RESEARCH ARTICLE

Risk Factors and Prognostic Factors of Acute Renal Failure in Patients Admitted to an Intensive Care Unit, Tehran-Iran

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ABSTRACT

Acute renal failure (ARF) is defined as a sudden and continuous decrease of glomerular function associated with azotemia, and may be followed by decreased urinary output. There is a high incidence of ARF in ICU patients with a high mortality rate. Many factors can promote ARF development or influence its outcome. This study was done to assess the incidence, risk factors, outcome and treatment of patients who develop ARF in ICU. One hundred seventy five patients admitted to general ICU were studied. The impact of some factors such as age, sex, hypertension, length of stay in ICU, sepsis, oliguria, surgery, consumption of nephrotoxic drugs such as aminoglycosides and underlying chronic renal failure on development and prognosis of ARF was evaluated. ARF developed in 42(24%) patients with the mortality rate of 59.5%. Among factors studied, only use of aminoglycosides was statistically significant in relation to ARF development (P= 0.041), and the factors found to be associated with increasing mortality were hypertension (P=0.015) and prolonged stay in the ICU (P=0.012). In conclusion, among the prognostic factors, two were associated with a worse outcome of patients with ARF: hypertension and prolonged stay in the ICU. Unfortunately, the rapidly-changing clinical status of critically ill patients prohibits the clinician to make a clear decision on the prognosis of patients.

Keywords: *Acute renal failure, Risk factors, Prognostic factors, Intensive care unit*

Acute renal failure (ARF) is a potentially-reversible reduction in the capacity of the kidney to excrete nitrogenous wastes and maintain fluid and electrolyte homoeostasis, which usually occurs over hours to days [1]. This condition leads to progressive increase of nitrogenous compounds concentration (creatinine and blood urea nitrogen (BUN)) in plasma and can affect 5 to7% of all hospitalized patients [2]. It occurs mostly as part of a multiple organ dysfunction syndrome and sepsis, but it can also occur as a separate event [3]. Despite the recent technological advances, there is still a high incidence of ARF in intensive care unit (ICU) leading to high mortality [4-8] or requirement of renal replacement therapy (RRT) in approximately 6% of patients [5]. There is no standard definition of ARF, but common criteria are either biochemical (a rise in serum creatinine of 50 µmol/L, or of 50% from baseline, or beyond a set level, for example, >500 µmol/L), or clinical (oliguria with urine output < 400 ml/day). A combination of both, or the need for renal transplant is considered ARF [9,10].

Few researches have conducted concerning appropriate use of medical resources in renal failure. Identification of risk factors and poor prognostic markers in ICU patients can help in planning strategies to prevent ARF and to prioritize the utilization of sparse and expensive therapeutic modalities. Several risk factors involved in the genesis of ARF have been analyzed in the medical literature. Sepsis, state of shock, surgery, mainly, complex heart and vascular surgeries, advanced age, infections, use of contrast, and drug toxicity proposed by several investigators in earlier studies [7,11-15]. Similarly, the risk factors for mortality are also multiple in patients with ARF. Studies have demonstrated the importance of age, sepsis, oliguria, infection, multiple organ dysfunction and male gender, the latter possibly due to preexistent vascular disease [4,6,7,12,14,16-19]. The delay before ARF onset and length of stay in the ICU seem to be important, probably because they are markers of the severity of the patient's condition [20].

The aim of this study was to evaluate the incidence of ARF among ICU patients with normal renal function

Table 1. General characteristics of the 175 patients studied

Age (years)	53.1±12.9
Gender	
Female	85(48.6%)
Male	90(51.4%)
Chronic diseases	
CRF	17(9.7%)
Hypertension	93(53.1)
Cirrhosis	35(20%)
Malignancy	70(40%)
Chronic heart disease	100(57%)
Type of ARF	
Oliguric	125(71.4%)
Non-oliguric	50(28.6%)
Surgical group	75(43%)
Non-surgical group	100(57%)

Data were reported as means ± SD or as number of patients, with percent given in parentheses. All percentages refer to the total number of patients (N=175). CRF= chronic renal failure. ARF= acute renal failure.

on admission, as assessed by creatinine levels, and to analyze the risk and prognostic factors of ARF and its impact on the clinical course as well as the mortality of these patients.

PATIENTS AND METHODS

This cross-sectional study was conducted in the general ICU of a teaching general hospital affiliated with Tehran University of Medical Sciences from June 2002 to October 2003, in which 175 patients who met the inclusion criteria including absence of acute renal failure at the time of admission to ICU and minimum age of 18 years, were assessed prospectively. ARF was defined as a creatinine level above 1.5 mg/dl. Patients with progressive chronic renal failure are enrolled in this study only if they show acute renal failure (due to present chronic failure). On admission, demographic data (gender and age) were collected, as well as cause of admission and prior admission data (underlying chronic disease). Full medical history were taken by a general practitioner and any drug and non-drug sensitivity, serious problems that patients occasionally encountered, electrolyte and acid-base disorders, prescribed drugs, their dosage, time intervals and also recovery process of the disease, were recorded. If a patient met the inclusion criteria, his/her disease process was controlled and any therapeutic procedures are evaluated. For included patients, the relationship between some factors and ARF occurrence and its healing or mortality rate, was evaluated. These factors included age, sex, hypertension, length of stay in ICU, sepsis, oliguria,

surgery, consumption of nephrotoxic drugs such as aminoglycosides and underlying chronic renal failure. Patients were followed until ICU discharge or death. Statistical analysis was performed for determining the effect of each factor on ARF. The relationship between these variables and ARF occurrence and also its mortality, is evaluated using Pearson, Chi-square, Fisher's Exact and Student t-test, with the level of significance set at $p<0.05$. Patient conditions for sepsis diagnosis were selected according to criteria mentioned by American College of Chest Physician and Society of Critical Care Medicine Consensus Conference.

RESULTS

The demographic and overall features of the study population are shown in Table 1. The 175 patients fulfilling the criteria included 90(51%) men and 85(49%) women of mean age 53.1 ± 12.9 Years (18 to 86). ARF as defined by a creatinine level above 1.5 mg/dl, developed in 42(24%) patients with 59.5% resulting in death.

Analysis of certain risk factors related to ARF development is shown in Table 2. Only use of aminoglycosides, which are known to be nephrotoxic, has demonstrated to be significantly associated with ARF happening.

Among the prognostic factors shown in Table 3, two were associated with a worse outcome of patients with ARF: hypertension and prolonged stay in the ICU.

DISCUSSION

Acute renal failure is the acute loss of renal function over a period of hours or days. It is a common complication in intensive care unit patients. Despite improvements in medical and dialytic therapies, mortality rate for patients with complicated ARF remains tragically high. ARF in critically-ill patients is multifactorial in origin. Recognizing risk factors permits the timely-institution of proper treatment, which is the key to reducing untoward outcomes. We studied 175 patients admitted to general ICU and described the relationship between development and prognosis of ARF and the findings by age, gender, sepsis, surgery, underlying disease, type of ARF, which can be oliguric, and/or non-oliguric and ICU length of stay.

The incidence of ARF in population studied was 24%, which is higher than that reported in other series of ICU patients [3,16,21]. The whole mortality was

Table 2. Analysis of risk factors for the development of acute renal failure

Characteristics	ARF patients	Non-ARF patients	*p* value
Age (years)	47.1±13.2	53.4± 15.5	0.254
Male gender	64	46	0.401
Sepsis	25.8	74.2	0.009
Surgery	59.5	40.5	0.066
ICU length of stay (days)	9±4	7±3	0.364
Hypertension	57	43	0.569
Use of nephrotoxic drugs			
Aminoglycosides	48	52	0.041
Radiocontrast media	18	82	0.010

Data were analyzed statistically by the Pearson, Chi-square, Fisher's Exact and Student t-test. Data are reported as means ± SD or as percent of patients in parentheses. ARF= acute renal failure. CRF= chronic renal failure. ICU= intensive care unit.

Table 3. Analysis of prognostic factors for mortality of patients with acute renal failure

Characteristics	Survivors (N=17)	Non- Survivors (N=25)	p value
Age (years)	50.3±7.3	72.4± 6.5	0.041
Male gender	9	13	0.119
Sepsis	32	63	0.030
Oliguria	41.6	66.6	0.035
ICU length of stay (days)	4±2	11±5	0.012
Hypertension	53	76	0.015

Data are reported as means ± SD or as percent of patients in parentheses. ICU= intensive care unit.

about 59.5% in our department which is comparable to that found in literature [22-25].

According to our data, there was no significant difference in mean age between patients with and without ARF (47.1 ± 13.2 years and 53.4 ± 15.5years, respectively, with p = 0.254). Also, the outcome of ARF was independent of age (p = 0.041). In some recent studies, advanced age is considered as a factor indicative of a poor prognosis [26-30]; however, some others demonstrated that patient's age does not worsen the outcome of ARF [12,31-33].

In one study, age, sex, oliguria and in particular hypertension showed to be associated with ARF mortality [34]. In present study, the relationship between hypertension and ARF development was not significantly improved (p = 0.569), but it was found to be significant in predicting mortality due to ARF (p = 0.015).

Despite some previous studies which observed a trend towards an increasing number of ARF cases among male patients compared to female patients [3] and also showed male gender to be an effective factor on ARF mortality [30], in our study no significant difference was found between sex and ARF development (p = 0.401) or mortality (p = 0.119). Of 25 non-survivors due to ARF, 13(50.8%) were male and 12(49.2%) were female.

Of 175 patients screened, 17(10%) had chronic renal failure (CRF). After evaluating the effect of underlying CRF on the outcome of ARF, it is revealed that there is no statistically-significant relationship between development (p = 0.065) and prognosis (p = 0.057) of ARF and pre-existing CRF as a risk factor. A recent study determined underlying renal pathology as a leading precipitating cause for renal failure [23], however, the other one demonstrated that chronic renal dysfunction can be a risk factor for ARF development [35].

Earlier studies have described three factors associated with the most frequency with mortality or recovery of hospitalized patients diagnosed with ARF: length of stay in the ICU, sepsis and oliguria. Mean bed occupancy on this ICU for ARF patients was longer than that of non-ARF patients (10 ± 4 days vs. 6 ± 3 days, respectively). ICU length of stay has no effect on developing ARF (p = 0.364) but is completely effective on ARF recovery or mortality (p = 0.012). This finding has also been reported by others [12], whereas in some other studies, hospitalized duration has not shown to be a significant predictor of ARF outcome [14].

Sepsis carries a high morbidity and mortality further enhanced by ARF. Septic patients with ARF often are more seriously ill and have a higher mortality [16]. In the group of 31 patients with severe sepsis, 8(25.8%) developed ARF versus 74.2% in non-septic patients. So, in spite of most of the recent studies, which found sepsis to be a significant risk factor for ARF development [3,29,36-38] and also a predictive factor for poor outcome [38-41], in this study it is not improved to have significant effect on ARF development (P= 0.009) and its mortality (P= 0.030).

Oliguria has been considered a clinical feature of acute renal failure which prognoses its outcome. Most studies indicate that non-oliguric forms of ARF are associated with less morbidity and mortality than oliguric forms [27,28,42]. In present study, 71.4% were recorded as having oliguric ARF (urine output <400 ml/day). The mortality rate was 66.6% in oliguric and 41.6% in non-oliguric patients (p = 0.035). It is demonstrated in many studies that oliguria is a prognostic factor of poor outcome of ARF [29,37,43]. The result of this study is consistant with others which have considered oliguria to be the major predictor of non recovery of renal function.

ARF development after surgery often results in high morbidity and mortality [26,32]. Out of total of 175 patients, 75(43%) underwent surgery that 59.5% of these patients developed postoperative ARF. As it is clear, ARF development did not significantly differ between the two groups (p = 0.066).

Regarding nephrotoxic drugs (aminoglycosides and radiocontrast media such as barium sulfate and meglumin compound), only the use of aminoglycosides was significantly more frequent among subgroup of surgical patients (30.7%), with p = 0.01. Of 46 patients taken aminoglycosides, 22(48%) affected with ARF. So, we found that aminoglycoside therapy is statistically significant in developing postoperative ARF (p = 0.041).

ARF management is directed at treating any life-threatening features (hypotension, shock, respiratory failure), attempting to halt or reverse the decline in renal function, and if unsuccessful, providing support by renal replacement anticipating renal recovery. Fluid balance, the treatment of less severe acidosis, the use of diuretics and dopamine, as well as the relief of obstruction are all issues in the further management of the patient [44]. Intravascular volume is a crucial factor in the maintenance of organ function. It is therefore an essential task of critical care management to restore

intravascular volume to achieve adequate systemic circulation [45]. There is a theoretical rationale for the use of diuretics in ARF. Diuretics can help to maintain a homeostatic fluid balance during an episode of ARF and are often given if the patient is compromised by excessive fluid. The decrease in urine production seen in the oliguric phase of renal failure can have catastrophic effects, resulting in fluid overload and pulmonary oedema, which can lead to respiratory distress [46]. A reduction in urine output can also lead to hyperkalaemia, hyponatremia, metabolic acidosis and uraemia. It is for these life-threatening complications associated with oliguric ARF that health care professionals feel that the use of drugs promoting diuresis and electrolyte clearance will be beneficial [47]. In our department, if ARF in the patient was not due to obstructive azotemia, then in order to fluid balance and restoring urinary output, diuretics such as furosemide and acetazolamide were administered. Dopamine (1.5-3 µg/kg/min) was used in 5 of 42 (11.9%) patients with ARF. Furosemide with a dose of 200 mg, twice daily or 10-20 mg/kg was administered in 17(9.71%) patients. Also, acetazolamide was administered using 500 ml normal saline in order to eliminate oliguria. Dialysis and hemodialysis were used in 12(6.8%) patients. In this department, continuous renal replacement therapy (CRRT) was not done for any patients.

Acute renal failure is associated with fundamental alterations of metabolism and immunocompetence with the induction of a pro-oxidative and proinflammatory state. A rise in mortality rates of patients with ARF will be observed if underlying or hospital-acquired malnutrition exists [48]. So, whenever possible, enteral nutrition should be provided in patients with ARF because even small amounts of luminal nutrients will help to maintain intestinal function. Nevertheless, in many patients, total parenteral nutrition (TPN), at least supplementary and/or temporarily, will become necessary [49]. In this department, TPN was used for all patients if necessary but its administration was not due to metabolic disorders resulting from ARF in any patients.

Despite our best therapeutic efforts, ARF is a serious condition that carries a considerable mortality. Recovery of renal function is often incomplete and chronic renal failure may result, with its associated increased cardiovascular mortality and attendant risks of later progression to end stage disease [50]. Once ARF is established, a precise diagnosis should be sought and appropriately treated, and further insults avoided. The cornerstone of effective management remains regular reassessment of the patient's clinical and biochemical status, and recognition of the need for additional intervention, including timely and effective renal replacement therapy [44].

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