Acute renal failure in an intensive care unit

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ABSTRACT

Objective: To determine the clincal course and outcome of acute renal failure in an intensive care unit set-up.

Methods: All patients admitted to the intensive care until who developed acute renal failure were prospectively studied over a 3-year period from 1996 to 1999, at King Fahd Hospital of the University, Al Khobar, Kingdom of Saudi Arabia. They were investigated for the causes of their acute renal failure, given appropriate treatment and their course carefully documented until discharge from the intensive care unit.

Results: Forty-seven patients (29 male and 18 female) were studied. The majority were Saudis (81%). The age range was 28-81 years with a mean of 53 ± 14 years. Renal causes, 31 cases (66%), were the most frequent causes of acute renal failure. Pre-renal causes occurred in 12 cases (25.5%) and post-renal causes in 4 cases (8.5%). Three quarters of the causes were medical and one quarter surgical. Septicemia (22 cases), dehydration with hypovolemia (8 cases) and myo/hemoglobinuria (5 cases) were the leading medical causes. Fifteen patients (32%) died in the intensive care unit while 32 were discharged (68%). Multiple organ dysfunction, disseminated intravascular coagulopathy, acute respiratory distress syndrome and diabetes mellitus were the major factors that adversely affected mortality. There was a statistically significant difference in the length of intensive care unit stay of the survivors (5.7±2.6 days) compared to the deceased (11±5.8 days) (P<0.005). Renal replacement therapy was performed in 15 patients (10 continuous veno-venous hemodialysis and 5 conventional hemodialysis). Almost 3 quarters (73%) of the deceased required renal replacement therapy.

Conclusion: The development of acute renal failure in the setting of an intensive care unit carried a poor prognosis. Renal causes are responsible for 2 in 3 cases. Septicemia, dehydration/hypovolemia, myo/hemoglobinuria are the leading medical causes while multiple organ dysfunction, disseminated intravascular coagulopathy, acute respiratory distress syndrome and diabetes mellitus increase mortality. The poor prognosis of patients developing acute renal failure in the intensive care unit can be improved if attention is paid to prevention of septicemia, dehydration, prompt and aggressive treatment of multiple organ dysfunction, disseminated intravascular coagulopathy, acute respiratory distress syndrome and diabetes mellitus.

Keywords: Acute renal failure, intensive care unit.

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Acute renal failure (ARF) is a shared responsibility between Nephrology and Critical Care physicians. However, there seems to be a wide difference between the ARF cases observed in the Intensive Care Unit (ICU) compared to those observed in other areas of the hospital, particularly when looking at the mortality rate. The mortality in the ICU patients was 70% in some studies[1] while it may reach 50%-90% in others.[2] This high mortality was explained by the difference between multiple organ dysfunction (MOD) versus single system failure.[3,4] Other factors, however, need to be evaluated. Prediction of which ICU patients are likely to develop ARF would be useful. However, scoring systems such as Acute Physiological and Chronic Health Evaluation (APACHE) have been disappointing in this regard.[5] The presence of other parameters such as sepsis, dehydration, hypovolemia, myo and hemoglobinuria or both, MOD and diabetes mellitus (DM) may be more helpful.

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Different risk factors for the development of ARF in the ICU population as well as those affecting the outcome were studied before, but is far from being complete or conclusive.[6] Infection, however, is said to increase the risk of death associated with all factors.[7] There is, however, no honogenous agreement with regards to the most important factor responsible for ARF in the ICU, while some authors believe that it is the severity of circulatory shock, others think that it is the presence of MOD and many think that complicated sepsis is still the leading factor.[1,4,6]

Although patients with ARF are now older and sicker than in the past, mortality remains constant or even slightly lower, which suggests a better management of the syndrome. Different techniques have been recently introduced in managing those acutely ill patients, including a variety of extracorporeal renal replacement procedures.[2] The low efficacy arteriovenous procedures (continuous arteriovenous hemofiltration (CAVH) and continuous arteriovenous hemodialysis (CAVHD)) have been abandoned for the veno-venous, pump-driven techniques (continuous veno-venous hemofiltration (CVVH) and continuous veno-venous hemodialysis (CVVHD). Up to now there is no consensus whether continuous or intermittent renal replacement therapy (RRT) is more advantageous. In many cases, oliguric patients with circulatory instability will be treated by CVVH, even though there is no prospective study to show that in terms of outcome, continuous treatment is superior to intermittent hemodialysis.[2,7]

In concert with the search for ARF prevention and regeneration/repair strategies, it is imperative to focus efforts to reduce ICU, ARF mortality. Septic ARF is a dominant problem in managing ICU patients requiring RRT. Due to hemodynamic instability, it is difficult to manage these patients with traditional intermittent hemodialysis (HD), continuous RRT is used with greater frequency in the United States of America and Australian ICUs.[8,9] There is also emerging literature examining the use of RRT to remove septic inflammatory mediators.[10] There are still many unanswered fundamental questions in this area creating serious obstacles to the design and execution of clinical studies to improve the outcome.

Methods. A prospective study was carried out on 47 ARF patients who had acute renal failure in the ICU of King Fahd Hospital of the University during a 3-year period (1996-1999) to define prognosis factors and outcome. Age, sex, cause of renal failure, systemic infections, presence of MOD dysfunction during the disease course, need and type of RRT and length of stay in ICU were recorded. Acute renal failure was defined as elevation of serum creatinine above 165 umol/L or creatinine clearance less than 50ml/min.

Patients were divided into 2 groups: Medical Group - those who had acute renal failure during the course of an acute medical illness and Surgical Group - those who developed acute renal failure as a complication of surgical maneuver. Detailed information was prospectively obtained and analyzed by the investigators. A data forum was developed for the purpose of the study and the diagnostic category was established according to the modified APACHE III diagnostic category list. Specific information was obtained regarding the following items: Starting date of ARF, volume status of the patient, type of organism in septic patients, the presence or absence of evidence of MOD, the presence or absence of hemo- or myoglobinuria, the presence of diagnostic data of disseminated intravascular coagulopathy (DIC), the presence of diagnostic data of acute respiratory distress syndrome (ARDS), pre-existing chronic disease, type and duration of surgery, starting date of renal replacement therapy and the reason for its initiation, and the type of RRT used. Upon discharge from ICU, data was obtained on duration of ICU stay, time on ventilation, number of days of RRT, organ and patient outcome.

Statistics. Individual predicted risk of death was calculated from the SPAS II scores of each patient. Descriptive statistics and comparisons were performed using the statistical analysis package of the spreadsheet software (Microsoft Excel 97; Microsoft Corporation, Redmond, WA).

Table 1 - Clinical features of critically ill acute renal failure patients.

Diagnosis	Survivors n (%)	Non-survivors n (%)	Statistical significance
n of cases	32 (68)	15 (32)	-
Duration of stay in ICU	5.7+2.6 days	11.4±5.8 days	P<0.005
Diabetes Mellitus	8 (25)	9 (60)	P<0.005
Diabetes+Hypertension	6 (40)	3 (20)	NS
Anemia	19 (59)	10 (67)	NS
Metabolic acidosis	30 (94)	14 (93)	NS
Leukopenia	7 (22)	4 (27)	NS
MOD	2 (6)	8 (53)	P<0.001
Sepsis/Septic Shock	9 (28)	13 (87)	P<0.001
ARDS	1 (3)	4 (27)	P<0.001
DIC	1 (3)	7 (47)	P<0.001
Need for mechanical ventilation	4 (12.5)	13 (87)	P<0.001
Need for vasopressor support	5 (16)	14 (93)	P<0.001
Duration of RRT	5.25 days	6.62 days	-
Need for Dialysis at ICU discharge	4 (12.5)	- -	-

n=number, ICU=intensive care unit, MOD=multiple organ dysfunction, ARDS=acute respiratory distress syndrome, DIC=disseminated intravascular coagulopathy, RRT=renal replacement therapy, NS=not significant

Table 2 - Summary of the major patient's characteristics.

Diagnosis	n of cases (%)
n of pre-renal disease	12 (25.5)
n of intrinsic renal disease	31 (66)
n of post-renal disease	4 (8.5)
Sepsis	22 (63)
Dehydration and hypovolemia	8 (23)
Myo/Hemoglobinuria	5 (14)
Need for RRT	15 (32)
CVVHD	10 (21)
Hemodialysis	5 (11)
Survivors	32 (68)
Non-survivors	15 (32)
need for dialysis at ICU discharge	4 (8.5)

n=number, RRT=renal replacement therapy, CVVHD=continuous veno-venous hemodialysis, ICU=intensive care unit

Comparisons between survivors and non-survivors were performed using either the chi-square test for nominal variables or student's t test for numerical variables for all the patients.

Results. Forty-seven critically ill adult patients developed ARF during the 3-year study period. Their age ranged between 28-81 years with a mean age of 53±14. Saudis constituted 81% of the patient's population. Twenty-nine (62%) were male and 18 (38%) female. The clinical features of the 47 patients admitted to ICU who developed ARF are summarized in Table 1. The major diagnoses of the patients are shown in Table 2. Medical causes were responsible for ARF in 35 cases (74.5%) while surgical complications were the triggering factors in 12 cases (25.5%). Of the 22 septic cases 10 were diagnosed as bacterial pneumonia, 7 urinary tract infection, 2 with spontaneous bacterial peritonitis, 2 immuno-compromised due to chemotherapy and one with complicated wound.

Renal replacement therapy was required in 15 cases (32%), 8 cases (53%) for volume overload, 5 cases (33%) for severe and persistent oliguria and 2 cases (13%) for hyperkalemia with severe metabolic acidosis. The modality of RRT was CVVHD in 10 patients (67%), with conventional hemodialysis in 5 (33%) of them (Table 2). There were no differences in outcome between these 2 modes of RRT. Seventeen of the 47 cases (36%) involved in the study were diabetic. The duration of stay in the ICU was 5.7±2.6 days in the survivors and 11.4±5.8 in the deceased. The difference was statistically significant ($P<0.005$). At the end of the study, 15 patients (32%) died while 32 (68%) survived (Table 2).

The factors affecting mortality are shown in Table 3. Other factors such as anemia, leukopenia, site of infection, type of organism that causes sepsis and metabolic acidosis did not significantly influence the outcome.

Table 3 - Factors affecting mortality.

Factors	n of Cases (%)	n of Deaceased (%)
Mulitple organ dysfunction	10 (21)	8 (47)
Disseminated intravascular coagulopathy	8 (17)	7 (35)
Acute respiratory distress syndrome	5 (11)	4 (27)
Diabetes mellitus	17 (36)	9 (60)

n=number

Discussion. The definition of ARF rests on arbitrary cut-off points.[11,12] These dividing lines vary from study to study making comparisons difficult. Biochemical subdivisions have no clear association with outcome. Severe ARF is no longer a disease of Nephrology Wards, it is now frequently managed in ICU due to its association with MOD.[12] The factors predisposing to and complicating ARF in the Medical ICU and their relative influence on outcome during ARF are unclear and need more study. Several factors: age, prior chronic renal disease, sepsis and MOD have been discussed in previous articles but whether or not the outcome of ARF is dependent on factors predisposing to ARF is not yet clear.[6,7,13] Sepsis and hypovolemia are the major medical causes of ARF in the ICU. This information highlights the fact that any success in decreasing the incidence of ARF in the ICU is likely to be based on the development of more effective ways for the prevention and rapid treatment of sepsis. However, isolated ARF is uncommon in the ICU.[13] More than 80% of patients with severe ARF of critical illness have associated respiratory and circulatory failure or both (MOD).[6,14,15] In this study the pre-renal causes of ARF constitutes approximately one-fourth (25.5%) of the patient population and they responded well to conservative management. Aggressive conservative management in those patients who have pre-renal azotemia prevents further development of acute parenchymatous kidney failure and improves the

outcome. There is little data in severe ARF associated with trauma which supports the view that early intervention with continuous replacement therapy may improve survival[16] but the situation is obviously different.

The mortality rate of ARF in different literature is 50%-80% and has not declined significantly since the initial marked benefit of acute dialysis therapy.[14,17] In this study the mortality rate was 32% which may reflect better care, aggressive approach and early attempts at controlling sepsis and hypovolemia, although may be attributable to the fact that those with pre-renal azotemia were included.

Uncontroversial indications for RRT include uremic symptoms (anorexia, nausea, vomiting) or signs (uremic pericarditis, bleeding, encephalopathy), hyperkalemia refractory to medical management, volume overload unresponsive to fluid restriction and diuretics, metabolic acidosis that is severe or accompanied by volume overload, certain dialyzable intoxications (such as lithium, toxic alcohols, salicylates), some cases of hypocalcemia, hyperphosphatemia, or hypercalcemia, and anuric ARF unresponsive to acute interventions (reversal of pre-renal factors, relief of obstruction).[11]

In this study, the main indications for starting RRT were significant volume overload, persistent oliguria, severe hyperkalemia and the blood urea nitrogen (BUN)/creatinine values. The precise timing of RRT initiation, however, is a matter of clinical judgment.[17] In addition, RRT is commonly initiated when the BUN concentration reaches 100mg/dl, and repeated to maintain a pre-dialysis BUN below 80mg/dl.[13] In the United States of America ICU survey of ARF cases found that the mean BUN and creatinine values at initiation of RRT were 98 and 4.5mg/dl.[16] This pattern of practice is based primarily on early experience suggesting that uremic bleeding diathesis and hemorrhage were reduced when hemodialysis was initiated before the BUN exceeded 100mg/dl.[18,19] In this study the cut-off points were BUN 150mg/dl or above or serum creatinine 5mg/dl or above. Similarly, the threshold to initiate RRT to remove volume varies among clinicians.[20] The inability to severely restrict fluid intake in ICU patients results in adverse effects of volume overload more frequently than in less severely ill patients with ARF.[20] Almost all our seriously hypervolemic patients who did not respond to diuretics were exposed to RRT.

Sepsis is a complex process and may lead to ARF, which is often multi-factorial, particularly in ICU patients. For example septic shock causing ischemia in combination with nephrotoxic antibiotic and myoglobinuria is not an uncommon combination in this setting.[21,22] In this study, no nephrotoxic antibiotics were used and all septic patients did not manifest myoglobin in urine leaving us with the 2 factors: sepsis and hypotension. Infection alone can activate the immune system in which the kidney is an innocent bystander. Acute renal failure may be the presenting finding in patients with traumatic rhabdomyolysis, as the case with our patients, or non-traumatic rhabdomyolysis from infections or cocaine use.[23,24] Hemoglobinuric renal failure may be the initial presentation in patients with acute intravascular hemolytic event or those with DIC as the case with our patients. Obstruction of the collecting system generally must involve both kidneys or a solitary kidney to cause significant renal failure. Obstruction of the urinary tract at any level may cause ARF. Thus bladder outlet obstruction from prostate enlargement, tumor, or urethral stricture, ureteral obstruction by tumor, stone, papillae or fibrosis or even massive crystal (uric acid, acyclovir, calcium oxalate) deposition in the tubules can cause obstruction leading to ARF. In this study the causes of obstruction were prostatic tumors and renal stones. In either case surgical treatment was offered.

In conclusion, the development of ARF in the setting of an ICU carried a poor prognosis. Renal causes are responsible for 2 in 3 cases, septicemia, dehydration/hypovolemia, myo/hemoglobinuria are the leading medical causes while MOD, DIC, ARDS and DM increase mortality. The poor prognosis of patients developing ARF in the ICU can be improved if attention is paid to prevention of septicemia, dehydration, prompt and aggressive treatment of MOD, DIC, ARDS and DM.

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