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## Factors associated with mortality in acute renal failure (ARF) in children

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**Abstract** Objective: To assess the factors that affect the mortality in acute renal failure (ARF) in children. Patients and methods: We studied 149 patients with ARF and described the findings by age, gender, pathophysiological mechanism of renal damage, and type of renal damage, which can be oligoanuric and/or septic. We used multiple logistic analysis, Cox analysis for survival, and Kaplan–Meier curves. Results: The male/female ratio was 91/58. The most affected age groups were newborns (44.3%) and infants (37.6%). The ARF mechanism was ischemic in 87 cases (58%) and the most frequent clinical type was nonoliguric in 118 cases (79.2%). In the multiple logistic regression analysis, only oliguria ( $P=0.07$ ) and age group ( $P=0.049$ ) were associated with mortality. In the survival analysis using the Cox method, oliguria ( $P=0.003$ ) and sepsis ( $P=0.03$ ) were associated with mortality. The survival curves showed that the cumulative probability of dying in the first 10, 20, or 40 days after the event was 75, 70, and 45% respectively. When oliguria was present, the survival at day 10 was 47% and when sepsis was present it was 68%. Conclusion: Oliguria, age, and sepsis are factors associated with mortality in children with ARF.

**Keywords** Acute renal failure (ARF) · Mortality · Oliguria · Children · Sepsis

### Introduction

Acute renal failure (ARF) is a condition with increasing incidence in the pediatric, infant, and newborn population [1]. This is because of the increased possibility of preventing death in children exposed to severe and potentially fatal injuries, who will eventually develop ARF.

The epidemiological characteristics of this condition may be similar in developed countries. In low income countries, however, important differences must be taken into account relating to the level of poverty and access to, and the quality of, health services [2].

It is, nevertheless, still important to identify risks associated with major mortality, because this is the only way to achieve successful intervention in preventing death in children with established ARF [3, 4, 5, 6, 7, 8, 9, 10, 11].

The aim of this study was to analyze the risk factors for death in children with acute renal failure in a public general hospital in Metropolitan Lima (Cayetano Heredia Hospital). We describe our five years of experience in pediatric nephrology.

### Patients and methods

In this study we included all children between 0 and 14 years old seen between July 1, 1996 and June 30, 2001 by the Nephrology Unit of the Hospital Nacional Cayetano Heredia (HNCH) with diagnosis of acute renal failure. This was defined as sudden loss of renal function and was identified by an increase in serum creatinine levels for the child's age [12].

We collected the following data for each patient: age, gender, clinical presentation, type of renal failure (oliguric, nonoliguric), predominant physiopathological mechanism (ischemia, interstitial nephritis, urinary tract obstruction, nephrotoxicity, glomerular damage), final outcome, and associated diseases.

Oliguric ARF was defined as urine flow less than  $1 \text{ cc kg}^{-1} \text{ h}^{-1}$ , and pathophysiological mechanism was defined according to the main mechanism of injury. Sepsis was defined by the presence of bacteria isolated from the blood.

Data were analyzed with the statistical package SPSS V9, using nominal multiple regression analysis to evaluate variables related to death risk. Cox linear regression was used to evaluate the risks associated with mortality in ARF as a function of the variables that reached statistical significance ( $P<0.05$ ). In the tables shown, the chi-square test or Fisher's exact test for categorical variables was also used.

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**Table 1** Clinical presentation of ARF in children by age group

Age group	Type of presentation	
	Nonoliguric, n (%)	Oliguric, n (%)
Premature newborns (n=35)	32 (91)	3 (9)
On term newborns (n=31)	20 (65)	11 (35)
Infants (n=56)	43 (77)	13 (23)
Schoolchildren (n=27)	23 (85)	4 (15)
TOTAL (n=149)	118 (79)	31 (21)
P=0.046		

**Table 2** Type of damage in ARF and age group

Age group	Type of damage			
	Tubular necrosis, n (%)	Interstitial nephritis, n (%)	Glomerular disease, n (%)	Other, n (%)
Premature newborns (n=35)	12 (34)	22 (63)	0 (0)	1 (3)
On term newborns (n=31)	19 (61)	8 (26)	3 (10)	1 (3.0)
Infants (n=55)	40 (73)	10 (18)	0 (0)	5 (9)
Schoolchildren (n=26)	8 (31)	4 (15)	13 (50)	1 (4)
Total (n=147)	79 (54)	44 (30)	16 (11)	8 (5)
P=0.000				

**Table 3** Clinical presentation of ARF and type of damage in children

Type of damage	Type of presentation	
	Nonoliguric, n (%)	Oliguric, n (%)
Pre-renal (n=8)	1 (12)	7 (88)
ATN (n=79)	59 (75)	20 (25)
ATIN (n=44)	42 (95)	2 (5)
Glom-dis. (n=16)	14 (88)	2 (12)
Total (n=147)	116 (79)	31 (21)
P=0.001		

**Table 4** Mortality in ARF by age group

Age group	Mortality	
	Alive, n (%)	Dead, n (%)
Premature newborns (n=35)	21 (60)	14 (40)
On-term newborns (n=31)	17 (55)	14 (45)
Infants (n=56)	43 (77)	13 (23)
Schoolchildren (n=27)	23 (85)	4 (15)
Total (n=149)	104 (70)	45 (30)
P=0.027		

**Table 5** Mortality in children with ARF and sepsis

Sepsis group	Mortality	
	Alive, n (%)	Dead, n (%)
Without sepsis (n=73)	58 (79)	15 (21)
With sepsis (n=76)	46 (61)	30 (39)
TOTAL (n=149)	104 (70)	45 (30)
P=0.012		

**Table 6** Mortality in ARF and clinical presentation in children

Type of presentation	Mortality	
	Alive, n (%)	Dead, n (%)
Nonoliguric (n=118)	88 (75)	30 (25)
Oliguric (n=31)	16 (52)	15 (48)
Total (n=149)	104 (70)	45 (30)
P=0.013		

newborns (44.3%), 56 infants (37.6%), and 27 children of school age (18.1%).

The clinical presentation was nonoliguric in 118 patients (79.2%) and oliguric in 31 patients (20.8%). The main mechanisms of ARF were tubular necrosis in 79 patients (54.5%), acute interstitial nephritis in 44 patients (30.3%), glomerular disease in 16 patients (11.0%), and other causes in six patients (4.1%). Age group was associated with the clinical presentation ( $P=0.046$ ) (Table 1) and type of damage ( $P=0.000$ ) (Table 2). There was also an association between the type of damage and clinical presentation ( $P=0.001$ ) (Table 3). In multinomial logistic regression analysis, only oliguria ( $P=0.07$ ) and age group ( $P=0.049$ ) were associated with mortality (Tables 4, 5, 6, 7). In the Cox model survival analysis, oliguria ( $P=0.003$ ) and sepsis ( $P=0.03$ ) influenced survival (Table 8).

Survival curves showed that the probability of dying in the first 10, 20, or 40 days after the event was 75, 70, and 45% respectively (Fig. 1). When oliguria was present, survival at 10 days was 47% (Fig. 2); when sepsis was present it was 68% (Fig. 3).

## Results

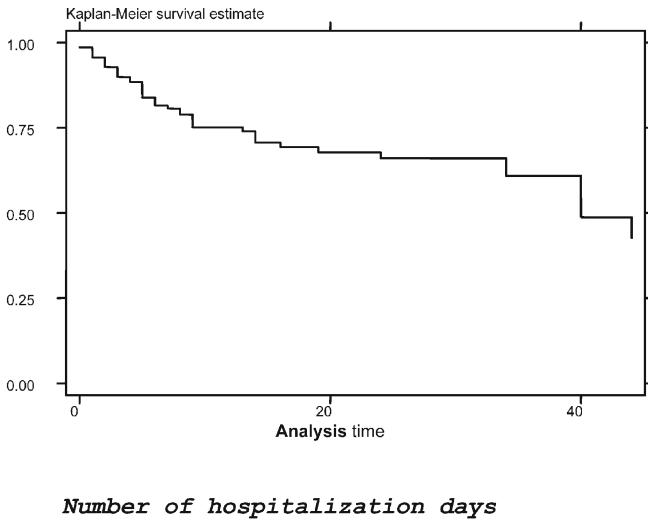
In total, 149 children were identified as having acute renal failure. The male/female ratio was 1.58/1. There were 66

**Table 7** Factors associated with death in children with ARF (multiple logistic regression)

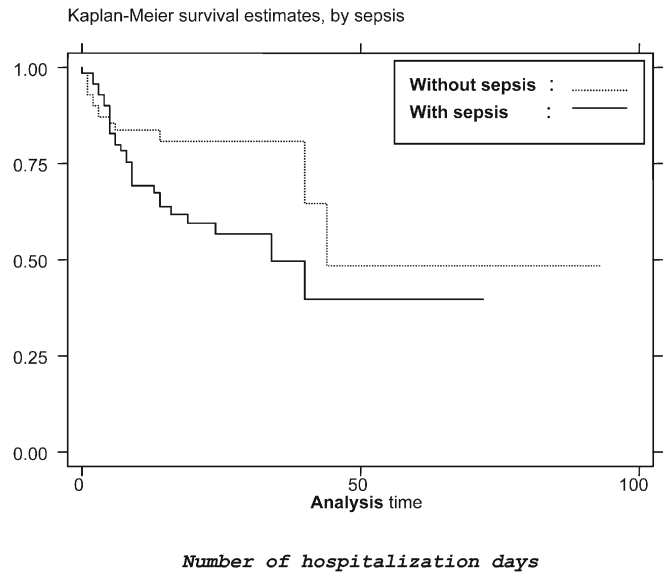
Final	Odds ratio	Std error	P	95% Confidence interval
Age group	0.6725664	0.1357228	0.049	0.4588601–0.9988637
Sepsis	1.988849	0.8347443	0.101	0.8736594–4.527532
Oliguric	3.242836	1.420801	0.007	1.373989–7.653614

**Table 8** Factors associated with survival in ARF (Cox analysis)

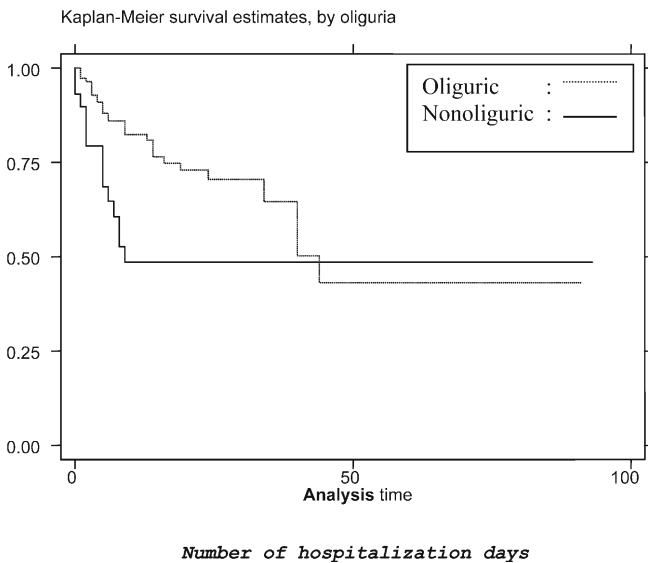
Final	Haz. ratio	Std error	P	95% Confidence interval
Sepsis	2.058415	0.683471	0.030	1.073747–3.946061
Oliguric	2.714372	0.910012	0.003	1.407013–5.236493



**Fig. 1** General survival of pediatric ARF (149 children)



**Fig. 3** Survival in ARF related to sepsis in (149) children



**Fig. 2** Survival in ARF related to oliguria in 149 children

**Discussion**

In the literature from high-income countries cardiovascular surgery and uremic hemolytic syndrome are the

most important risk factors associated with mortality in ARF in the pediatric population [13, 14, 15]. Arora et al. described a significant association between mortality in ARF and cardiovascular surgery and uremic hemolytic syndrome in 80 children less than 16 years old in India [3, 14].

After a study in New Zealand, on the other hand, Wong reported 27% mortality in children with ARF of etiologies other than uremic hemolytic syndrome and none in children with that disease [16].

The published results differ in clinical characteristics. This is clearly expressed in Hentschel’s review (1996) from Germany, in which he refers to mortality data in infants with acute renal failure varying from 25 to 78%, reporting, however, that renal disease by itself represents 0.9% of all deaths in children [1].

It is important to note that the results described in our population are not applicable to other populations. We can, however, describe coincidences in age group, where the vast majority show the high mortality associated with renal failure in newborns. A study group in Malaysia reports a mortality of 37.4% in very low weight newborns. Here a logistic regression analysis reports ARF as a risk factor for mortality [17]. Likewise, Hentschel reports premature birth as a risk factor for ARF [1]. However,

Airede describes his experience of renal failure in newborns in Nigeria, finding a mortality of 51.2% in a four-year case series with an incidence of 3.9/1000 live births [18]. Moghal reports his experience of acute renal failure in children in the Children's Hospital in Birmingham, UK; he found an incidence of 0.8 per 100,000 inhabitants, with hemolytic uremic syndrome the most common cause in 45% of cases. In the newborn group, ARF was related to surgery to correct congenital heart malformations in 63% and a global mortality rate of 25% [13, 14].

With regard to the type of clinical presentation in oliguric and nonoliguric ARF, we found that oliguric types had a worse outcome. This must be rapidly investigated, because this is seldom described in the literature as a prognostic factor in mortality related to ARF [19].

When we add sepsis, the situation becomes catastrophic and our series coincides with reports by Vega in a case series at Viña del Mar (Chile), in which he describes mortality in patients that developed ARF with sepsis (56 vs. 42.7%). Likewise Bhutta in Karachi (Pakistan) reports that sepsis in newborns was one of the major causes of morbidity and mortality among a cohort of 292 newborns; in a logistic regression model he found in the patients with sepsis and ARF an OR of 11.2 with death risk [8, 20].

In summary, we can confirm that for newborns with oliguria and sepsis the probability of dying is very high among our population, which agrees with most reports [7, 9, 10, 11, 21, 22]. We therefore recommend that physicians in charge of the treatment of a group with these characteristics should be alert to any manifestation that may predict the future of an infant patient with acute renal failure and mortality.

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