ACUTE RENAL FAILURE - CHANGING TRENDS

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ABSTRACT

A prospective study of 120 patients of acute renal failure was done at CH (EC) Calcutta to document the changing trends in the incidence and etiology of acute renal failure and to assess the prognostic factors. Mean age of patients was 33.7 ± 20.2 years. 75% had a medical risk factor. The etiological factors were volume depletion (13.3%), septicaemia (25.6%), falciparum malaria (16.6%), a transplant related renal failure (5.7%) and drugs (16.7%). Renal histology showed acute tubular necrosis to be the most common lesion (53.3%). In 13.3% patients who died with acute renal failure, associated infection and multisystem involvement was more common.

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KEY WORDS : Acute renal failure

Introduction

Several studies have documented the causes of acute renal failure (ARF) [1]. The frequency of these risk factors besides showing regional differences have changed over a period of time. Despite regular use of dialysis and major improvement in management techniques over past decades, mortality rates after ARF have not changed dramatically and one third patients with medical causes are reported to die during ARF [2].

This study was taken to document the changing trends in the incidence and etiology of ARF and to identify the prognostic factors contributing to mortality amongst patients of ARF.

Material and Methods

One hundred and twenty patients of acute renal failure (ARF) were identified at CH (EC) Calcutta between Jan 1990 and July 1992. Acute renal failure was defined as acute reduction in renal function resulting in serum creatinine greater than 2 mg/dl or an increase in serum creatinine of at least 0.5 mg/dl for patients with a base line serum creatinine greater than 2 mg/dl. Base line serum creat-

inine was the most recent value obtained within the previous 6 months. For patients not having a creatinine determination in prior 6 months but having an admission value greater than 2 mg/dl, the presence of ARF was retrospectively defined by a decrease in serum creatinine of 50% within one month of admission [3].

Patients were categorised as having a medical, surgical or an obstetrical cause for ARF. Patients with pre-renal azotemia and urinary tract obstruction were not included in the study. The only exception being when either of these were secondary to drugs. Pre-renal azotemia was considered to be present when there was evidence of intravascular depletion, heart failure or drug induced renal hypoperfusion and improvement in creatinine was noted with correction of volume disturbance or discontinuation of drugs. Acute intrinsic renal failure was considered when there was no response in clinical course to either volume repletion or discontinuation of the offending drugs and the urine sediment contained renal tubule epithelial cells and muddy brown granular casts [3].

A comparison was made of the incidence and causes of acute renal failure in the

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present study (period B) with that in the preceding 30 months (period A).

In 45 patients renal tissue was obtained for histological examination either by a percutaneous renal biopsy or at necropsy. The factors associated with higher mortality were identified and their frequency compared in those who died with ARF with those who survived.

Results

One hundred and twenty patients of ARF were identified. Mean age of patients was 33.7 ± 20.2 years and 65% were males. Seventy five percent patients had a medical risk factor. A surgical cause was detected in 24.2% and in 0.8% patients an obstetric cause was identified. Comparison of the risk factors for ARF during the two study periods (Table 1) showed a decreased incidence of volume depletion and a higher incidence of septicaemia during the present study. Falciparum malaria continued to be an important etiological factor. Urinalysis in patients with falciparum ARF showed varying degree of proteinuria and microscopic abnormalities. Extra renal manifestations in this group included hepatocellular jaundice (80%), cerebral malaria (26.7%), intravascular haemolysis (20%), septicaemia (26.7%) and dysenteric malaria (13.3%).

A spectrum of renal transplant related ARF was also seen. Three patients suffered from

acute rejection, one had acute pyelonephritis of the transplanted kidney and yet another developed *de-novo* crescentic glomerulonephritis. 16.7% patients had drug induced ARF. Gentamicin in 10 patients and captopril in 3 patients were suspected to be the primary cause. Ampicillin was considered the offending agent in a patient who had ARF with nephrotic range proteinuria.

The miscellaneous group included patients with acute pancreatitis, seizures, electrical injury, intra cerebral haemorrhage and unidentified causes.

In the present study (period B) renal biopsies were done in 45 patients. Acute tubular necrosis was the most common lesion (53.3%). The other lesions included diffuse proliferative glomerulonephritis (8.9%), crescentic glomerulonephritis (6.7%), renal vasculitis (4.4%) and acute interstitial nephritis (4.4%). In 22.2% biopsies besides acute tubular necrosis, mesangial proliferation was a prominent feature.

The overall mortality in patients with ARF was 13.3%. A significant difference was noticed between the characteristic of survivors vis a vis those who died (Table 2). Four patients of falciparum malaria who died, had also cerebral malaria, three had associated blood culture positive gram negative septicaemia, and a metastatic cerebral abscess was seen in one patient. In yet another patient massive intravascular haemolysis was documented.

TABLE 1

Medical causes of acute renal failure

Etiology	Period A 1987-89		Period B 1990-92	
	Nos	%	Nos	%
Volume depletion	22	(29.7%)	12	(13.3%)
Septicaemia	12	(16.2%)	23	(25.5%)
Falciparum malaria	20	(27.1%)	15	(16.7%)
G-6 PD deficiency	-	-	1	(1.1%)
Snake bite	2	(2.7%)	4	(4.4%)
Drugs	8	(10.8%)	15	(16.7%)
Transplant	-	-	5	(5.6%)
Glomerulonephritis	6	(8.1%)	8	(8.9%)
Miscellaneous	4	(5.4%)	7	(7.8%)
	74		90	

TABLE 2

Characteristics of survivors

Variables	Survivors (n = 78)	Death (n = 12)	'p'
Age (mean $\pm$ SD years)	37 $\pm$ 9.2	46.16 $\pm$ 15.4	NS
Septicaemia	18	5	NS
Falciparum malaria	11	4	NS
Oliguria	15	12	< 0.05
Mean peak S. creatinine	7.56 $\pm$ 3.6	10.2 $\pm$ 4.2	< 0.05
Dialysis	44	12	< 0.05
Days of hosp. stay	45	5	< 0.05

n = number

Discussion

The etiology of ARF is closely linked to the prevailing socio-economic and environmental condition in a given geographical location. Consequently the pattern of ARF in the tropics differs markedly from that of economically advanced countries. Within India itself there are differences in the etiology of ARF in different parts of the country. Moreover the pattern of ARF in the country has changed considerably in recent years [1]. An analysis of our own data collected over the last six years brings out these changes distinctly (Table 2). A high incidence of surgical ARF (24%) was seen in the present study and obstructive uropathy was a major cause. Trauma and post operative complication contributed to 7.5% cases of surgical ARF.

Septicaemia accounts for 2% to 8% cases of ARF and a higher incidence has been reported in hospital acquired ARF [4]. The older age group, multiple therapeutic and diagnostic procedures and prolonged hospitalisation probably accounted for the increased incidence of septicaemia. In the post transplant period, acute rejection [5] is a common cause for ARF and was seen in two of our patients. As reported earlier, the classical signs of acute rejection viz fever, oliguria and graft tenderness were masked in patients on cyclosporine therapy [5]. Acute pyelonephritis of the grafted kidney may present with acute worsening of renal function in the absence of systemic signs [6] as was seen in our patients. Recurrence of glomerulonephritis in the transplanted kidney has been documented, however, *de novo* crescentic glomerulonephritis which occurred in our patients is distinctly uncommon [7].

In twenty three (12.5%) of our patients, ARF was attributed to drugs, with aminoglycosides being the principal offending agents. The clinical presentation in these patients was of non oliguric ARF, which recovered on discontinuing the drugs. Renal failure is a well known complication of therapy with angiotensin converting enzyme inhibitors and nonsteroidal anti inflammatory drugs [8].

Although these drugs may cause intrinsic renal disease the rapid reversal of renal functions on stopping captopril in our patients, was consistent with a haemodynamic rather than a structural alteration. In renal transplant cases the induction of acute reversible renal failure by angiotensin converting enzyme (ACE) inhibitors is not only a clue to the presence of graft artery stenosis but also a good predictor of the success of revascularization. Unfortunately, renal artery occlusion has been observed occasionally after administration of captopril in patients with renovascular hypertension. This precludes the systemic use of this medication in patients with graft-artery stenosis [9]. One patient on ampicillin developed hypersensitivity vasculitis and ARF with nephrotic range proteinuria. The renal biopsy was suggestive of acute interstitial nephritis.

Thirty five (17.8%) of the ARF patients treated at this centre were associated with malaria. This contrasts with the much lower incidence reported by Mahakur *et al* [10] and highlights the geographical variation in the incidence of malaria ARF. Majority of cases with ARF had falciparum infection, of these 4% had vivax infection in addition. Only one patient had a pure vivax infection superimposed on G-6-PD deficiency and developed ARF due to intravascular hemolysis.

The overall prevalence of ARF in falciparum malaria is about 1% but it has been reported in upto 60% of patients with severe infection [11]. The presence of cerebral and hepatic involvement in our patients suggests, they had a more severe form of infection. In this series, 66.7% patients of malarial ARF had nonoliguric acute renal failure and all patients had varying degree of proteinuria. Although oliguria was usual in the early descriptions of ARF, it is now clear that urine volumes may vary from severe oliguria to severe polyuria. Both patterns may arise from the same insult, but it is probable that the non oliguric pattern results from less severe injury [12].

The most common histological abnormal-

ity in malaria ARF was acute tubular necrosis, however associated mesangial proliferation was seen in 10 patients. The hypercellularity was due to mesangial proliferation, increased mesangial matrix and mononuclear cell infiltration. These changes were probably responsible for the development of proteinuria and urinary sediment changes.

Several factors have been described to cause renal ischaemia and tubular injury in falciparum malaria. These include hypovolaemia, intravascular hemolysis, intravascular coagulation, endotoxaemia, catecholamine release and the hemorrhheologic changes induced by parasitized erythrocytes [10].

The overall mortality of patients with ARF in the present study was 13.3%. On comparing the characteristics of survivors with those who died, we found fewer survivors had infection as an underlying cause; significantly less number of patients were oliguric, and dialysis was needed in less number of patients. A negative correlation was found between the duration of hospitalisation and mortality. Analysis of prognostic factors showed that these patients had a severe systemic disease ending fatally within a short time.

In summary, a changing pattern in the cause of ARF was observed. Falciparum ARF continued to be a significant risk factor. A spectrum of renal histologies was documented with acute tubular necrosis being the most common lesion. A higher mortality was seen in patients who had infections as a cause of ARF, in patients who had a multisystem involvement and those who had oliguric

ARF, the latter representing the more severe forms of ARF.

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