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Prognosis of acute renal failure in children in intensive care unit: A pilot study.

Batouche DD[1*], Kerboua K[2]

[1]Service de Réanimation Pédiatrique, CHU, Oran, Algeria.
[2]Service d'Immunologie, Hôpital Militaire Régional, Oran, Algeria.

Abstract

Introduction: Acute renal failure (ARF) is a rare pediatric disease. Despite significant advances in the methods of treatment, still the disease presents high mortality rates.

Objective: The aim of the study was to analyze the prognostic factors that determine the rates of morbidity and mortality among children suffering with acute renal failure and admitted to Paediatric Intensive Care Units in Oran (Algeria)

Patients and methods: A retrospective study was conducted of the data obtained from the Pediatric Intensive Care Unit of the University Hospital of Oran. The prognostic factors associated with ARF were recorded for of 260 patients over a period of 20 years. The parameters that were noted at the time of admission of ICU patients are: age, sex, clinical severity, underlying diseases, type and ARF mechanism, diuresis, the time to onset of ARF (ARF early: 1 to 2 days, late ARF: 3 days), the concentration of creatinine, use of mechanical ventilation, associated organ failure, diuretics administration, the use of positive inotropes, the need for renal replacement therapy (RRT), outcomes of the treatment and follow-up data of one year. All these data were collected and analyzed statistically. PRISM score and pediatric RIFLE criteria at the time of admission were used to characterize the patients.

Results: The mean age of pediatric patients was 77.261 ± 4.401 months. ARF was diagnosed in 38% of the patients at the time of admission while 61.5% acquired it in the hospital. Renal replacement therapy was administered in 63% of the cases. The overall mortality was 24%. The results of Univariate analysis revealed significant association of the clinical score severity at admission (p=0.0025), oligo anuria (p=0.0043), age<12 months, creatine at admission (p=0.0017), more than two organ failure and vasopressives drugs (p=0.0037). Interestingly, mortality was found to be associated with the PRISM score at baseline (RR: 2.1 [CI: 1.5 to 6.8], sepsis complicated by more than two organ failure (RR: 17.25 [CI: 2.8 to 33.9]; p=0.002) and age less than 1 year.

Conclusion: The findings of the present study highlight the most relevant prognostic factors associated with occurrence of morbidity or mortality in pediatric ARF patients. Further clinical studies should be conducted for the application of these parameters as prognostic factors in future recommendations.

Keywords: Acute renal failure, Pediatric, Sepsis, Dialysis treatment, Prognosis.

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Introduction

Acute Renal Failure (ARF) is a rare pediatric disease. It is considered as one of the most dangerous diseases due to high morbidity and mortality rates. Several prognostic factors of ARF have been studied in pediatric intensive care units in the recent years [1-4].

The biochemical indicators of acute renal failure (ARF) include serum creatinine value of 5 mg/L associated with 25% reduction in glomerular filtration rate as compared to the baseline functions. The severity of the ARF is defined by the pediatric RIFLE criteria [5].

The aim of the study was to analyze the prognostic factors associated with morbidity and mortality in children affected with acute renal failure and admitted to Paediatric Intensive Care Units in Oran (Algeria).

Methods

This retrospective study was conducted during January 1995 to May 2015. A total of 260 patients from different pediatric

wards of Oran hospitals were enrolled for the study. Patients with complications requiring dialysis were included, but cases of newborn ARF and ARF resulting from chronic renal failure or heart surgery under extra corporeal circulation were excluded.

The different parameters recorded at the time of admission to ICU included: age, sex, severity assessed by the PRISM score, pediatric RIFLE criteria, the underlying disease, type and ARF mechanism, diuresis, the time to onset of ARF (ARF early: 1 to 2 days, late ARF=3 days), creatinine levels, usage of mechanical ventilation, associated organ failure, diuretics administration, the use of positive inotropes, the need for renal replacement therapy (RRT) and patient outcomes and follow up data for 1 year [6]. The efficacy of the prognostic factors was investigated by univariate and multivariate analyses.

The factors were compared for patients both alive and deceased using test Khi2, and the Odds Ratio (OR) in order to measure the strength of the association between the different variables. The significance level was set to a value of $p<0.05$. Multivariate statistical analysis was carried out to analyze mortality factors by logistic regression model.

Results

A total of 260 patients were admitted with a hospital prevalence of 3.07% at the time of admission. The mean age of the patients studied was 77.261 ± 4.401 months (range 1 month-16 years). It was found that the most affected age group was of infants 1 to 11 months with a total of 79 cases (Figure 1).

The time of the ARF onset from the 1st disorder was 5 ± 0.622 days. The clinical characteristics of patients at the point of admission are shown in Table 1. Oliguria was found to be the major symptom, with a frequency of 90%, Followed by acute respiratory distress at 31%. Mechanical ventilation was required for 21.5% of patients and signs of circulatory failure were observed in 26% of the patients. 39% of patients were comatose and 13% experienced convulsions Table 2.

Mechanisms and causes of the ARF: The pathophysiological key elements identified from the investigation were used in the classification of ARF into functional IRA or pre-kidney, renal parenchymal or organic, or post-renal type (Figure 2). Functional acute renal failure was presented in 30.8% of cases while organic or parenchymal acute renal failure accounted for 63.1% of cases followed by the post-renal at 6.1%.

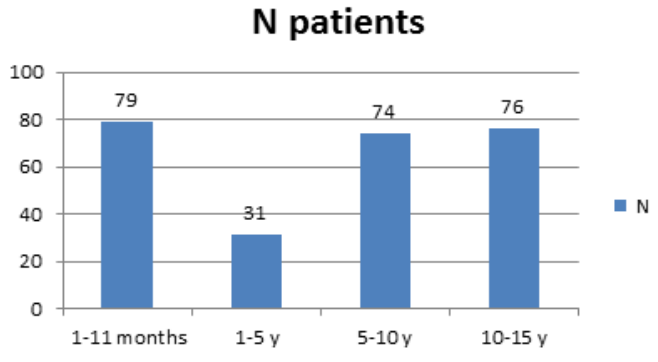

Figure 1: *Number of patients by age group.*

Table 1. *Clinical characteristics of patients at admission*

Clinical Disorders	N	(%)
1. Oligoanuria	234	(90)
2. Hypotension	67	(25)
3. Hypertension	54	(20)
4. Acute respiratory distress	85	(31)
5. Edema	46	(17)
6. Coma	102	(39)
7. Convulsions	34	(13)
8. Acute edema of the lungs	25	(9)
9. Icterus	04	(1,5)

Table 2. *The main causes of the ARF in children*

Causes	n	%
Causes functionnal ARF	**81**	**30.8**
1. Deshydratation 2. hypovolemia (absolute or relative)		21.10 09.70
Organic causes of ARF	**164**	**63.13**
1. ATN 2. Glomerulopathies 3. Vascular nephropathy		51.53 09 2.60
Post renal causes of ARF	**15**	**6.1**
Compression or obstruction of the urinary		5.0
tract (non-tumor diseases and/or tumor)		1.18

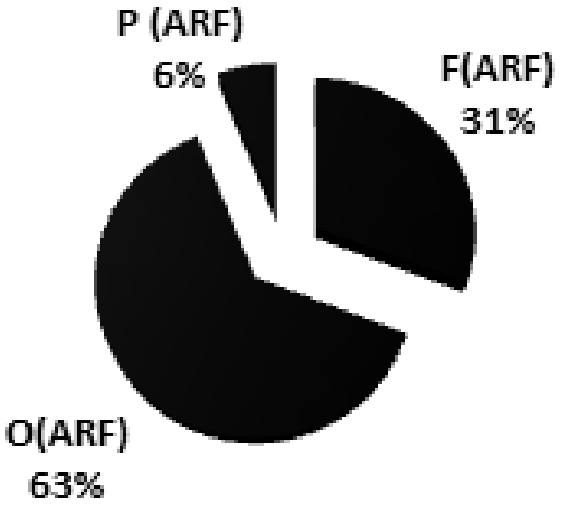

Figure 2: *Mechanism of ARF [F (ARF): Functional Acute Renal Failure; O (ARF): Organic Acute Renal Failure; P (ARF): Post Renal Acute Renal Failure]*

Acute tubular necrosis (ATN) was present in 51% of patients. An exogenous (septic, toxic, ischemic) and an endogenous (rhabdomyolysis, crush syndrome, hemolysis, and tumor lysis syndrome). Etiological research on anamnesis, clinical and biological elements allowed distinguishing the primary ARF or finding on admission (38% of cases) and secondary or acquired ARF during hospitalization (61%) (Table 3).

The ARF is defined according to its characteristics shown in Table 4. Diuresis during the first 8 hours of admission is preserved in 26 patients, and 234 patients were in trace anuria. The average value serum creatinine of 31.811 mg/l

***Table 3**. The ARF types in our study*

Nature of ARF	Number
ARF present on admission	
AGN	27
NS	17
obstruction, compression of the urinary tract	16
DKA	15
HUS	12
Collagenoses, hypertensive nephropathy	07
cardio-renal Syndrome	06
Total	100
ARF acquired in the hospital	
ATN (exogenous and endogenous toxic)	48
ATN (infection)	45
ATN(ischemic, hypovolemia	41
Nephrotoxicity (TB, Ch)	14
Post -opératoire	12
Total	160

GNA: Acute Glomerulonephritis; SN: Nephrotic Syndrome; ACD: Diabetic Ketoacidosis; HUS: Haemolytic Uraemic Syndrome; ATN: Acute Tubular Necrosis; Ch: Chemotherapy and TB: Tuberculosis

***Table 4.** ARF characteristics*

Parameters	Value	Number
Diuresis : Oliguria Anuria preserved		 129 105 26
Mean serum creatinine (mg/l)	31 .811 ± 10.031	
Mean serum uremia (g/l)	1.6 g/l ± 0.55	
Rifle: Rifle(R) Rifle(I) Rifle(F)		 76 119 65

Rifle (R): Rifle risqué; Rifle (I): Rifle injury; Rifle (F): Rifle failure

± 10.031 mg/l (range 18-104 mg/l) and the median value 28 mg/l, and that of plasma urea is 1.6 g/l ± 0.55 (range 0.6-3 g/l) and the median value of 1.5 g/l. The RIFLE criteria helped to highlight RIFLE (R) in 76 patients, RIFLE (I) in 119 patients and RIFLE (F) in 65 patients.

The most important mortality risk factors associated with the ARF are young age (RR=0.33; CI 95%=0.14-0.17), the test RIFLE -F: 77% (RR=1.61; CI95=1.43 to 1.95), clinical severity score at admission defined by PRISM (RR=2.01; CI95% CI: 1.5 to 6.83]; the presence of sepsis (RR=4.8; 95% CI: 2.9-7.8) and failure of more than two organs including hemodynamic, respiratory and haematological factors (Table 5).

Discussion

Our study enrolled children from different pediatric wards of the University Hospital of Oran, Pediatric Nephrology of the Pediatric Hospital of Canastel-Oran, Surgery department of the of Emir Abdelkader Oncology Center-Oran and different pediatric wards of different health establishments of Oran prefectures. In an epidemiological point of view, despite the limited literature about the analytical and descriptive surveys in this field, it was found that the ARF is less common in children than in adults. However, newborns are especially vulnerable with an annual incidence of 19.7 per 100 000, as compared to 3.7 for total pediatric ARF rate and 17.2 in adults [7-10].

The incidence of the ARF in the present study was 3.07%, however, children in post cardiac surgery with bypass and newborns were not included in the current study. The data obtained showed that 63.4% of the ARF cases were attributed to organic causes: 53.5% of ATN, 9% of glomerular and 2.6% of vascular nephropathy.

In this study, the overall mortality rate (24%) was similar to that reported in the previous studies. It is well known that ARF is a partial determinant of the motalities reported [10,11]. The specific severity indices were characterized by the severity score based on PRISM [6]. It was observed that PRISM score >10 is a statistically significant risk factor for the occurrence of ARF [2]. The PRISM scores of dead children at the time of admission was significantly higher as compared to survivors PRISM $_{\text{dead patients}}$=10.9 ± 1.5 PRISM $_{\text{survivors}}$=21.03 ± 4.1 (p=0.0025; RR=2.01 CI95%=1.5 to 6.83). It was also observed that the use of vasoactive drugs and the ventilator setting was associated with a poor prognosis.

The mortality rates were particularly higher within 24 h of admission for infants and the difference was significant in these patients (p=0.03) which concord with the previous reports [2,12]. This difference could be explained on the basis of quality and precocity of care: the condition of patients admitted to the ICU was more severe due to delay of the circulatory failure diagnosis, and its initial management. Despite the consensual recommendations for the treatment of septic shock in children and newborn of 2002 updated in 2007, most of the pediatric intensive care unit still lacks the optimal care methods required in such conditions [13].

The worst prognosis was observed in patients with a complicated sepsis DMV. Higher mortality rate was observed in septic children (54%) as opposed to 06% of non-septic children. Septic patients face significantly higher risk with an OR 4.8 [95% CI: 2.9 to 7.8]. The presence of more than two organ failure has made the poor prognosis with a statistically significant difference (p<0.002) and RR17, 25 [95% CI: 2.8 to 33.9]. Several previous studies confirm the findings of the present investigation regarding the mortality rate in the ARF and most significantly in patients with severe sepsis complicated MOF [2,14,15].

In concordance with recent reports, the present study also concluded that diuresis could influence the prognosis of the ARF. In fact, patients with preserved diuresis have a better prognosis than those with oligomeric diuresis [4,16]. The mortality rate among non oligoanuriques subjects was 5% versus 95% for subjects oligoanuriques (p=0.0043).

In 2007, Akcan-Arikan and Zappetelli adapted the RIFLE criteria pediatric version among 150 children admitted to intensive care and recorded a 25.8% mortality with RIFLE (F) [5,17]. 77% of patients were classified as RIFLE (F) and were immediately treated by renal replacement therapy, while 8% of them died.

Table 5. *Global Patient characteristics by comparing prognostic variables*

Parameters	Survivors N (%) 197 (75,7)	Deceased N (%) 63 (24)	p	RR
Age 1-11 months 1-5 years 5-10 years 10-15 years	 46 (23.3) 25 (12.6) 61 (30.9) 65 (33)	 33 (52.3) 6 (9.5) 13 (20) 11 (17)	0.03	1.02 [95% CI: 0.45-2.1]
Diuresis Oligoanuria	148 (86)	60 (95.2)	<0.0043	
MV	8 (4.7)	48 (85.7)	<0.005	
HD support	2 (1.17)	48 (74)	<0.0037	
RIFLE (F)	16 (8)	49 (77)		1.61 [95% CI: 1.43-1.95]
mean serum creatinine (mg/l)	28.3 ± 11.395	34.8 ± 11	<0.0017	
PRISM	10.9 ± 1,5	21.03 ± 4.1	<0.0025	2.01 [95% IC: 1.5-6.83]
sepsis	11 (6)	34 (54)	<0.001	4.8 [95% IC: 2.9-7.8]
MOF ≥ 2	1 (0.5)	40 (63.5)	<0.002	17.25 [95%IC: 2.8-33.9]
With RRT DP HDI d without RRT	111 (68) 05 106 86	53 (32.1) 43 10 10	<0.001 <0.005	
ARF primary (at admission) ARF secondary (acquired)	94 103	6 57	0,001	0.33 [IC à 95% (0.14–0.37]

MV: Mechanical Ventilation; HD support: Hemodynamic Support; PRISM: Pediatric Risk of Mortality Score; MOF: Multiorgan Failure; RRT: Renal Replacement Therapy; PD: Peritoneal Dialysis; HDI: Daily Intermittent Hemodialysis

However, the present study has some limitations: The definition used for the severity of acute renal failure does not confer with the 2007 classification of acute renal failure according to the p RIFLE criteria. The children were retrospectively classified according to blood levels of creatinine and urine output using the p RIFLE criteria [5,17].

In addition, several publications emphasized that the ARF threatening hospital-acquired remains are severe [18-22]. Thus, ARF occurring during hospitalization or during the ICU stay (160 patients) has a poor prognosis compared to the ARF present at admission (100 patients). The hospital acquired ARF objectified with a death rate of 36% as compared to 6% of those admitted with ARF, with RR 0.33 (CI95%=0.14 to 0.37).

The need for RRT is a predictor of mortality: Several studies have shown that children hospitalized in intensive care units followed by the administration of the RRT technique (An important oligoanuria, sepsis, multiorgan failures) have a mortality rate of 40% [14-16,20,22-26]. In the present study 32% of the dialysis patients died and the high rate of death can be explained by the need for peritoneal dialysis in children with aged <12 months in septic shock with MOF.

The second weak point of our study is the treatment by renal replacement therapy .In the present study, the treatment of the patients was restricted to peritoneal dialysis and hemodialysis intermittent. Effects of continuous haemofiltration as compared to conventional dialysis brings more income in a state of shock or in an unstable patient as metabolic control is continuous and progressive [27,28]. This technique, although attractive did not seem feasible in our unit for lack of non-availability of the technical platform for the duration of the retrospective observational study [29-31]. The data collected from these studies suggest that none of these techniques has benefited over the other in terms of survival.

Currently, due to the effectiveness of techniques of renal replacement therapy, mortality is often linked to the etiological context and not to the ARF consequences. In the recent times no patient dies due to ARF complications, instead it happens due to underlying clinical contexts. Independent prognostic factors were found by the multivariate analysis. According to their decreasing RR, they consist on the sepsis with organ failure, clinical severity at admission, and the very young age of the infant. As for renal functional outcome: 72% of the patients had a follow-up of a year and it was observed that they all recovered positively after the acute episode. ATN seemed to induce fewer sequelae than glomerulopathy which in 3% of the cases caused chronic renal failure.

Conclusion

Acute Renal Failure (ARF) is a rare disease in pediatrics, but is considered as a serious event because the circumstances are multifactorial and mortality associated. The results obtained in the present study demonstrated the various prognostic factors of ARF and their impact on morbidity and mortality in children. The prognosis is influenced by infant

age, the severity of the clinical picture at the point of hospital admission, by the presence of severe sepsis and the existence of associated visceral organ failures. The improved prognosis of acute renal failure in children must go through a strategy of prevention, and hence support the need for recommendations tailored to pediatrics by future clinical research.

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Correspondence to:

Batouche DD,
Maitre de conferences,
Réanimation pédiatrique,
Anesthesia reanimation pédiatrique,
Coop 19 join ilot 9 villa 124 hai khemisti big el djir oran,
Algeria.
Tel: 00213771799324;
E-mail: khedidjabatouche@yahoo.fr