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Original Article

Acute renal failure in children: outcome and prognostic factors

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Abstract

Background Acute renal failure (ARF) is an emergency condition with a high mortality rate despite the long-known dialysis and advanced supportive care. Only few studies on prognostic factors of ARF in children are available in the literature, which are difficult to compare to each other due to the different definitions of the ARF outcome used.

Objective To find out the clinical and laboratory characteristics of children with acute renal failure and the prognostic factors affecting the outcome.

Methods This observational prospective study was conducted on children with acute renal failure hospitalized in the Department of Child Health, Cipto Mangunkusumo Hospital, between July and December 2001. Patients with acute on chronic renal failure were excluded. Clinical and laboratory data were taken at the time of diagnosis and the outcomes were noted after 2 weeks of observation. We classified the outcome as cured, uncured, and dead. Analytical study was done to find out the relationships among various prognostic factors.

Results Fifty-six children with ARF were recruited in this study. Male to female ratio was 1.3:1; the mean age was 4.4 year-old. The most frequent presenting symptom was dyspnea (34%), followed by oliguria (29%). The most frequent primary disease was malignancy (20%). Most of the patients had renal-type of ARF (73%). The outcomes were cure (71%), no cure (16%), and death (13%). Bivariate analysis and logistic regression revealed that younger age (OR=13.6; 95%CI 1.01;183.60) and the need for dialysis (OR=10; 95%CI 1.53;65.97) had significant relationships with mortality or no cure.

Conclusion We should be aware when finding ARF patients less than 5 year-old and have the indications for dialysis, due to the poor prognosis they might have **[Paediatr Indones 2003;43:205-210].**

Keywords: *acute renal failure, children, outcome, prognostic factors.*

Acute renal failure might be a serious complication of various diseases, medical or surgical interventions.[1-3] Most of the ARF patients present the symptom of oliguria, so that patients easily develop fluid overload which leads to edema, hypertension, seizures, congestive heart failure, pulmonary edema and respiratory failure.[4,5] Therefore, early recognition of ARF is very important to prevent such complications.

The prognosis of ARF in children is still poor despite the advanced management.[1] The mortality rate of ARF greatly depends on the severity of the disease and also the promptness and accuracy of the management.[2,6] Studies reporting prognostic factors of childhood ARF are rare and not comparable due to different definition of outcome used. To our knowledge, there had been no such study done in Indonesia. Various prognostic factors of childhood ARF are age, primary disease, the severity of renal impairment, clinical manifestations, laboratory results, complications, the need for dialysis, and nutritional status.[3,7-9] The aims of this study were to describe the clinical and laboratory characteristics of ARF patients in the Department

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of Child Health, Cipto Mangunkusumo Hospital and the prognostic factors affecting the outcomes.

Methods

This observational prospective study was conducted on ARF patients who were hospitalized or patients who developed ARF during their hospitalization in the Department of Child Health, Cipto Mangunkusumo Hospital, between July and December 2001. We divided the study into 2 parts. The first part was a descriptive study describing clinical and laboratory characteristics at the time of diagnosis and the outcomes after 2 weeks of observation. The second part was an analytical study to find out the relationships between various prognostic factors and the outcomes. All the patients aged between 1 month–18 year-old and had informed consents. Patients with acute on chronic renal failure were excluded. Acute renal failure was defined as sudden decrease of renal function, marked by GFR <80mL/minute/1.73m^2,[11,12] while hypertension was defined as mean systolic and diastolic blood pressures >95th percentile for specific sex and age.[13] Oliguria was urine output <1ml/kgBW/hour and non-oliguria was urine output ≥1 ml/kgBW/hour.[14] Indications for dialysis were the presence of ureum level of ≥200mg/dL, serum potassium ≥7.5mEq/L, intractable metabolic acidosis, clinical manifestations of fluid overload or general deterioration.[3,4,15,16] The outcomes were classified as cure when GFR ≥50 ml/mt/1.73m^2, no cure when GFR <50 ml/mt/1.73m^2, and death if during the observation the subject died.

Serum ureum and creatinine levels were performed in patients at high risk of getting ARF, and then the glomerular filtration rate (GFR) were assessed using the Schwarts formula.[10] Data of anamnesis, physical examination, urine output and laboratory findings (hemoglobin, serum albumin, cholesterol, electrolytes, urinalysis, and blood gas analysis) were collected. Patients were observed in 2-week period during the therapy based on the standard ARF management and the underlying diseases. Complications during the care and the need of dialysis were noted. At the end of observation, the GFR was reassessed and subjects were classified into died, cured, and uncured.

Data were analyzed using SPSS program version 10.00 and were presented in absolute numbers and percentages. We assessed all variables in each outcome group and analyzed them with bivariate and multivariate analyses. Bivariate analysis was performed using chi square test with 95% confidence interval, and multivariate test was analyzed using forward and backward stepwise logistic regression. To have the OR value and do the multivariate analysis, the table was changed into a 2x2 table; hence the columns of outcomes of death and no cure were merged into one column. Age was divided into <5 year-old and ≥5 year-old; nutritional status was divided into undernourished and well nourished; and type of ARF was divided into renal and extra renal ARF (pre renal and post renal).

Results

Characteristics of subjects

During 6-month period of study, out of 534 hospitalized patients, there were 61 ARF patients and 5 of them were excluded. Male to female ratio was 1.3:1.1. The youngest patient was one month-old while the oldest was 13 years old, and the mean age was 4.4 years. Half of the subjects were undernourished. (**Table 1**)

Table 1. Distribution of ARF patients based on demographic characteristics and nutritional status

Characteristics	n	%
Sex		
Male	32	57
Female	24	43
Age group (years)		
<1	12	21
1 - <5	23	41
5 - <10	14	25
≥10	7	13
Nutritional status		
Malnourished	2	4
Undernourished	28	50
Well-nourished	22	39
Overnourished	4	7

Table 2 shows that the most frequent clinical manifestation was dyspnea (34%), followed by oliguria in 29% including one patient with anuria. Most of the subjects had anemia (71%) and hypoalbuminemia (34%).

The most frequent underlying disease was ma-

TABLE 2. DISTRIBUTION OF CLINICAL MANIFESTATIONS AND LABORATORY FINDINGS

	n	%
Clinical manifestations		
Dyspnea	19	34
Seizure	12	21
Unconscious	10	18
Hypertension	7	13
Digestive tract bleeding	6	11
Pulmonary edema	3	5
Congestive heart failure	3	5
Oliguria	16	29
Laboratory findings		
Anemia	40	71
Uremia	19	34
Hypoalbuminemia	30	54
Hypocholesterolemia	26	46
Hyponatremia	26	46
Hyperkalemia	5	9
Metabolic acidosis	16	29

Note: each patient might have more than 1 clinical manifestations

lignancy, found in 17 patients (30%). Nearly 75% of the subjects had renal type of ARF (41), whereas the others had pre renal (8) and post renal ARF (7). The indications for dialysis was found in 19 subjects, but only 2 underwent this procedure. After 2 weeks of observation 40 subjects were cured, 9 were uncured and 7 died.

Bivariate analysis (**Table 3**) found that the younger the subject, the higher the mortality rate was (OR=6.33; 95%CI 1.27;31.57). Mortality rate was higher in subjects with oliguria than non-oliguric ones (OR=4.00; 95%CI 1.15;13.95). Seventy-one percents of subjects with renal-type ARF had an improvement of renal function within 2 weeks. There were more deaths among the subjects who had the indications for dialysis (OR=14.14; 95%CI 3.51;57.06). Mortality rate among patients with hypoalbuminemia (OR=3.67; 95%CI 1.01;3.34) and metabolic acidosis (OR=6.06; 95%CI 1.68;21.82) was higher than that of patients with normal albumin level and without metabolic acidosis.

Multivariate analysis found that factors of age (<5 year-old) and the need for dialysis had significant relationships with the occurrence of death and no cure in the ARF subjects.

Discussion

Our study found that male to female ratio was 1.3:1, which was similar to the result of Gallego *et al* who found a ratio of 1.1:1 among his 92 subjects.[17] Previous studies reported that there is no predominance of a certain sex over the other.[1,2,6,17] The subjects were mostly aged between 1-<5 year-old (41%) with the mean age of 4 years and 4 months (SD 3 years and 7 months). This was similar to the study by Arora *et al* who found that the mean age was 5.7 years.[18]

Most of the subjects were undernourished (50%). This was probably due to the low socio-economic status of most patients treated in our ward. Malnourished subjects tended to have a lower rate of curability compared to those who had better nutritional status. This finding was in accordance with the study of Fiaccadori *et al*[19]

TABLE 3. BIVARIATE ANALYSIS RESULTS FOR DIED AND UNCURED PATIENTS AMONG THE SUBJECTS

Prognostic factors	c^2	p	OR	**95%CI**
Sex	1.23	0.27	1.99	0.58; 6.78
Age group	5.97	0.02*	6.33	1.27;31.57*
Nutritional status	6.96	0.74	0.82	0.26;2.61
Oliguria	5.04	0.03*	4.00	1.15;13.95*
Type of ARF	0.04	0.85	1.14	0.30;4.29
Need for dialysis	16.86	0.00*	14.14	3.51;57.06*
Anemia	0.14	0.71	1.29	0.34;4.81
Uremia	2.58	0.11	2.64	0.79;8.76
Hypoalbuminemia	4.14	0.04*	3.67	1.01;13.34*
Hypocholesterolemia	2.33	0.13	2.50	0.76; 8.25
Hyponatremia	2.81	0.25	2.20	0.75;6.48
Hyperkalemia	0.35	0.55	1.76	0.27;11.69
Metabolic acidosis	8.41	0.00*	6.06	1.68;21.82*

* p<0.05

Bivariate analysis on 7 clinical manifestations found dyspnea, decreased level of consciousness, digestive tract bleeding or pulmonary edema were significantly correlated with the outcome (dead or uncured). We cannot compare this result to any other studies due to the different clinical manifestations used. Gallego *et al* reported that patients on ventilator had a higher mortality rate (75%).[17]

Oliguric ARF patients, especially patients with anuria, had much lower GFR, that leads to a longer period of azotemia, so that complications to other organs were higher.[5,16] Our study showed that mortality rate among the oliguric subjects was significantly higher than that of the non-oliguric subjects (OR=4.00, p=0.025). Obialo *et al* also reported a significant mortality among the oliguric patients (RR 17.0; 95%CI 6.2;46.6).[20]

Subjects with prerenal or post renal type of ARF have better prognosis than those with the renal type if they were diagnosed early and treated adequately. In the pre- and post renal ARF, the kidney function usually returns to normal quickly, whereas in the renal type there is already an abnormality in the glomeruli, tubules or vascularization, so that fluid restriction and or diuretic administration may be useless which results in the worsening of fluid overload.[5,16] This study found that the types of ARF did not influence the outcome significantly, probably due to the uneven distribution and severity of the underlying disease in the post renal ARF subjects.

To find out whether a prolonged prerenal ARF is still in the prerenal phase or already developed into renal phase, we should perform urine index examination (urine density and osmolality) or excretion fraction of sodium (FENa).[16] FENa is the best choice but this procedure is technically difficult since it needs 24-hour urine collection.

ARF patients with fluid overload or severe uremic manifestations had the indication for dialysis,[2,4,21] but due to unaffordable cost of this procedure, only 2 out of 19 patients underwent dialysis. Our study found that among the 19 patients indicated for dialysis, 7 died (37%) and 7 were cured (37%), while among the group not indicated for dialysis no death occurred and mostly were cured (76%). This results was similar with other studies that found more deaths and less cure among subjects indicated for dialysis.[3,4,8,9] Brivet reported that mortality rate of ARF patients with and without dialysis was 64% and 43%, respectively.[9] Arora *et al* found the rate was 53% and 20%, respectively.[18] Gallego *et al* found that the death rate among ARF patients who need dialysis was 79%.[17]

Uremia intoxication in ARF patients may lead to seizures, decreased level of consciousness, digestive tract bleeding, susceptibility to infection, where such conditions are the most important causes of death.[2,16] Our study found that mortality rate among subjects with uremia was higher than that of those with normal level of ureum, although it was not statistically significant. This was probably due to the lower cut off point used in this study i.e., ≥40mg/dL. Gallego *et al* found that ureum level was higher among the dead and not-cured group (non-survivors) than that among the survivors (28.6mmol/L vs. 15.2mmol/L; p=0.00).[17]

Hypoalbuminemia and metabolic acidosis had significant relationships with the outcome. Many studies revealed that prognostic factors for death in ARF were uremia, hypoalbuminemia, hypocholesterolemia, and the need for dialysis. Severe metabolic acidosis is one of the reasons for dialysis.[9,20,22,23] Obialo *et al* reported that hypoalbuminemia and hypocholesterolemia in ARF had a very significant relationship with death (p<0.0001).[20]

Forward and backward stepwise logistic regression analysis in our study found 2 variables (out of 13 independent variables) as the prognostic factors of death and no cure. Those variables were age and the need for dialysis. The younger the age, the higher the mortality rate and the lower the cure rate. (OR=13.63 and 95%CI 1.01;183.60) This might be explained by the fact that toddlers are more susceptible to disease/infection than the older age-group. Chevalier *et al* found that the younger the age, the worse the prognosis, especially in ARF patients aged less than 1 month-old.[24]

Studies on prognostic factors of ARF found that oliguria, hypoalbuminemia, hypocholesterolemia, the use of mechanical ventilation, sepsis, and multiorgan failure were predictors of death in ARF.[20,22,23] Arora *et al* found anuria, the need for dialysis, complications of the neurological and respiratory systems as the predictor factors of bad outcome. The more organ functions impaired, the worse the prognosis was.[18] Gallego *et al* found that factors having positive correlation with death were hypotension, the need for dialysis, the use of mechanical ventilator, uremia, complications developed in the respiratory,

neurology, hematology systems, and the occurrence of shock. All the dead ARF patients had complications of more than 3 organ systems.[17]

We concluded that a consideration should be taken in dealing with children suffering from ARF especially in those younger than 5 year-old and have indication for dialysis.

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