

Epidemiology of acute renal failure in hospitalized patients: experience from southern Saudi Arabia

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وبائيات الفشل الكلوي الحاد في مرضى المستشفيات؛ خبرة المنطقة الجنوبية للمملكة العربية السعودية
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الخلاصة: على الرغم مما تحقّق من تقدّم في الرعاية الصحية فإنّ المراضة والوفيات المرتبطة بالفشل الكلوي الحاد لا تزال مرتفعة. وتحدّد هذه الدراسة تواتر وسبببات الفشل الكلوي الحاد في مرضى المستشفيات في المملكة العربية السعودية على مدى سنتين. ومن بين الحالات المئة والخمسين من الفشل الكلوي الحاد كانت 38.0% منها مكتسبة من المجتمع في حين كانت 62.0% منها مكتسبة من المستشفيات. وكان السبب الرئيسي للفشل الكلوي هو النخر الأنبوبي الحاد في 93 مريضاً، ولاسيّما ذلك الناجم عن الإنتان (24.7%) ثم ذلك الناجم عن الإقفار (12.7%) وعن انحلال العضلات المخططة ولاسيّما ذلك الناجم عن حوادث المرور (10.7%)، وعن الأدوية (7.3%) وعن الملاريا وعن لدغات الأفاعي (4.6%). وقد مات من مجمل المرضى 40% وشفي 48% آخرون شفاءً تاماً، فيما أصبح مريض واحد (0.7%) معتمداً على الديال. وتمثّلت العوامل المرافقة لسوء المآل في تقدّم العمر فوق ستين عاماً، وكون الفشل الكلوي الحاد مكتسباً من المجتمع، وزيادة قمة آزوت اليوريا في الدم على 160 مغ/دل، وامتداد فترة الفشل الكلوي الحاد لأكثر من أسبوع، والحاجة للديال ووجود مرض كبدي مرافق.

ABSTRACT Despite advances in health care, morbidity and mortality associated with acute renal failure (ARF) remain high. This study determined the frequency and etiology of ARF in hospitalized patients in Saudi Arabia over 2 years. Of the 150 cases of ARF, 38.0% were community-acquired and 62.0% hospital-acquired. The main cause was acute tubular necrosis (ATN) in 93 patients, due to sepsis (24.7%), ischaemia (12.7%), rhabdomyolysis (mainly from road traffic accidents) (10.7%), drugs (7.3%) and malaria and snake-bites (4.6%). Overall, 40% died, 48% made a full recovery and 1 patient (0.7%) became dialysis-dependant. Factors associated with poor prognosis were: age 60+ years, community-acquired ARF, peak blood urea nitrogen > 160 mg/dL, duration of ARF > 1 week, need for dialysis and associated chronic liver disease.

Epidémiologie de l'insuffisance rénale aiguë chez des patients hospitalisés : expérience en Arabie saoudite méridionale

RESUME Malgré les progrès réalisés dans les soins de santé, la mortalité et la morbidité associées à l'insuffisance rénale aiguë demeurent élevées. Cette étude a permis de déterminer la fréquence et l'étiologie de l'insuffisance rénale aiguë chez des patients hospitalisés en Arabie saoudite sur une période de 2 ans. Parmi les 150 cas d'insuffisance rénale aiguë, 38,0 % étaient des cas communautaires et 62,0 % des cas nosocomiaux. La principale cause était la nécrose tubulaire aiguë chez 93 patients, due à la septicémie (24,7 %), suivie par l'ischémie (12,7 %), la rhabdomyolyse (principalement due aux accidents de la route) (10,7 %), les médicaments (7,3 %) ainsi que le paludisme et les morsures de serpent (4,6 %). Globalement, 40 % des sujets sont décédés, 48 % ont guéri complètement et seul un patient (0,7 %) est devenu dépendant de la dialyse. Les facteurs associés à un mauvais pronostic étaient l'âge avancé (plus de 60 ans), l'origine communautaire du cas d'insuffisance rénale aiguë, un pic élevé d'azote uréique dans le sang (> 160mg/dL), une insuffisance rénale aiguë de longue durée (> 1 semaine), la nécessité d'une dialyse et une maladie hépatique chronique associée.

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Introduction

Acute renal failure (ARF) is a frequent complication in hospitalized patients. Despite substantial advances in renal replacement therapy and health care delivery, morbidity and mortality rates associated with ARF have remained high [1–3]. Although reliable statistics on the prevalence of ARF among different tropical countries are not available, statistics based on referrals to dialysis units suggest that the condition is more common in the tropics. Earlier reports from the Middle East have indicated that the incidence of ARF is several times higher in the region than elsewhere [4–6].

Snakebite, malaria, liver diseases and road traffic accidents are common health problems in Saudi Arabia [7–9], and the contribution of these conditions to the development of ARF have not been studied before. This report was undertaken to study the pattern of ARF in hospitalized patients in southern Saudi Arabia.

Methods

A prospective study was made of all adult patients (15 years and over) with ARF during a 2-year period (January 1999 to December 2000) attending Asir Central Hospital, southern Saudi Arabia. Children were not included.

The diagnosis of ARF was based on history, physical examination, laboratory data and clinical course. To select cases for the study, ARF was defined as a sudden deterioration in renal function presenting either as oliguria (urine volume \leq 400 mL/day) for at least 48 hours or as a rise in serum creatinine level of more than 50% and \geq 2 mg/dL. To ensure accurate diagnosis all cases were evaluated and followed up by a nephrologist until their renal functions normalized, they were discharged from the

hospital or they died (average period 3 weeks). Consent was obtained from patients who required kidney biopsy.

Cases were divided into community-acquired ARF, defined as renal failure developing outside the hospital, and hospital-acquired ARF, defined as renal failure that developed during hospitalization for non-renal-related problems in patients whose serum creatinine level on admission was normal.

The data were studied and coded. Analysis was carried out using *SPSS*, version 10. The chi-squared test, Student *t*-test and Fisher exact test were used as tests of significance at the 5% level of significance. Multivariate logistic regression analysis was carried out to study potential factors that might affect survival of acute renal failure. Age, peak blood urea nitrogen (BUN), acquiring ARF during hospitalization, duration of renal failure and having concomitant liver disease were included in the logistic regression model. Serum plasma urea was tested using enzymatic methods and serum creatinine using spectrophotometry.

Results

There were 150 patients with ARF in this study: 58.7% males and 41.3% females. The mean age of patients was 58.9 ± 22.5 years and 57.3% were 60 years or over (Table 1). Total admissions to the hospital during the study period were 26 000 patients, giving an incidence of ARF among hospitalized patients of 0.6%.

The mean duration of ARF was 10.7 ± 9.2 days (range 1–46 days). One-fifth of patients (21.3%) required dialysis while 78.7% did not require dialysis intervention. The mean duration of dialysis treatment was 6.1 ± 6.9 days (range 1–40 days).

Table 1 Distribution of acute renal failure cases by age and sex

Age group (years)	Male		Female		Total	
	No.	%	No.	%	No.	%
<20	5	5.7	1	1.6	6	4.0
20-44	26	29.5	13	21.0	39	26.0
45-59	12	13.6	7	11.3	19	12.7
60+	45	51.1	41	66.1	86	57.3
Total	88	58.7	62	41.3	150	100.0

A majority of patients (93, 62.0%) acquired ARF in hospital after admission for other reasons, while the other 57 patients (38.0%) were admitted primarily due to ARF (Table 2). Associated medical diseases were cardiac problems in 16.0% of patients, diabetes in 15.3% and hepatic problems in 10.7% (Table 2).

The commonest cause of ARF was acute tubular necrosis (ATN) in 93 (62.5%) of the patients (Table 2). Sepsis was the leading cause of ATN (37/93 cases), followed by ischaemia (19/93) and rhabdomyolysis of different etiologies (16/93); 10 of the rhabdomyolysis cases were traumatic following road traffic accidents. ARF was drug-induced in 11 cases due to aminoglycoside antibacterials. Snakebite and malaria comprised 7 cases.

The outcome of renal failure is seen in Table 3. Overall, 60 (40.0%) ARF patients died, 72 (48.0%) achieved full recovery and only 1 patient (0.7%) became dialysis-dependant. Uncontrolled sepsis and multi-organ failure was the leading cause of death (39/60 cases); other major causes of death were hepatic failure (6/60) and myocardial infarction (6/60). All patients with chronic liver diseases who developed ARF during hospitalization died.

Table 2 Profile of acute renal failure (ARF) cases by associated medical diseases, place of initiation and primary cause

Variable	No. of cases	% (n = 150)
<i>Associated disease</i>		
None	87	58.0
Cardiac	24	16.0
Diabetes	23	15.3
Hepatic	16	10.7
<i>Place of initiation</i>		
Hospital	93	62.0
Medical ward	(40)	(26.7)
Surgical ward	(26)	(17.3)
Intensive care unit	(23)	(15.3)
Burns unit	(4)	(2.7)
Community	57	38.0
<i>Primary cause of ARF</i>		
Acute tubular necrosis	93	62.5
Sepsis	(37)	(24.7)
Ischaemia	(19)	(12.7)
Rhabdomyolysis	(16)	(10.7)
Drugs (aminoglycosides)	(11)	(7.3)
Malaria	(5)	(3.3)
Snakebite	(2)	(1.3)
Other	(3)	(2.0)
Pre-renal failure	36	23.3
Glomerulonephritis	10	6.7
Obstructive uropathy	4	2.7
Interstitial nephritis	5	3.4
Vascular lesions	2	1.4
Total	150	100.0

n = total number of cases.

Table 4 shows a comparison of hospital- and community-acquired ARF cases. Mortality was significantly more frequent in hospital-acquired ARF than community-acquired ARF. On the other hand, full recovery was significantly more frequent in community-acquired ARF than hospital-acquired ARF.

Table 3 Outcome of acute renal failure

Outcome	No. of cases	% (n = 150)
Full recovery	72	48.0
Partial recovery	17	11.3
Dialysis-dependent	1	0.7
Death	60	40.0
Sepsis and multi-organ failure	(39)	(26.0)
Myocardial infarction	(6)	(4.0)
Hepatic failure	(6)	(4.0)
Gastrointestinal bleeding	(4)	(2.7)
Cerebral haemorrhage	(3)	(2.0)
Arrhythmia	(2)	(1.3)
Total	150	100.0

n = total number of cases.

Factors that determined the survival of our study population are shown in Table 5. Age less than 60 years, low peak BUN, hospital-acquired ARF, short duration of ARF, no concomitant liver disease and no

intervention with dialysis were good prognostic factors for better patient survival.

Discussion

In recent years, improvements in socioeconomic conditions, rapid industrialization, expanding medical facilities and developments in prevention have led to a near eradication of ARF due to infection and obstetric accident. ARF in industrialized societies is now largely a consequence of road traffic and industrial accidents, cardiovascular surgery, drugs, multi-organ failure and renal transplant rejection [10]. The patterns of ARF encountered in the tropics have shown changes similar to those in the industrialized countries, although at a slower pace [11]. Among the medical causes of ARF, etiological factors leading to ARF in tropical countries are different from those seen in the industrialized world. Diarrhoeal diseases, intravascular haemolysis due to glucose-6-phosphate de-

Table 4 Distribution of cases: comparison of hospital- and community-acquired acute renal failure (ARF)

Factor	Hospital-acquired ARF (n = 93)	Community-acquired ARF (n = 57)	P-value
Primary cause	Acute tubular necrosis	Glomerulo-nephritis	
Mortality (%)	51.6	21.1	< 0.05
Need for dialysis (%)	19.4	24.6	NS
Full recovery (%)	37.6	64.9	< 0.05
Mean age ± s (years)	61.25 ± 22.18	55.1 ± 22.78	NS
Male (%)	55.9	63.2	NS
Female (%)	44.1	36.8	NS

s = standard deviation.

n = total number of cases.

NS = not significant.

Table 5 Multivariate logistic regression model: adjusted odds ratio (OR) and 95% confidence intervals (CI) of potential determinants of survival in cases of acute renal failure

Factor	Adjusted OR	95% CI	P-value
Age < 60 years	3.2	1.3–8.2	0.014
Peak BUN (< 160 mg/dL)	3.1	1.2–8.2	0.018
Hospital-acquired renal failure	5.0	1.9–12.5	0.001
No liver disease	5.1	1.2–21.3	0.025
Duration of renal failure (< 1 week)	3.9	1.5–11.1	0.004
No dialysis	10.7	3.0–37.5	0.000

BUN = blood urea nitrogen.

hydrogenase (G6PD) deficiency, copper sulphate poisoning, snakebite and insect stings together constitute over 40% of all cases of ARF in India, problems that are rarely encountered in western Europe and the USA [12,13].

The incidence of ARF among our hospitalized patients was 0.6%. This is in agreement with reports from the Middle East and industrialized countries where the incidence of ARF was reported to be between 0.1%–1.5% [14–16]. Although the spectrum of the different etiological factors for ARF was not different from previous reports from the region, there were, however, 2 new factors contributing to the cause of ARF in this study, namely snakebite and malaria. Although these 2 tropical problems contributed only to 4.6% of the causes of ARF, they have not been reported previously in other studies. Snakebite and malaria are common health problems in southern Arabia [7,9] and ARF is a common complication of these conditions. The overall prevalence of ARF in *Plasmodium*

falciparum malaria can reach up to 60% of inpatients with heavy parasitaemia [17,18]. The incidence of ARF following snakebite is reported to be 13%–32% in India and snakebite contributes to 3% of the causes of ARF [12]. Although it is a common health problem, particularly in southern Arabia, the true incidence of ARF following snakebite is not known and few case reports have been published [19,20].

ATN was the commonest reason for ARF seen in our hospitalized patients. Sepsis and ischaemic causes were the commonest causes of ATN in this study, and this is similar to other reports [3–5]. Rhabdomyolysis of different etiologies contributed to 10.7% of ARF cases in our study. This finding is also unique to our study and has not been seen in previous reports from neighbouring countries [4–6,10]. Rhabdomyolysis is defined as injury to skeletal muscle cell of such severity that their contents are released into the circulation. Myoglobinuria is a consequence of rhabdomyolysis. Rhabdomyolysis is caused by either traumatic or non-traumatic factors. In the tropics, the common causes of non-traumatic rhabdomyolysis leading to myoglobinuric ARF include: eclampsia, prolonged labour, poisoning with mercuric chloride or zinc phosphide, status epilepticus, viral myositis, burns and electrical injury [21]. The incidence of post-traumatic ARF has been reported to be 3%–12% [22,23]. Two-thirds of rhabdomyolysis cases in our study were the result of road traffic accidents. Based on this study it is difficult to estimate the risk of ARF following road traffic accidents and further studies are needed.

Nephrotoxicity from drugs remains an important cause of ARF, both in nephrology units and intensive care units as well as in general surgical and medical wards. Drug-induced ARF comprised 7.3% of

cases in our study. In a North American general hospital the incidence of drug-induced ARF was estimated to be 20% [24]. Different studies from the Middle East have reported higher incidences of drug-induced ARF, up to 24% reported from Kuwait [4]. Our data showed a lower incidence than previously reported [4,24].

The mortality rate in this study was 40.0%. This is in agreement with the general impression that, despite impressive advances in the management of patients with ARF, there has been little improvement in survival rates [25]. The main causes of death in our population were uncontrolled sepsis and multi-organ failure in 39 cases (26.0%). All patients with chronic liver disease who developed ARF during hospitalization died. ARF complicating chronic liver diseases is not infrequent in this region where there is high prevalence of chronic carrier state for viral hepatitis [8]. In one study from Saudi Arabia 4 out of 18 deaths in ARF were caused by hepatic failure [21].

In our study, hepatic failure was the main cause of death in 4.0% of cases.

Patients who developed ARF in hospital show a higher mortality rate and less chance of their renal function recovering to normal. This can be explained by the fact that those patients who acquired renal failure during hospitalization are already ill and have concomitant medical problems such as chronic liver disease. A better survival rate was observed in younger patients, low peak BUN, short duration of ARF (< 1 week) and in those patients who did not require dialysis treatment.

In summary, ARF remains one of the major medical problems that require special attention in hospitalized patients. Despite the developments in diagnostic techniques and the availability of dialysis in most referral hospitals, the morbidity and mortality associated with ARF remains high. Appropriate treatment and avoidance of toxic agents in hospitalized patients may help to reduce the mortality in those at high risk.

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