DGAFMS MEDICAL MEMORANDUM

ACUTE RENAL FAILURE

DEFINITION

1. Acute Renal Failure (ARF) is defined as an abrupt and usually reversible impairment of the excretory functions of the kidneys leading to accumulation of nitrogenous waste products as well as water, electrolytes and non-volatile acids.

AETIOLOGY

2. The diverse causes of ARF may be divided into :-

I. Prerenal causes

(a) Decreased effective blood volume :

(i) Blood loss – Acute haemorrhage of any cause
(ii) Fluid loss _ Burns, vomiting, diarrhoea, diuretic abuse, excessive sweating, polyuria of salt-losing renal disease, adrenaline insufficiency.
(iii) Combined fluid and blood loss - massive trauma
(iv) Extracellular fluid sequestration – pancreatitis, burns, crush syndrome, nephrotic syndrome, severe malnutrition, advanced liver disease.

(b) Circulatory insufficiency :-

(i) Myocardial pump failure – Massive infarction, cardiac arrhythmias, cardiac tamponade, severe cardiomyopathy, ruptured valves.
(ii) Vascular pooling – Septic shock, anaphylactic shock, septic abortion, severe hypotension of any cause, antihypertensive therapy.

(iii) Mechanical occlusion of renal arteries.

(iv) Severe renal vasoconstriction – Sepsis, Drugs eg. NSAIDs, alpha-adrenergic agonists, Hepatorenal Syndrome.

II. Acute Intrinsic Renal Causes

(a) Prerenal causes persisting beyond 6-8 hours.

(b) Nephrotoxins:

(i) Pigments – Haem as in IV Haemolysis, Mismatched blood transfusion, Blackwater fever, drug-induced haemolysis, Disseminated intravascular coagulation (DIC), snake envenomation; Myoglobin liberated from damaged muscles as in crush syndrome, status epilepticus, heat stroke, unaccustomed severe physical exertion, eclampsia, snake envenomation.

(ii) Drugs and exogenous toxins - Aminoglycosides, Glycopeptides (eg. Teicoplanin, Vancomycin), antirmalignancy drugs (eg. Cisplatin), Amphoterecin B, Heavy metals, Carbon tetrachloride, Methyl Alcohol, radioopaque contrast media, NSAIDs.

(c) Renal Vascular Disorders – Vasculitides, Malignant Hypertension, Scleroderma, Thrombotic Thrombocytopenic Purpura (TTP), Haemolytic–Uraemic Syndrome (HUS), Disseminated Intravascular Coagulation, Renal Artery Thrombosis, Renal Vein Thrombosis.

(d) Glomerulonephritis - Postinfectious GN, Membranoproliferative Glomerulonephritis (MPGN), Rapidly progressive Glomerulonephritis (RPGN).

(e) Interstitial Nephritis
(i) Drug-induced (eg. Penicillins, Sulphonamides, Rifampicin, Phenytomin, Allopurinol, cimetidine, Ciprofloxacin, Furosemide, Thazides, etc)

(ii) Infections.

(iii) Hypercalcaemia.

(iv) Infiltrative Disorders (eg. Sarcoidosis, Lymphoma, Leukemia)

(v) Connective Tissue Diseases.

III Postrenal causes (Obstructive Uropathy)

(a) Intrarenal / Intratubular :

(i) Crystal deposition – Uric Acid, oxalic Acid, Methotrexate, Acyclovir, Sulfonamides.

(ii) Protein deposition – Light chains, myoglobin, haemoglobin.

(b) Extrarenal

(i) Ureteral / Pelvic -

(a) Intrinsic - due to tumors, clots, pus, fungal balls, necrosed papilla, stones.

(b) Extrinsic – Retroperitoneal / Pelvic malignancy, Retroperitoneal fibrosis, accidental ligation.

(ii) Bladder – Stones, Tumors, Neurogenic bladder, Prostatic Hypertrophy/Malignancy.
(iii) Urethra - Strictures, meatal stenosis, phimosis.

3. Common clinical settings in which ARF is often seen and hence should be looked for, include:

   (a) Elderly
   (b) Surgery, Postoperative state, following massive trauma
   (c) Pregnancy
   (d) Malignant Diseases
   (e) Rhabdomyolysis of any cause
   (f) Sepsis/Multiorgan failure esp in ICU setting
   (g) NSAID and Nephrotoxic drug administration.
   (h) Complicated Diabetes Mellitus.

4. Clinical course of ARF is highly variable depending upon the underlying cause of renal failure and the promptness with which effective remedial measures are instituted. In hospital setting, a majority of ARF may be nonoliguric due to early detection during routine biochemical monitoring. On the other hand, a large proportion of community acquired ARF may be oliguric/oligoanuric.

5. Presence or absence of oliguria is a reflection of the residual GFR. A nonoliguric ARF is usually associated with lower morbidity and mortality and a better long-term outcome.

6. Oliguria with avid salt and water retention are the hallmarks of reversible prerenal azotaemia. In a variety of acute intrinsic renal failures and Postrenal azotaemias, ARF may be nonoliguric. Further, intravenous fluid and diuretic administration may alter the course of ARF in the hospital.

**DIAGNOSTIC APPROACH.**

7. As mentioned in the definition, ARF is a potentially reversible impairment of renal function. Some of the causes are amenable to specific therapeutic intervention provided they
are applied early in the course of the disease. Therefore, early detection and timely evaluation are keys to successful management.

8. A thorough history must be obtained and carefully analysed. Especially important is the history of any recent loss or sequestration of extracellular fluid volume, of sepsis and of recent exposure to nephrotoxic drugs or NSAIDs. Detailed history of any unusual urinary symptoms viz. hematuria, oliguria, dysuria, pyuria, gravelluria or flank pain may offer clues to an intrinsic renal disease.

9. Meticulous examination and recording of vital parameters, haemodynamic data, intake and output and daily weight is of paramount importance. The clinical chart should also record serial urinalysis and renal function parameters as well as the drugs administered. Analysis of clinical charts may be of great diagnostic assistance.

10. Physical examination is of value in confirming/excluding prereal and postrenal causes of ARF and the presence of a systemic disorder that could result in ARF. The state of hydration, postural hypotension, pedal oedema/anasarca and signs of congestive cardiac failure can all be determined on a thorough physical examination.

11. Urinalysis is the next critical step. Immediately after history taking and physical examination, a urine sample should be obtained and analysed. If patient is unable to void, a straight bladder catheter (viz a feeding tube) may be introduced under strict asepsis and the urine thus obtained be subjected to routine and microscopic examination.

12. ‘Dipsticks’ are available for detection of occult blood by orthotoluidine test and for presence of proteins, and can be used at the bedside. The sediment obtained after spinning the urine in a centrifuge should next be subjected to microscopic examination. Very few formed elements or only hyaline casts suggest prerenal or postrenal azotaemia. In Acute Tubular Necrosis (ATN), brownish pigmented cellular casts and many tabular epithelial cells are commonly present. Microscopic haematuria usually results from acute glomerulonephritis or structural disorders such as stones, tumors, infections or trauma. Dysmorphic RBCs as seen by phase contrast microscopy suggest glomerular hematuria.
13. RBC casts are pathognomonic of a rapidly progressive glomerulonephritis. Presence of a large number of polymorphonuclear leucocytes suggests pyelonephritis or acute papillary necrosis. Eosinophiluria and eosinophilic casts on Hansel’s stain support a diagnosis of acute allergic interstitial nephritis.

14. Combination of muddy brown pigmented casts and positive occult blood test in the absence of RBCs suggest haemoglobinuria or myoglobinuria. Presence of large number of hexagonal uric acid crystals suggests a diagnosis of acute uric acid nephropathy. Crystals of oxalic acid appear ‘back-of-envelope’ shaped. Broad casts in the urine are pathognomonic of chronic renal failure.

15. Urine flow rates are another important consideration. Oliguria is defined as passage of < 400ml urine per day. Anuria is defined as passage of < 100ml urine per day. Absolute anuria is defined as absence of any urine at straight bladder catheterization. Sustained anuria is usually seen in total urinary tract obstruction. Other causes include severe RPGN, mechanical obstruction to renal blood flow and acute diffuse cortical necrosis. Oliguria is usually a feature of prerenal ARF. A variety of acute intrinsic renal diseases cause ARF which is nonoliguric at presentation. These include ATN due to minoglycoside and radio-contrast nephrotoxicity, cranial trauma, polytrauma, postoperative ARF and myoglobin-induced ARF.

16. A sample of urine should be saved for determination of various urinary indices. These have been listed in Table 1. A careful analysis of these indices helps in differentiating a prerenal ARF from one due to ATN, though no single index is absolutely diagnostic.

Table 1

<table>
<thead>
<tr>
<th>Ser No</th>
<th>Index</th>
<th>Prerenal</th>
<th>ATN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Uosm (mOsm/kg)</td>
<td>&gt; 500</td>
<td>&lt; 350</td>
</tr>
<tr>
<td>2.</td>
<td>UNa (mEq/L)</td>
<td>&lt; 20</td>
<td>&gt; 40</td>
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</table>
3. U/P Creatinine ratio  > 40  < 20

4. FE Na  < 1  > 2
   (U/P Na / U/P creatinine x 100)

5. Renal failure Index  < 1  > 2
   (UNa / U/P Creatinine)

6. Blood Urea : Creatinine Ratio  > 30:1  < 20:1

7. FE Uric Acid  < 7  > 15
   (U/P Uric Acid / U/P creatinine x 100)

17. Another important consideration is exclusion of an obstructive uropathy. This is a significant cause of ARF in the community and has excellent potential for full recovery following urologic intervention provided a diagnosis is reached early in its course. A solitary kidney, absolute anuria or widely fluctuating urinary volumes, recent surgery on genitourinary tract or retroperitoneal space, prostatic/pelvic/abdominal malignancy and a normal urinalysis are clues to suggest that a search for potential obstruction should be made.
18. Ultrasonography of the abdomen is now widely available, is non-invasive, quick and a very useful tool to look for extrarenal obstruction. Hydronephrosis with hydroureter, bladder tumours, calculi and structural abnormalities can be picked up with a high degree of sensitivity on USG. However, a normal or minimally dilated pelvicalyceal system and ureter do not exclude an obstructive uropathy. A plain x-ray abdomen is of value if urolithiasis is suspected. IVU should generally be avoided in ARF as information obtained is insufficient and risk of aggravation due to nephrotoxicity of radiocontrast is real. In tertiary care centres, retrograde pyelography(RGP), computed tomography (CT) and radioisotope renography may be employed if there is reasonable suspicion of obstructive uropathy.

19. Renal biopsy may be considered in ARF if the following are present :-

(a) No obvious cause of ARF evident.
(b) Either historic or clinical evidence of extrarenal/multisystem disease.
(c) Heavy proteinuria and persistent haematuria with dysmorphic RBCs or RBC casts in urine.
(d) Marked hypertension in the absence of significant volume expansion.
(e) Prolonged oligoanuria lasting longer than 2-3 weeks and
(f) Anuria in the absence of obstruction.

FORCED DIURESIS AS A DIAGNOSTIC AID

20. This is often employed to differentiate ATN from perennial ARF but it should only be resorted to (a) after a careful history, physical examination, unnalysis and study of renal indices.
(b) where dialysis facilities are available in the event of a failed trial of forced diuresis.
(c) after adequate hydration has been achieved as indicated by clinical parameters and CVP monitoring.

21. Use of 20% mannitol has not been shown to be of any advantage in several trials. On the other hand, conversion of an oliguric ARF into a nonoliguric ARF does confer some survival benefit. Additionally, it makes subsequent management of the patient a little less difficult, by allowing a greater amount of fluid infusion which is often required for drug delivery, maintenance of haemodynamic stability and delivery of adequate nutrition.

22. A practical way of inducing forced diuresis is to infuse 120 mg of Furosemide IV at the rate of 10-20 mg/minute and carefully recording urine output over next two hours. If the urine flow rate remains less than 30 ml/hour, a second dose of 240 mg may be infused. If, at the end of fourth hour, the urine output remains less than 30 ml/hour, a third dose of 480 mg may be given. If this also fails to induce diuresis, the trial should be abandoned.

PREVENTION OF ACUTE RENAL FAILURE

23. In view of high morbidity and mortality of ARF as well as the high cost of treatment of a severe ARF, it is imperative that maximum effort is directed towards its prevention. The preventive strategies applicable to predominantly medical settings of ARF are:

(a) Identification of high risk patients for pharmacologic agent induced anephrotoxicity.

(b) Minimisation of use of potential nephrotoxins

(c) Aggressive surveillance for nephrotoxin-induced renal dysfunction

(d) Use of volume expansion, diuretics and renal vasodilators in selected clinical settings. The preventive strategies applicable to predominantly surgical/trauma/ICU settings include:-

(i) Aggressive resuscitation

(ii) Preoperative optimisation of cardiovascular haemodynamics

(iii) Elevation of systemic oxygen delivery in selected critically ill patients

(iv) Optimisation/minimisation of use of potential nephrotoxins
(v) Minimisation of use, and length of use of invasive lines and catheters to avoid nosocomial sepsis.

**MANAGEMENT OF ARF**

24. Briefly the conservative management of ARF entails the following steps:-
   
   (a) Exclude reversible/treatable causes of ARF.
   (b) Achieve and maintain euvoletic state
   (c) Attempt to establish a urine output if patient is oliguric
   (d) Provide adequate nutrition
   (e) Minimise use of invasive lines and procedures
   (f) Monitor vitals, weight, intake and output
   (g) Monitor drug usage carefully and modify drug doses and dosing intervals appropriately
   (h) Monitor and treat for clinical and biochemical complications
   (j) Institute renal replacement therapy

25. Maintenance of adequate nutrition is vital to recovery though a very difficult task in view of the restrictions necessary in the face of acute renal failure. Unless the patient is hypercatabolic as in pancreatitis, burns, polytrauma, sepsis or following recent major surgery, restriction of proteins to less than 20 gm/day is well tolerated for a few days and helps to reduce the load on kidneys. Sodium intake needs to be judiciously restricted and potassium intake needs to be strictly curbed unless serial biochemistry reveals hypokalaemia. Caloric requirement is 20 Kcal/kg/day but may be as high as 35 Kcal/kg/day in hypercatabolic states. A majority of calories need to be supplied in the form of carbohydrates and fats. Patients on dialysis may be permitted upto 1 gm/kg/day of proteins of high biological value.

26. As has been emphasised many times in the preceding discussion monitoring has to be meticulous. Sample monitoring charts are given in appendix A and B to this memorandum. These can be suitably modified for a given clinical setting but should form the mainstay of management and evaluation of response to treatment.
27. The most important complications of ARF include hyperkalaemia, metabolic acidosis, fluid overload and infections. Other complications encountered in some patients are bleeding tendency, dysnatraemia, encephalopathy and hyperuricaemia.

28. Hyperkalaemia is a medical emergency and needs to be looked for at all times during the course of ARF. Frequent serum potassium and ECG monitoring are essential. Hyperkalaemia is very common in certain settings viz rhabdomydysis, tumor chemotherapy, extensive haemolysis and polytrauma needing multiple blood transfusions. Rate of rise of serum potassium is probably more significant than an absolute level of serum potassium. However, absolute value of potassium more than 6 mEq/L should be treated. ECG changes seen are symmetric increase in amplitude with peaking of T waves in praecordial leads V2-V4, flattening of P waves, widening of QRS complex, prolongation of PR interval, and finally, a sine wave pattern with eventual cardiac arrest in ventricular asystole.

29. Emergency measures to treat hyperkalaemia include:-
   (a) IV calcium gluconate (1-3 doses of 10 ml of 10% solution)
   (b) Salbutamol Nebulisation (10-20 mg over 10 minutes; may be repeated every 4-6 hours).
   (c) Insulin Glucose (10 U crystalline Insulin S/C with 50 ml of 50% Dextrose IV bolus plus 500 ml of 10% Dextrose over next 4-6 hours)
   (d) Sodium Bicarbonate (50-100 ml IV only if pH in ABG is <7.20 or there is clinical evidence of severe metabolic acidosis
   (e) Potassium Exchange Resins (25-50 gm in 50% Dextrose or 70% Sorbital either orally or as retention enema)
   (f) Haemodialysis

30. Volume overload should be prevented rather than treated through meticulous monitoring of intake/output, JVP and CVP and daily weight record. Pulse oximetry and sometimes, X-Ray chest may help detect an impending pulmonary oedema. The complication is most often seen in oligoanuric ARF. If forced diuresis trial has failed the only management of this complication is by providing haemodialysis or continues ultrafiltration.

31. Severe metabolic acidosis is an important metabolic complication of severe ARF and may be life threatening. It is particularly fatal if respiratory compensation is compromised due to thoracic trauma, respiratory infections, pulmonary oedema or a comorbid chronic respiratory disease. Careful monitoring of pulse oximetry, arterial blood gases and pH, and
judicious correction by infusing sodium bicarbonate may be attempted but severe acidosis often requires haemodialysis.

32. Infection control is of paramount importance to achieve recovery and survival in patients of ARF. Preventive strategies have already been discussed. A high index of suspicion and frequent culturing of blood and body fluids followed by specific antimicrobial therapy in appropriately modified doses should be the standard of care.

33. Conjugated estrogens and cryoprecipitate may be judiciously administered in those patients of ARF who manifest bleeding tendencies. Haematocrit should be maintained at around 30-35% through transfusion of packed RBCs.

**MONITORING DRUG THERAPY IN ARF**

34. Drugs that are directly nephrotoxic have been mentioned in preceding discussion. Apart from these, a host of drugs and their metabolites are dependent on the kidneys for their elimination. It is logical that the dosages of these drugs, and in certain cases, dosing intervals need to be appropriately modified in a setting of ARF. All textbooks of medicine carry comprehensive guidelines in this regard. Therapeutic Indexes and product literatures also provide useful information regarding dosages and dosing intervals in ARF. For application of these guidelines, it is important to determine the creatinine clearance of the patient. A simple and practical formula for calculation of creatinine clearance has been provided by Cockcraft and Gault, and is enumerated below:

\[
\text{Creatinine clearance (CCr)} = \frac{(140-\text{Age}) \times \text{Wt (Kgs)}}{72 \times \text{S-Cr (mg/dl)}}
\]

It is important to note that in females, due to a smaller muscle mass, the value obtained needs to be reduced to 85% i.e. calculated CCr x 85/100.

**RENNAL REPLACEMENT THERAPY**

35. While there is little doubt that severe hyperkalemia, severe metabolic acidosis, fluid overload not responsive to fluid restriction and diuretic therapy, encephalopathy and symptoms of uremia are indications for renal replacement therapy, in the last two decades a
general consensus has emerged that dialysis should probably be initiated ‘prophylactically’ before its need is precipitated by a complication of ARF.

36. For a primary care physician it is sufficient to know that apart from the indications mentioned in the preceding paragraphs, dialysis should be offered early to severely oliguric/anuric patients, e patients with a rapid rate of rise of urea/creatinine irrespective of the absolute values and patients in ICU setting with polytrauma or multiorgan failure due to sepsis.

37. While haemodialysis is available in Nephrology centres located at New Delhi, Mumbai, Kolkata, Lucknow, Chandimandir, Pune and Bangalore, all medical specialists have been trained to perform emergency bedside peritoneal dialysis to combat a metabolic complication of ARF. Besides, Govt medical college hospitals and civil institutions located in most large cities may be able to provide emergency dialysis till the patient is stabilised for evacuation to a service nephrology centre.

**ARF IN ARMED FORCES**

38. ARF is common in war casualties due to extensive muscle trauma, hemorrhage, enhanced risk of infection and prolonged shock. Even peacetime soldiering exposes armed forces personnel to polytrauma and conditions such as heat stroke, infections and prolonged shock in hostile and remote terrains. Prompt and aggressive treatment of shock, broad spectrum antibiotics, high dose diuretic and cautious mannitol infusions in cases of extensive muscle damage, and early evacuation to a secondary or tertiary care centre preferably by air should be the standard of care in these patients.

**CONCLUSIONS**

ARF is a common clinical problem associated with high morbidity, mortality and cost of care. However it is a potentially reversible condition provided it is recognised early, diagnosed properly and managed promptly and effectively. The primary care physician has as important a role to play as the tertiary care subspecialist. This memorandum elucidates
general guidelines for the diagnosis and management of Acute Renal Failure. Attention to preventive strategies and intensive monitoring with timely intervention to maintain the “milieu interior” as close to normal as possible will go a long way in improving the outcome of patients of ARF.

CLINICAL CHART

DATE

Name: ___________ Age/Sex: ___________ Identification No: ___________ Diagnosis: ___________

Total Fluids to be given =
IV =
Oral =

Intake (Previous 24 Hrs):
Output (Previous 24 Hrs):
Net Balance:
Wt:

Appendix B

INVESTIGATION CHART
<table>
<thead>
<tr>
<th>Name :</th>
<th>Age/Sex :</th>
<th>Diagnosis :</th>
<th>Identification No</th>
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<table>
<thead>
<tr>
<th>Date/Time</th>
<th>B-Urea/BUN (mg/dl)</th>
<th>S-Creatinine (mg/dl)</th>
<th>S-Na (mEq/L)</th>
<th>S-K (mEq/L)</th>
<th>pH</th>
<th>PaO₂</th>
<th>PaCO₂</th>
<th>BE</th>
<th>βHCO₃</th>
<th>S-O₂</th>
<th>Proteins</th>
<th>RBC/Hpf</th>
<th>WBC/Hpf</th>
<th>EC/Hpf</th>
<th>Casts</th>
<th>Spot Na⁺</th>
<th>Calcium (mg/dL)</th>
<th>Phosphorous (mg/dL)</th>
</tr>
</thead>
</table>

**Special Investigations with date**

1. ECG
2. CXR PA View
3. USS Abdomen
4. 24 hrs U-proteins
5. Others