
Not done	1 (16.7)	5 (83.3)	0 (0.0)		6
Diagnosis				0.047	
Respiratory failure	4 (36.3)	4 (36.3)	3 (27.3)		11
SIRS/Sepsis	7 (28.0)	8 (32.0)	10 (40.0)		25
HT/Trauma	2 (50.0)	1 (25.0)	1 (25.0)		4
Heart PS	5 (29.4)	11 (64.7)	1 (58.9)		2
General PS	3 (60.0)	2 (40.0)	0 (0.0)		17
Others	6 (85.7)	1 (14.3)	0 (0.0)		7
MV				0.030*	
Yes	13 (28.9)	19 (42.2)	13 (28.9)		45
No	14 (58.3)	8 (33.3)	2 (8.3)		24
Vasoactive drugs				0.001*	
Yes	13 (27)	20 (41.7)	15 (31.3)		45
No	14 (66.7)	7 (33.3)	0 (0)		24
Nephrotoxic drugs				0.002*	
Yes	10 (23.3)	20 (46.5)	13 (30.2)		43
No	17 (65.4)	7 (26.9)	2 (7.7)		26
Peritoneal dialysis				0*	
Yes	0 (0.0)	2 (25.0)	6 (75.0)		8
No	27 (44.3)	25 (41.0)	9 (14.7)		61
Outcome				0.002**	
Discharge	23 (44.2)	23 (44.2)	6 (11.6)		52
Death	4 (23.5)	4 (23.5)	9 (53)		17
<b>Total</b>	<b>27</b>	<b>27</b>	<b>15</b>		<b>69</b>

\*Fisher's exact test; \*\* Pearson's Chi-square test. PIM - pediatric index of mortality; SIRS – systemic inflammatory response syndrome; HT – head trauma; PS – post-surgery; MV –mechanic ventilation





AKI – acute kidney injury; PD – peritoneal dialysis.

**Figure 3 – Distribution of the patients admitted to the intensive care unit according to the maximal level of acute kidney injury during the time of stay versus death rate and renal replacement therapy need.**

## DISCUSSION

AKI has a known catastrophic impact on critically ill patients. It is common among them, and its cause is mostly multifactor. AKI may progress to renal failure, preventing the kidneys to play their most important role, homeostasis.

During the study were admitted to the PICU 245 patients, 235 complied with the inclusion criteria, and among them, the AKI incidence was 30.6% (69 patients). Ostermann and Chang<sup>(5)</sup> studied adult patients from the United Kingdom and Germany, and found a 35.8% incidence, while Host et al.<sup>(22)</sup> found a 67.2% incidence and in a multicenter study, and Bagshaw et al.<sup>(9)</sup> found an 36.1% incidence. Among children Akcan-Arikan et al.<sup>(23)</sup> found an 82% incidence, while Plötz et al.<sup>(26)</sup> found 58%.

Regarding the AKI level, the maximal RIFLE score found during the patients stay was 39.1% R, 39.1% I and 21.8 F, while Akcan-Arikan et al.<sup>(23)</sup> found 48.8%, 26% and 25.2%, respectively, and Plötz et al.<sup>(26)</sup> 52%, 37% and 11%, respectively.

The variable AKI incidences could be explained by the different populations studied, and also by the different ICU characteristics. Specially regarding pediatric studies with all patients under MV, while in this study only 65.2% needed ventilatory support.

Of the 69 patients who developed AKI at any time of their stay, 36.2% were diagnosed AKI in the first day. Similarly, in the Plötz et al.<sup>(26)</sup> study,

45% of the patients were diagnosed AKI in their first 24 hours. Akcan-Arikan et al.<sup>(23)</sup> identified AKI in 42.3% of their sample. These data emphasize the sensitivity of the pRIFLE criteria for diagnosis AKI.

Aiming to evaluate if more severe patients had increased AKI sensitivity versus less severe patients, the PIM II score was calculated. The isolated association between the PIM II and AKI identified higher means and medians for the exposed group, as anticipated by the authors. Similarly, this same association was found by Akcan-Arikan et al.<sup>(23)</sup> Conversely, Plötz et al.<sup>(16)</sup> in 2005, studying septic patients, identified no difference between the prognostic scores in patients who either developed or not AKI. In adults, the association of prognostic scores and AKI was clearly shown in the Bagshaw et al.<sup>(9)</sup> and Hoste et al.<sup>(22)</sup> studies.

The studies using the RIFLE criteria, both in adults and children, validated a positive statistically significant association between time of stay, both in the ICU or hospital, and AKI, proving a poorer prognosis predictor in critically ill patients. In this cohort we observed that the mean ICU stay time increased as the AKI severity progressed. Differently, Plötz et al.<sup>(26)</sup> showed no statistically significant differences between the control and AKI groups regarding the ICU time of stay. Akcan-Arikan et al.<sup>(23)</sup> not only showed a trend in the exposed group to stay longer in the ICU, but also observed that AKI was an independent factor for increased hospital stay risk. Similarly, in studies with adult patients using the RIFLE criteria, Hoste et al.<sup>(22)</sup> and Ostermann and Chang<sup>(5)</sup> identified the same associations for ICU time of stay.

Regarding mortality, several studies<sup>(5,7,9,16,19,22,26)</sup> have clearly shown that any degree of AKI is a poor prognosis indicator for critically ill patients. In this sample, we found that the in-hospital mortality of patients with the condition was ten times bigger than in the group with no AKI, according to the pRIFLE. Plötz et al.<sup>(26)</sup> identified a five times bigger mortality in patients with any level AKI. Akcan-Arikan et al.<sup>(23)</sup> found no statistically significant difference for both groups mortality. In adults, Hoste et al.<sup>(22)</sup> identified three times bigger mortality rates in the exposed group. Ostermann and Chang<sup>(5)</sup> identified that AKI patients had a four times bigger mortality versus non-AKI patients.

Regarding the mortality rates, we found that mortality increased in parallel with the AKI severity groups, which was also identified by other authors.<sup>(22,23)</sup> A similar mortality rate was found for AKI R and I levels (14.8%). The identification that the level R has increased progression to more severe levels, and high mortality rates in this level similar to level I (more severe), emphasize the relevance of the early diagnosis and therapy. It is thus suggested that early AKI diagnosis will result in improved prognosis and, specially, reduced mortality. Yet patients categorized as level F had a substantially higher mortality rate (60%) versus other AKI levels, showing that the level F represents a severe insult condition, with severe functional impairment and decreased reversibility, nevertheless the best of the therapeutic efforts.

Regarding the admission diagnosis, patients with SIRS/sepsis had a three times bigger AKI risk ( $p < 0.001$ ). Akcan-Arikan et al.<sup>(23)</sup> and Plötz et al.<sup>(26)</sup> also identified increased AKI incidence in these patients.

Patients admitted after heart surgery had 58.6% renal injury, and most of these patients had more severe renal injury. In a pediatric study, Perdensen et al.<sup>(27)</sup> found a 11.5% incidence. Kuitunen et al.<sup>(28)</sup>, evaluating adult patients, found a 19.3% rate, and these patients had less severe renal injury. This relevant difference may be explained by the fact of diagnosis of acute renal failure (ARF) in the pediatric study was made based on the urinary output (anuria or oliguria), hyperkalemia or volume excess, while in this study the pRIFLE criteria allowed earlier AKI diagnosis. This finding demonstrates the pRIFLE criteria sensitivity and applicability. The difference on AKI incidence in adult or pediatric patients following heart surgery is due to the more complex surgeries for congenital defects corrections. Alkan et al.<sup>(29)</sup> describe that younger patients, more complex cardiac defects, longer extracorporeal circulation, and lower heart output are risk factors for AKI. In this context, they propose using a prophylactic PD catheter in newborns or infants undergoing complex heart surgery. Regarding prognostic factors for AKI development as mechanic ventilation, nephrotoxic drugs and vasoactive amines need, it was shown that in the exposed group the AKI incidence was higher. These results were also reproduced in adult patients studies.<sup>(5,7,8)</sup>

In the studied group, RRT was required by 11.6% patients. In the Host et al.<sup>(22)</sup> study, this rate was 5.9%, and in the Akcan-Arikan et al.<sup>(23)</sup> 8.9% of the patients needed RRT, while in the study by Plötz et al.<sup>(26)</sup>, 10%. In all of these studies, the need of RRS was proportional to the AKI severity. Among the patients with any AKI level, eight underwent RRT. The vast majority of them were in the F level, representing 40% (6/15) of this subgroup. Akcan-Arikan et al.<sup>(23)</sup> found that 71% of the F level patients received RRT, and for Plötz et al.<sup>(26)</sup> this involved 14.3% of the patients. The different RRT indication in these three studies may be related to a lack of specific criteria for RRT indication and probably due to different population characteristics, although all were critically ill patients.

This study contribution has limitations. Firstly, a relatively small sample size with 235 patients, which however is in similar to other recent studies' samples in pediatrics. Secondly, this is a single center study, which may cause bias due to specific environmental characteristics including population, routines and RRT management and indication. Additionally, other biases may be present due to the heterogeneous distribution of some clinical features (age, severity scores, MV, VD, ND). These would be adjusted by a multivariate analysis in a regression test, not performed. However, this study proposal was based on a census, for which all patients complying with the inclusion criteria would constitute a cohort.

It is important to highlight that, nevertheless the validation of the new AKI criteria, this condition's diagnosis is troublesome as it is based in two functional abnormalities: serum creatinine changes (a GFR marker) and oliguria, both late renal impairment markers. Creatinine level may not change until 25-50% of the renal function is lost. Additionally, different analysis methods (Jaffé versus enzymatic) may lead to different serum creatinine values, and drugs leading to tubular creatinine secretion and increased bilirubin levels may impact the measurements by the Jaffé technique; and, in lower GFR conditions, the creatinine concentration may overestimate the renal function. The distribution volume, commonly changed in critically ill patients, may also impact the results, as does the patient's liver metabolism and body mass. For diuresis measurement, several limitations may be

commented. Its accuracy depends on catheterization, and the values may be changed by several drugs, specially diuretics and vasoactive amines.

On the other hand, we understand that this study is useful for pRIFLE criteria validation, and as it was prospectively used, allows to clearly show the accuracy and reliability of the described associations. Additionally, its contribution to demonstrate its use in the intensive care settings, especially for prevention, is undeniable.

Looking to future scientific progress, we believe that although pRIFLE in pediatrics publications are steadily growing, the articles are relatively scarce and conducted in single centers. An important step forward to widespread the acceptance of the pRIFLE criteria would involve conducting a larger and multicenter study.

## CONCLUSION

In this study the incidence of AKI in critically ill patients was high. AKI was directly related to increased mortality, with a ten times bigger risk of death versus patients without AKI.

Regarding the applicability of the pRIFLE criteria as a prognostic tool in ICU, the most severe AKI patients had a higher PIM II prognostic score.

The time of hospital stay was determinant. It was seen that patients staying longer had more severe AKI. Regarding the AKI-associated prognostic factors, it was identified that MV and VD need and exposure to ND lead to more severe AKI, and PD was required more frequently in the patients with more severe AKI.

The pRIFLE criteria were shown to be important for early AKI risk patients detection, suggesting that, with its use, earlier diagnosis will imply more careful and less delayed therapy, which in long term will lead to reduction in this disease related morbidity and mortality.

## RESUMO

**Objetivos:** Lesão renal aguda caracteriza-se pela redução súbita e, em geral, reversível da função renal com perda da capacidade de manutenção da homeostase do organismo. Em pediatria, as principais causas de lesão renal aguda são sepse, uso de drogas nefrotóxicas e isquemia renal nos pacientes criticamente enfermos. Nesses pacientes, a incidência de lesão renal aguda varia de 20 a 30%, resultando em aumento da taxa de morbi-mortalidade de 40 a 90%. Este estudo tem como objetivo avaliar a incidência de lesão renal aguda nos pacientes internados em unidade de terapia intensiva, classificar a gravidade da lesão renal aguda de acordo com o *Pediatric Risk, Injury, Failure, Loss, End-Stage* (pRIFLE), analisar a relação entre lesão renal aguda e a gravidade através do *Pediatric Index of Mortality* (PIM) e estudar os fatores prognósticos associados.

**Métodos:** Realizou-se um estudo prospectivo entre julho de 2008 a janeiro de 2009 dos pacientes internados na unidade de terapia intensiva pediátrica do Hospital Infantil Joana de Gusmão – Florianópolis (SC) - Brasil. Todos os pacientes foram analisados diariamente através do débito urinário e creatinina sérica e classificados de acordo com pRIFLE.

**Resultados:** No período de acompanhamento foram internadas 235 crianças. A incidência de lesão renal aguda foi de 30,6%, sendo que o pRIFLE máximo durante a internação foi de 12,1% para R, 12,1% para I e 6,4% para F. A taxa de mortalidade foi de 12,3%. Os pacientes que evoluíram com lesão renal aguda apresentaram risco dez vezes maior de óbito em relação aos não expostos.

**Conclusão:** Lesão renal aguda é uma entidade comum nos pacientes críticos. O diagnóstico precoce e a instituição imediata de medidas terapêuticas adequadas a cada situação clínica podem alterar o curso e a gravidade do envolvimento renal reduzindo a morbi-mortalidade do paciente.

**Descritores:** Criança; Rim/lesões; Mortalidade; Estado terminal

## REFERENCES

1. Andreoli SP. Acute kidney injury in children. *Pediatr Nephrol.* 2009;24(2):253-63.
2. Liberato Bresolin N, Toporovski J. Insuficiência renal aguda na sepse. *Arch Latinoam Nefrol Pediatr.* 2005;5(3):164-72.
3. Costa JAC, Vieira-Neto OM, Moysés Neto M. Insuficiência renal aguda. *Medicina (Ribeirão Preto).* 2003;36(2/4):307-24.
4. Fine DM. Acute renal failure in the critically ill. *Multiprofessional Crit Care Review Course*, 2005.
5. Ostermann M, Chang RW. Acute kidney injury in the intensive care unit according RIFLE. *Crit Care Med.* 2007;35(8):1837-43; quiz 1852.
6. Zappitelli M. Epidemiology and diagnosis of acute kidney injury. *Semin Nephrol.* 2008;28(5):436-46.
7. Barrantes F, Tian J, Vazquez R, Amoateng-Adjepong



- Y, Manthous CA. Acute kidney injury criteria predict outcomes of critically ill patients. *Crit Care Med.* 2008;36(5):1397-403.
8. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Ronco C; Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA.* 2005;294(7):813-8.
  9. Bagshaw SM, George C, Dinu I, Bellomo R. A multi-center evaluation of the RIFLE criteria for early acute kidney injury in critically ill patients. *Nephrol Dial Transplant.* 2008;23(4):1203-10.
  10. Liberato Bresolin N, Santos Bandeira MF, Toporovski J. Monitorização da função renal na insuficiência renal aguda. *Arch Latinoam Nefrol Pediatr.* 2007;7(1):20-34.
  11. Pannu N, Nadim MK. An overview of drug-induced acute kidney injury. *Crit Care Med.* 2008;36(4 Suppl):S216-23. Review.
  12. Bellomo R, Wan L, May C. Vasoactive drugs and acute kidney injury. *Crit Care Med.* 2008;34(4 Suppl):S179-86. Review.
  13. Schrier RW, Wang W. Acute renal failure and sepsis. *N Engl J Med.* 2004;351(2):159-69. Review.
  14. Schor N. Acute renal failure and the sepsis syndrome. *Kidney Int.* 2002;61(2):764-76.
  15. VA/NIH Acute Renal Failure Trial Network, Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, Choudhury D, et al. Intensity of renal support in critically ill patients with acute kidney injury. *N Engl J Med.* 2008;359(1):7-20. Erratum in: *N Engl J Med.* 2009;361(24):2391.
  16. Plötz FB, Hulst HE, Twisk JW, Bökenkamp A, Markhorst DG, van Wijk JA. Effect of acute renal failure on outcome in children with severe septic shock. *Pediatr Nephrol.* 2005;20(8):1177-81.
  17. Pollack MD, Patel KM, Ruttimann UE. PRISM III: an updated Pediatric Risk of Mortality score. *Crit Care Med.* 1996;24(5):743-52.
  18. Slater A, Shann F, Pearson G; Paediatric Index of Mortality (PIM) Study Group. PIM2: a revised version of the Paediatric Index of Mortality. *Intensive Care Med.* 2003;29(2):278-85.
  19. Bresolin N, Silva C, Hallal A, Toporovski J, Fernandes V, Góes J, Carvalho FL. Prognosis for children with acute kidney injury in intensive care unit. *Pediatr Nephrol.* 2009;24(3):537-44.
  20. Nguyen MT, Devarajan P. Biomarkers for the early detection of acute kidney injury. *Pediatr Nephrol.* 2008;23(12):2151-7.
  21. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P; Acute Dialysis Quality Initiative workgroup. Acute renal failure – definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care.* 2004;8(4):R204-12.
  22. Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, Kellum JA. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill patients: a cohort analysis. *Crit Care.* 2006;10(3):R73.
  23. Akcan-Arikan A, Zappitelli M, Loftis LL, Washburn KK, Jefferson LS, Goldstein SL. Modified RIFLE criteria in critically ill children with acute kidney injury. *Kidney Int.* 2007;71(10):1028-35.
  24. Schwartz GJ, Brion LP, Spitzer A. The use of plasma creatinine concentration for estimating glomerular filtration rate in infants, children, and adolescents. *Pediatr Clin North Am.* 1987;34(3):571-90.
  25. Kirkwood B. *Essentials of medical statistics.* Oxford: Blackwell; 1988.
  26. Plötz FB, Bouma AB, van Wijk JA, Kneyber MC, Bökenkamp A. Pediatric acute kidney injury in the ICU: an independent evaluation of pRIFLE criteria. *Intensive Care Med.* 2008;34(9):1713-7.
  27. Pedersen KR, Hjortdal VE, Christensen S, Pedersen J, Hjortholm K, Larsen SH, Povlsen JV. Clinical outcome in children with acute renal failure treated with peritoneal dialysis after surgery for congenital heart disease. *Kidney Int Suppl.* 2008;(108):S81-6.
  28. Kuitunen A, Vento A, Suojaranta-Ylinen R, Pettilä V. Acute renal failure after cardiac surgery: evaluation of the RIFLE classification. *Ann Thorac Surg.* 2006;81(2):542-6.
  29. Alkan T, Akçevin A, Türkoglu H, Paker T, Sasmazel A, Bayer V, et al. Postoperative prophylactic peritoneal dialysis in neonates and infants after complex congenital cardiac surgery. *ASAIO J.* 2006;52(6):693-7.