Chapter 129

Acute Renal Failure in India

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INTRODUCTION

Acute renal failure (ARF) is one of the most common clinical conditions encountered by physicians and nephrologists throughout the world. Due to the climatic conditions, overcrowding and poor socioeconomic factors, ARF in India differs from the world. There is no clear cut data on the incidence, causes and recovery from the disease. Most of the data available with nephrologists of various hospitals are of moderate to severe renal failure, since they are referred from other hospitals for further management. Acute renal failure is defined as an abrupt decline in glomerular filtration rate (GFR) resulting in progressive elevation of plasma urea and creatinine, the essential point to be established is that the renal failure is of short duration. Most common causes of ARF in India are acute diarrheal disease, malaria, leptospirosis, snakebite, insect stings, intravascular hemolysis due to septicemia, chemical poisoning like copper sulfate, vasomil and pregnancy. Overall, these causes constitute 40% ARF in India.

ACUTE DIARRHEAL DISEASE WITH ACUTE RENAL FAILURE

Diarrhea causes 5-10 million deaths in a year. In India, diarrheal disease is responsible for ARF in 35-50% of children dialyzed in a year. Acute renal failure due to diarrhea is not uncommon in adults and elderly people. Kidney receives almost one-fifth of the cardiac output. Due to severe diarrhea, fluid and electrolyte loss occurs, and leads to hypoperfusion despite its remarkable capacity to adopt during states of hypoperfusion. Still the kidney is more vulnerable to ischemic damage. It is because certain areas of the nephron, especially in the medulla are on the brink of hypoxia and prone to ischemic insult. Experimental evidence suggests that there is intense intrarenal vasoconstriction during shock, which contributes to ischemic injury. Another mechanism is tubular dysfunction. It is due to shedding of epithelial cells, whose adhesion causes tubular obstruction and back leak to interstitium. Renal failure is usually oliguric and presents with severe metabolic acidosis due to bicarbonate loss in diarrheal stools and renal failure.

Due to reduced tissue perfusion, lactic acidosis might also play a role. Severe acidosis leads to reduced cardiac output and arterial dilatation due to resistance to the vasoconstrictive action of catecholamines, resulting in hypotension. In addition, hypokalemia may occur due to loss of potassium, leading to paralytic ileus. Although acute tubular necrosis is the most common histological lesion, acute cortical necrosis can occur.

Management

Oral rehydration is advised in mild to moderate dehydration. In moderate to severe dehydration, intravenous (IV) fluids: normal saline or Ringer’s lactate is the ideal choice, since they stay in the intravascular compartment. Monitoring hydration status, urine output, serum potassium and metabolic acidosis are very essential. Once urine output is reduced and renal parameters elevated along with acidosis, dialysis needs to be planned to save the patient. All modalities of dialysis whether peritoneal or hemodialysis are ideal. In the author’s experience, peritoneal dialysis is an effective, simple and safe procedure which can be done by medicine postgraduate students and primary care physicians. Severe acidosis and prolonged hypotension due to severe dehydration are indicators of worst prognosis. Despite advances in the management of diarrhea, the mortality due to ARF is high due to late referral, severe acidosis, anuria, metabolic encephalopathy and multiorgan failure.

MALARIA

Malaria is widely prevalent and every year 300–500 million cases are recorded. The overall prevalence of ARF in falciparum malaria is less than 1%, but could go up to 60% in patients with heavy parasitemia. The reported incidence in different parts of India is 13% in North India, 17.2% in Orissa, 17.8% in Delhi and 22% in South India. Acute renal failure is usually seen by the end of the 1st week and mostly it is nonoliguric in 50–75% of cases. According to the recently revised World Health Organization (WHO) criteria, malarial ARF is defined as increase in serum creatinine, more than 3 mg/dL with 24 hours urine output less than 400 mL despite adequate hydration, in patients with peripheral smear positive for malaria. In a recent report, malarial ARF has been grouped into two categories. Patients with ARF and multiorgan failure are grouped under one category and patients who, even after treatment with antimalarial drugs, progress to develop renal failure, requiring dialysis for recovery are grouped under another category.

The pathogenesis is often multifactorial, involving a complex interaction of factors which include mechanical, immunologic, cytokine, humoral, acute phase reactants, nonspecific factors and hemodynamic components.

Mechanical Factors

The parasitized erythrocytes have reduced deformability and sequester in different capillary beds, leading to organ dysfunction.

Organ dysfunction occurs due to activation of complement, induction of cytokines such as tumor necrosis factor (TNF), interleukin (IL)-1, IL-6, IL-8 and soluble CD14. Cytokines and immunological factors not only facilitate cytoadherence but also have direct tubular effects. Various hormones like catecholamines and kinins can increase vascular permeability. Catecholamines and endothelins also can cause renal vasoconstriction. As an acute phase reaction, fibrinogen levels get elevated, increasing the viscosity of blood and rouleaux formation, thereby worsening organ dysfunction.
Several nonspecific factors like fever, hemolysis, intravascular coagulation, rhabdomyolysis and hyperbilirubinemia can contribute to the development of renal failure.6

**Treatment**

Quinine is the most widely used drug for malaria. Loading dose of 20 mg/kg followed by 10 mg/kg 8th hourly has to be administered. Dose modification is not required in mild to moderate renal failure. If the serum creatinine is more than 3 mg/dL, the dose interval is extended to every 12 hours. Artemether and artemisinin derivatives like artesunate can be given in severe malaria and no dose modification is required in renal failure.

Acute renal failure should be detected early and fluid challenge in the case of dehydration is essential. If there is reduced output with elevated renal parameters, dialysis needs to be planned. Prognosis is often determined by the degree of parasitemia and patients who are anuric and not dialyzed or referred in late stage have worst prognosis.

**LEPTOSPIROSIS ACUTE RENAL FAILURE**

Leptospirosis is a common zoonotic disease reported from many states in India. Renal involvement is the predominant manifestation of many types of severe leptospirosis. Acute renal failure is nonoliguric in about one fourth to half (50%) of the cases. The mechanisms of ARF in leptospirosis are direct bacterial invasion, nonspecific factors and immunological reactions. The passage of the leptospira through the glomerular blood initiates nonspecific glomerular changes. The organism is thought to migrate from peritubular capillary to the interstitium and finally reach the tubular lumen. Endotoxin may mediate renal tubular damage mediated by complement or bacterial enzymes; in addition hypotension and myoglobinuria all contribute to the renal involvement.7 Patients with severe leptospirosis present with high-grade fever, severe myalgia, jaundice, renal failure and hemorrhagic manifestations like subconjunctival hemorrhage, gastrointestinal (GI) bleeding and hemoptysis. Acute renal failure is the most serious complication and common cause of death in leptospirosis, because it presents with multiorgan failure.

**Diagnosis**

In the leptospiremia phase, the organisms may be demonstrated in the blood by dark ground microscopy. Serological methods are the main stay in diagnosis. They include complement fixation test, microagglutination, macroagglutination and enzyme-linked immunosorbent assay (ELISA). The microscopic agglutination test (MAT) uses live leptospiral antigens, and is highly sensitive and confirmatory. LeptoDipstick has recently been used to provide an early and accurate diagnosis.

**Treatment**

Leptospira are sensitive to various antibiotics, but crystalline penicillin is the drug of choice. In case of allergy, other drugs like doxycycline or quinolones may be tried. In case of renal failure, correcting volume depletion is the foremost aspect. Platelet and blood transfusion are needed in case of disseminated intravascular coagulopathy (DIC) and thrombocytopenia. Prognosis is bad in multiorgan failure.

**SNAKEBITE RENAL FAILURE**

Acute renal failure complicates 5–30% of snakebites and it is a preventable cause of renal failure in India. Viper bite accounts for the majority of snakebite-induced renal failure, but it also occurs with krait and sea snakes.3 Snake venom contains a variety of enzymes, polypeptides, glycoprotein and low-molecular-weight substances. Snake venom is a mixture of complex toxins like neurotoxins, myotoxins, hemotoxins, nephrotoxins and neurotoxins. Viper venom has mainly hemolytic and vascular toxic effects. Phospholipase A2 is the principal constituent in viper venom and it has damaging effect on mitochondria, vascular endothelium and membranes of red blood cells, leukocytes and platelets. Viper venom also contains arginine ester hydrolases which increase capillary permeability and cause shift of fluid from the vascular to the interstitial space. Kininogenase is another constituent, which mediates hypotension by the release of bradykinins. Hyaluronidase causes tissue damage and hemorrhaging causes spontaneous bleeding. Acute renal failure in snakebite is due to multiple factors like hypotension, hemolysis and direct toxic effects of snake venom.

**Clinical Features**

Local swelling with pain and bleeding from the site of bite along with systemic bleeding are common. Varying degrees of anemia due to DIC, prolonged clotting time, high colored urine with elevated renal parameters are prominent features. In the author’s study, he found that the compartment pressure was very high at the site of bite with cellulitis, which required surgical intervention. He compared the patients with high compartment pressure who had undergone surgical procedure, with patients who were not willing for surgical intervention. The recovery was good with less number of dialysis in those who had undergone surgical decompression and the mortality was very high in those who were not willing.9

**Treatment**

**Anti-Snake Venom**

In high-dose regime, 2 vials of anti-snake venom (ASV) diluted in 100 mL of dextrose/saline are administered over 2 hours followed by 10 vials in 500 mL of dextrose/saline over 4 hours. In the low-dose regime, 2 vials are given as initial dose followed by 4 vials administered over 4 hours. The mortality rate and percentage of cases requiring dialysis is more in the group who received the high-dose regime.10 Low-dose strategy has proved to be successful. Anti-snake venom is equine protein which is likely to cause subclinical toxic effects in the patient with multiorgan involvement. In case of anuria with elevated renal parameters, hemodialysis or peritoneal dialysis should be done, supported with blood transfusion if necessary. Early management of snakebite cases with ASV and adequate hydration can prevent renal failure. If renal failure sets in, dialysis is the choice. The prognosis is worse in patients with septicemia and DIC.

**WASP BITE ACUTE RENAL FAILURE**

Every year, more than 100 cases are admitted with wasp sting in the author’s hospital. Wasp belongs to the vespidae family. The site of bite is seen as an excavated area of about 0.5 cm in depth and 1 cm in diameter. Acute renal failure is secondary to hemolysis, rhabdomyolysis or both, but hypotension may also play a contributory role. The components of vespide venom can be categorized into three groups: (1) low-molecular-weight substances like acetylcholine, histamine serotonin, dopamin, adrenaline, nor adrenaline and kinins; (2) high-molecular-weight substances like cholinesterase, histidine, decarboxylase, phospholipases and disaccharidases; and (3) miscellaneous substances. Hemolysis results from direct action of a basic protein fraction and melitin in the venom. Sandbank et al.11 have postulated a direct nephrotoxic role of these venoms, based on the evidence obtained from their experimental studies. The author has observed in his study that patients with more than 10 sting marks have more chances of developing renal failure rather than one or two stings.12 Every patient must be admitted and urine for myoglobin and creatine phosphokinase (CPK) should be tested. In those with high colored urine and high CPK value, IV sodium bicarbonate...
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to alkalize the urine is required along with maintenance of fluid balance. Patients with persistent elevation of renal parameters and reduced urine output must be taken for dialysis. Early intervention has been found to save most patients. Late referral, multiple stings, hypotension and severe renal failure are indicators of high mortality.13

OBSTETRIC RENAL FAILURE

The incidence of obstetric renal failure has reduced drastically, but still continues to be a challenging problem in practice. Chugh et al.14 found a decrease from 22% in 1965–1974, to 9% in 1981–1986. In the author’s center, the incidence was 12.7%. The causes can be classified as prerenal, renal and postrenal.

Prerenal causes are hyperemesis gravidarum, persistent vomiting and uterine hemorrhage.

Postrenal causes are very rare. Brander et al.15 in his review, reported 14 cases with four cases associated with twin pregnancy and four with polyhydramnios. Rarely, tubular obstruction by uric acid can cause ARF.

Renal causes are pregnancy-induced hypertension, hemolysis, elevated liver enzymes levels and low platelets count (HELLP) syndrome, acute fatty liver, postpartum renal failure and hemolytic uremic syndrome.

Pre-eclampsia is characterized by heavy proteinuria, hypertension and edema occurring after 20 weeks of gestation. Pre-eclampsia as the cause of obstetric renal failure is reported in 11–21% of cases. In the author’s center, renal failure in pre-eclampsia/HELLP was 45% as against 28.5% in Gopal et al. series.

Septicemia due to septic abortion was the common cause of maternal death prior to legalized abortion.

Acute renal failure in septic abortion is due to infection and presents as hypercatabolic ARF. Most of the patients present in a state of shock with hypotension and jaundice. The pathogenetic mechanisms include hypotension, severe hemolysis, DIC and nephrotoxins used as abortifacients.

The prognosis and renal recovery is poor due to renal cortical necrosis. In the author’s center, 18% of obstetric renal failure patients had septic abortion.16

Management of Acute Renal Failure in Pregnancy

Regular antenatal check-up in high-risk patients, early detection of pre-eclampsia and regular monitoring of fetal status are essential. Early termination of pregnancy in high-risk patients with uncontrolled hypertension, fetal growth retardation, eclampsia, HELLP syndrome and acute fatty liver is necessary to prevent maternal death. With proper antenatal check-up, it is possible to treat both the etiological factor and renal failure without terminating pregnancy.

CHEMICAL TOXINS AND DRUGS

The incidence of drug-induced renal failure is increasing due to easy availability of over the counter medications namely nonsteroidal anti-inflammatory drugs and antibiotics. Drug-induced ARF accounted for 20% of all ARF in an Indian Study1 of which aminoglycosides accounted for 40% of the total cases.17

Copper sulfate related ARF is common in India due to easy availability. The incidence varies from center to center, 88% in Kilpauk Medical College (KMC), Chennai, 80% in Christian Medical College (CMC), Vellore and 8.8% in the author’s center. The symptoms appear within 15–30 minutes of ingestion, which include burning pain in the stomach, vomiting, nausea, diarrhea, malena, hematuria, severe jaundice and renal failure. Renal failure develops in 20–25% of cases.

MANAGEMENT

- Gastric lavage and maintenance of fluid balance
- Intravenous fluids and forced alkaline diuresis (FAD). FAD consisted of giving the following solutions (500 mL/hour) in rotation 500 mL of 0.9% sodium chloride, 400 mL of 5% dextrose with 100 mL of sodium bicarbonate (7.5%) and 500 mL of 5% dextrose with 10 mL of potassium chloride. Urine output was maintained at more than 6 mL/minute. If the urine output dropped below 2 mL/minute, frusemide 20–40 mg to be given intravenously. If there is no response, FAD has to be discontinued and patient must be taken up for dialysis.

CONCLUSION

Acute renal failure is a heterogeneous entity. Over the years, there is a declining trend in the incidence of diarrheal disease and hemolytic uremic syndrome. But the incidence of human immunodeficiency virus (HIV) associated ARF and hospital acquired renal failure is increasing. The incidence of hospital acquired renal failure varies from 4.9–7.2% and it is due to increasing use of nephrotoxic drugs, invasive procedures, intravenous catheters, major surgical procedure and sepsis. Mortality varies from 19–59%.18

The causes in India differ from that reported in western countries and the pattern is also changing over time. Without accurate data, it is not possible to assess the impact of various geographical and other factors in a diverse population like India’s. It is necessary to have a uniform registry to record the incidence and etiology of ARF in India.

REFERENCES

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