ORIGINAL RESEARCH

Study of clinical and laboratory profile of acute kidney injury at a tertiary care hospital

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ABSTRACT

Introduction: Acute kidney injury (AKI) is a common clinical problem in intensive care unit (ICU) patients and independently predicts poor outcome.[1] Recently, two large multi-centre cohort studies reported the occurrence of AKI in an estimated 36% of all patients admitted to the ICU[2]. Moreover, additional observational data indicate that the incidence of AKI is rising.[3,4]

Aims and Objectives: Analysis of the clinical spectrum and laboratory findings of AKI patients in ICU, identify the cause, risk and prognostic factors for AKI and analyzing the final outcome of the patients with AKI.

Material and Methods: Fifty patients with abnormal kidney size, abnormal cortico medullary differentiation and an absolute increase of Creatinine more than 1 to5 fold from the base line were included in the study. A thorough diagnostic evaluation by a detailed history, physical examination, urine analysis, complete blood picture (CBC), renal function test (RFT) and renal ultrasonography (USG) was recorded.

Results: Among the fifty patients with suspected AKI, ratio of oliguria and non oliguria patients was 4:1. Out of 10 non oliguria cases, one is snake bite, four poisoning, 2 acute diarrheal disease and 3 sepsis cases. The age group included 13-85 yrs with mean age group of 38.26 yrs. Conservative treatment given to 24 while 26 were kept on dialysis. Recovery was 90% in risk, 91.7% in injury cases while 61.1% among failure cases. Mortality was 20% among the study group.

Conclusion:AKI is usually asymptomatic and diagnosed when biochemical monitoring of hospitalized patients reveal a new increase in blood urea and serum Creatinine concentration. As the clinical and biochemical parameters indicate AKI, prompt treatment with Renal Replacement Therapy (RRT) helps in decreasing the morbidity & mortality.

Key words: Acute kidney injury Network, Acute Tubular Necrosis, Creatinine, Glomerular Filtration Rate, Oliguria, Renal function test, Renal Replacement Therapy

INTRODUCTION

Acute kidney injury is sudden decrease in Glomerular Filtration Rate (GFR) occurring over a period of hours to days resulting in failure of excretion of nitrogenous waste products and maintenance of fluid and electrolyte homeostasis by kidneys. A revision of the criteria was proposed by the Acute Kidney Injury Network (AKIN) - a group representing members of Acute Dialysis Quality Initiative, nephrology and critical care societies. Practically the definition of AKI is done as per the RIFLE criteria given below: (Fig.1).

The proposed diagnostic criteria for AKI is an abrupt (within 48 hours) reduction in kidney function defined as an absolute increase in serum Creatinine [level of > 26.4 mmol/L (0.3 mg/dl)] or a percentage increase in serum Creatinine level of > 50% (1.5 fold from baseline) or a reduction in urine output. These criteria should be applied in the context of the clinical presentation and following adequate fluid

resuscitation when applicable and classified the AKI into RIFLE criteria[5].

Overall incidence of AKI was 200 cases / million. Acute Tubular Necrosis (ATN) - 45%; Prerenal - 21%; Acute on CKD - 12.7%; obstructive -10%. Mortality was higher in AKI patients (45%) to other admitted patients (5.4%). Ostermann.M.Chang RW: CCM 2007 showed AKI as an independent risk factor for death[6]. They detected the following:

RIFLE class F has a mortality of 57%; RIFLE class I have a mortality of 45%; RIFLE class R have a mortality of 2%; compared to 8.4% of patients without AKI. The etiology of AKI varies from place to place. While in our country, Sepsis is the commonest cause. The incidence of insect bite induced AKI is higher in North India.[7] While leptospiral AKI is commonly encountered in Kerala and Chennai; Malarial AKI is common in eastern India[8]. AKI complicates approximately 5-7% of hospital admissions and up to 30% of admission to ICU[9]. Retention of nitrogenous waste products, oliguria (urine output- 400ml/day) contributing to extra cellular fluid overload and electrolyte and acid base abnormality are frequent clinical features. AKI is usually asymptomatic and diagnosed when biochemical monitoring of hospitalized patients reveal a new increase in blood urea and serum creatinine concentration.

For the purpose of diagnosis and management, AKI has been divided into three categories:

1. Disease characterized by renal hypo perfusion in which integrity of renal parenchyma is preserved (Pre renal);
2. Diseases involving renalparenchymaltissue (Intra renal);
3. Diseases involving acute obstruction of urinary tract (post renal).

AKI is often considered to be reversible, although a return to baseline serum Creatinine concentration post injury might not be always possible. To detect clinically significant irreversible damage that may ultimately contribute to chronic kidney disease and AKI has a significant in-hospital morbidity and mortality, the latter in the range of 30-60% depending on the clinical settingand presence or absence of non renal organ dysfunction.[3]

Etiology and Pathophysiology:[10,11]

AKI may be classified into 3 general categories, as follows:

Pre renal — as an adaptive response to severe volume depletion andhypotension, with structurally intactnephrons; Pre renal AKI represents the most common form of kidney injury and often leads to intrinsic AKI if it is not promptly corrected

Intrinsic — in response to cytotoxic, ischemic or inflammatory insults to the kidney, with structural and functional damage; Intra renal vasoconstriction is the dominant mechanism for the reduced Glomerular filtration rate (GFR). Glomerulo nephritis can be a cause of AKI and usually falls into a class referred to as Rapidly Progressive Glomerulo Nephritis (RPGN). Acute glomerulonephritis should be part of the diagnostic consideration in cases of AKI.

Post renal — from obstruction to the passage of urine. Causes of obstruction include stone disease; stricture; and intra luminal, extra luminal, or intramural tumors. Bilateral obstruction is usually a result of prostate enlargement or tumors in men and urologic or gynecologic tumors in women. If the site of obstruction is unilateral, then a rise in the serum creatinine level may not be apparent due to contralateral renal function. Although the serum creatinine level may remain low with unilateral obstruction, a significant loss of GFR occurs and patients with partial obstruction may develop progressive loss of GFR if the obstruction is not relieved. While this classification is useful in establishing a differential diagnosis,many patho physiologic features are shared among the different categories[12].

Patients who develop AKI can be oliguric or non oliguric; have a rapid or slow rise in creatinine levels, and may have qualitative differences in urine solute concentrations and cellular content.Clinical classification of AKI as oliguric or non oliguric based on daily urine excretion has prognostic value. Oliguria is defined as a daily urine volume of less than 400 mL/d and has a worse prognosis, except in pre renal failure. Anuria is defined as a urine output of less than 100 mL/d and, if abrupt in onset, suggests bilateral obstruction or catastrophic injury to both kidneys. Stratification of renal failure along these lines helps in decision-making (eg: timing of dialysis) and can be an important criterion for patient response to therapy.

A detailed and accurate history is crucial to aid in diagnosing the type ofAKI and in determining its subsequent treatment. Urine output history can be useful. Oliguria generally favors AKI. Abruptanuria suggests acute urinary obstruction, acute and severe glomerulo nephritis or embolic renal artery occlusion. A gradually diminishing urine output may indicate a urethral stricture or bladderoutlet obstruction due to prostate enlargement.

Because of a decrease in functioning nephrons even a trivial nephrotoxicinsult may cause AKI to be superimposed on chronic renal insufficiency[13].

Laboratory Studies for Diagnostic Evaluation:[13]

Several laboratory tests are useful for assessing the etiology of AKI, and the findings can aid in proper management. These tests include complete blood cell (CBC) count, serum biochemistry, urine analysis with microscopy andurine electrolytes.

- Blood urea nitrogen (BUN) and serum Creatinine
- Although increased levels of BUN and Creatinine are the hallmarks of renal failure, the rate of riseis dependent on the degree of renal insult as well as protein intake with respect to BUN[14].

- The ratio of BUN to Creatinine is an important finding, because theratio can exceed 20:1 in conditions in which enhanced reabsorption of urea is favored (eg: in volume contraction); this suggests prerenal AKI.
- BUN may be elevated in patients with GI or mucosal bleeding, steroid treatment or protein loading.
- Assuming no renal function, the rise in BUN over 24 hours can be roughly predicted using the following formula: 24-hour protein intake in milligrams X 0.16 divided by total body water in mg/dL added to the BUN value.
- Assuming no renal function, the rise in Creatinine can be predictedusing thefollowing formulas:
- For males: weight in kilograms X [28 – 0.2(age)] divided bytotal body water in mg /dL added to the Creatinine value
- For females: weight in kilograms X [23.8 – 0.17(age)]divided by total body water added to the Creatinine value
- As a general rule, if serum Creatinine increases to more than 1.5 mg / dL / day, rhabdomyolysis must be ruled out.
- CBC count, peripheral smear and serology - decreased Hb% will be observed in AKI Patients in kidney diseases, Malarial Parasites can be observed in peripheral smear.
- The presence of myoglobin or free hemoglobin, increased serum uric acid level and other related findings may help further define the etiology of AKI.
- Serologic tests for antinuclear antibody (ANA), ANCA, anti Glomerular basement membrane (anti GBM) antibody, hepatitis and antistreptolysin O (ASO) and complement levels may help include and exclude glomerular disease.
- Urinalysis:
- Findings of granular, muddy- *a*ar cell casts also supports the diagnosis of ATN. Often, oxalate crystals are observed in cases of ATN.
- Reddish brown or cola-colored urine suggests the presence of myoglobin or hemoglobin.
- The dipstick assay may reveal significant proteinuria, which would suggest glomerular or interstitial disease.
- The presence of Red Blood Cells (RBC) in the urine is always pathologic. Eumorphic RBCs suggest bleeding along the collecting system. Dysmorphic RBCs or RBC casts indicate glomerular inflammation, suggestingglomerulonephritis is present.
- The presence of White Blood Cells (WBC) or WBC casts suggests pyelonephritis or acute interstitial nephritis.
- The presence of uric acid crystals may represent ATN associated with uric acid nephropathy.
- Calcium oxalate crystals are usually present in cases of ethylene glycol poisoning.
- Urine electrolyte findings also can serve as valuable indicators of functioning renal tubules.
- The fractional excretion of sodium (FENa) is the commonly used indicator and can be a valuable test for helping to detect extreme renal avidity for sodium in conditions such as hepato renal syndrome.
- Bladder pressure: Intra-abdominal pressure of <10 mm Hg is considered normal. Patients with a bladder pressures above 25 mm Hg should be suspected of having AKI as a result of abdominal compartment syndrome.
- Emerging biomarkers: A number of biomarkers are being investigated to risk stratify and predict AKI in those at risk for the disease. The reason for this is because creatinine is a late marker for renal dysfunction and once elevated, reflects a severe reduction in GFR. The most promising biomarker to date is urinary neutrophil gelatinase - associated lipocalin (NGAL), which has been shown to predict AKI in children undergoing cardiopulmonary bypass surgery.
- Imaging Studies[15]
- Renal ultrasonography is useful for evaluating existing renal disease and obstruction of the urinary collecting system.
- Ultrasonographic scans or other imaging studies showing small kidneys suggest chronic renal failure.
- Doppler ultrasonography - Doppler scans are useful for detecting the presence and nature of renal blood flow and can be quite useful in the diagnosis of thromboembolic or renovascular disease.

Material and Methods

Fifty patients admitted in Intensive medical Care Unit, GGH, Nellore, with absolute increase in serum creatinine of more than or equal to 0.3mg/dl (>26.4 µmol/L) and decreased urine output of <0.5ml/Kg body weight /hr were included in the study. A percentage increase of serum creatinine of more than equal to 50% (1-5 fold from baseline) was considered for inclusion. Patients with CKD were excluded.

A thorough diagnostic evaluation was done by a detailed history, physical examination, urinary analysis, CBC, RFT, Renal USG. In appropriate place, serology for enteric fever, peripheral smear for MP/MF, other related investigations were done. The patients were started on appropriate therapy, once the diagnosis was made. Wherever possible the etiological factors were treated. RRT was given according to the clinical and biochemical indications.

Results

Among the total 50 cases, Males were 28 (22 oliguric & 6 non-oliguric) and females were 22 (18 oliguric & 4 non-oliguric) with maximum incidence in the age group 21-30 years followed by 41 -50 years. Mean age was 38.26 yrs (Table:1 & Fig:2). There were 8

patients above the age of 60 years. Five of them were at risk, one developed injury and two of them developed failure according to RIFLE criteria.

The presentation was predominantly oliguric. Out of the ten non oliguric patients four (4) patients were of poisoning, two (2) were due to Acute Diarrhoeal Diseases (ADD), three (3) cases of sepsis and one (1) case of snake bite (Table:2).

The most common cause of AKI in critically ill patients was sepsis (19). The second common cause was ADD (15). Next to it was the snake bite (7) with prolonged Whole Blood Clotting Time and 7 cases of poisoning due to insecticide poisoning. Two cases of malaria were Plasmodium falciparum species (Fig: 3).

According to RIFLE criteria, 20 cases classified under class R (risk). All the patients under this class were treated conservatively. While the patients who came under class I (injury) were 12 of whom 8 were treated with dialysis. The F (Failure) class constituted 18 patients who were all treated with dialysis. Between Hemodialysis (HD) and Peritoneal Dialysis (PD), the former is the preferred mode (Fig:4).

Two patients who were at risk expired. Both were cases of sepsis that were onionotropic and ventilatory support managed conservatively for the AKI. The only patient who died of Injury was also a case of sepsis with multiorgan dysfunction (MOD) (Table:3).

Table: 1 Presenting Features in the study group (n=50)

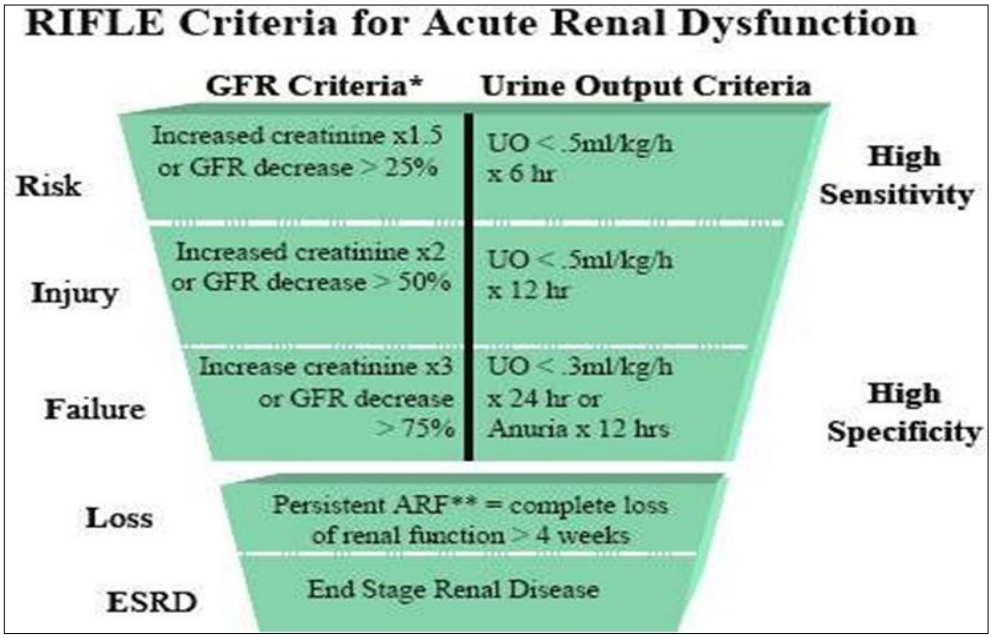
Urine Output	Males	Females	Total
Oliguric	22	18	40
Non oliguric	6	4	10
Total	28	22	50

Table:2 Causes of Non Oliguric AKI (n=10)

Etiology	No of case
Poisoning	4
Sepsis	3
ADD	2
Snake bite	1
Total	10

Table: 3 Outcome of AKI

Outcome	Survived	Percentage	Expired	Percentage	Total
Risk	18	90%	2	10%	20
Injury	11	91.7%	1	8.3%	12
Failure	11	61%	7	39%	18



Source: Results of the second Acute Dialysis Quality Initiative consensus conference (May 2002)[5].

Fig 1: RIFLE criteria for acute renal dysfunction

R is risk group, I for injury group, F for failure group, L for loss, E for ESRD (end stage renal disease).

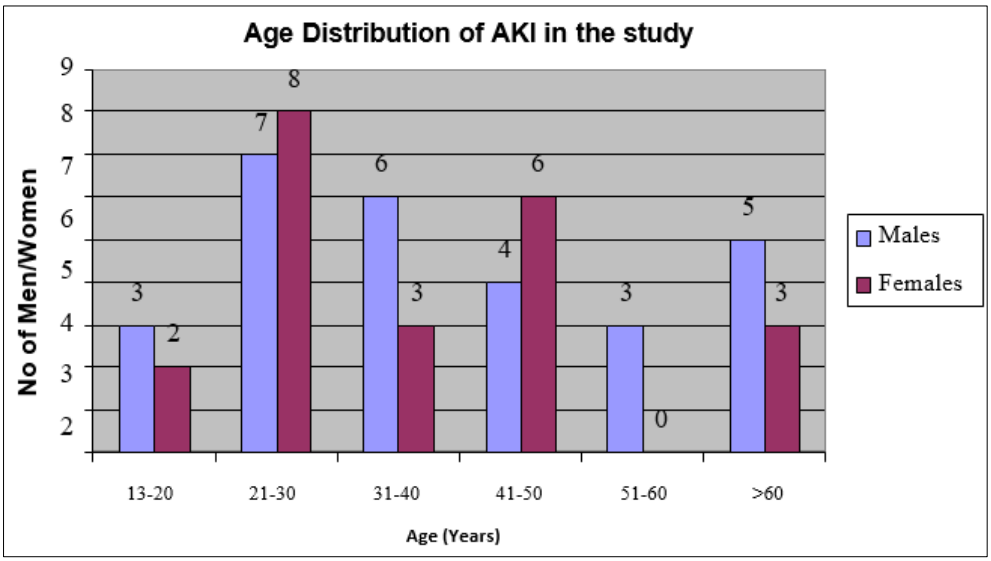


Fig 2: Age Distribution of AKI in the Study (n=50)

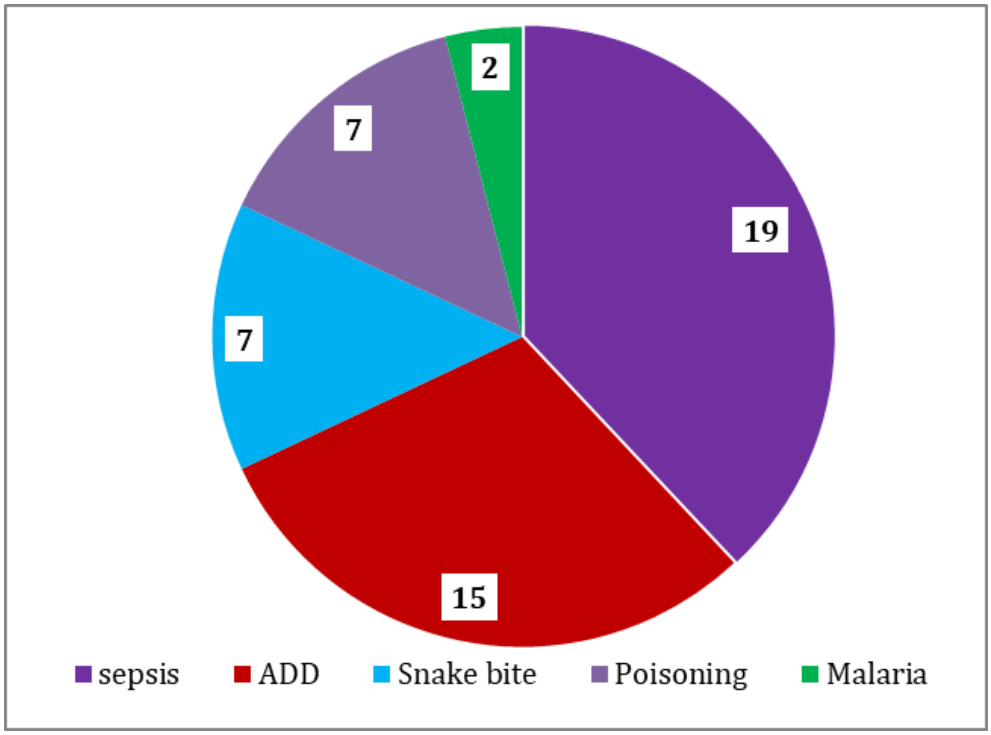


Fig 3: Etiological Profile of AKI

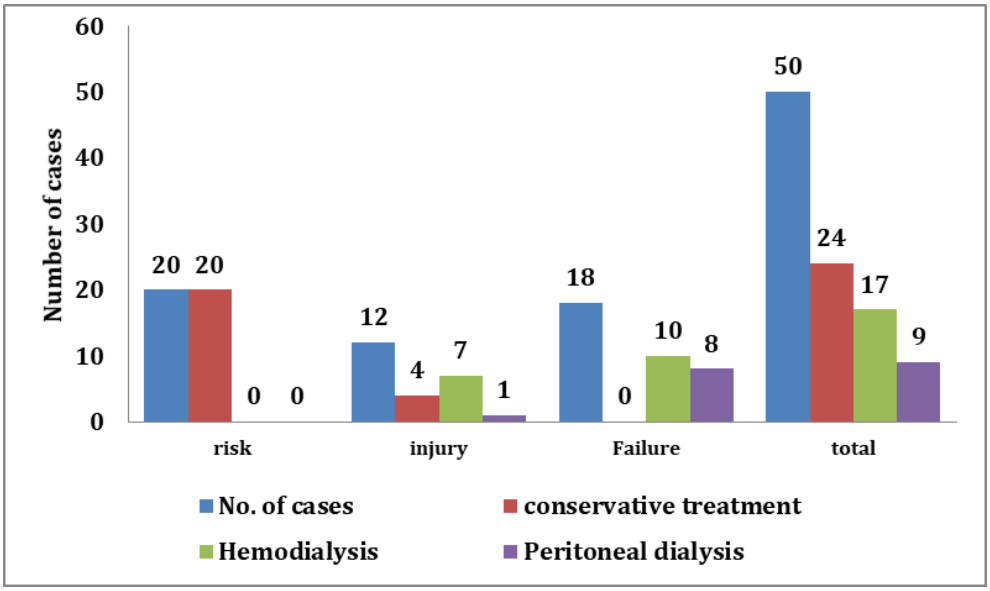


Fig 4: Management of AKI

Co-morbid Conditions Associated

There were 3 cases of isolated diabetes alone. 4 patients had diabetes and systemic hypertension (SHT) in combination. There were each one isolated cases of SHT, coronary artery disease (CAD) and chronic liver disease. MOD was present in 7 cases, of which only one survived. Totally 10 patients had ionotropic or a ventilatory support of which 7 of them expired. 85% morality was observed among patients with MOD and ionotropic support.

Discussion

AKI is a potentially fatal but reversible renal disease. The etiology, course, outcome differ in various parts of the world and also within India due to its climatic and geographic diversity and the variable standards of medical care. In our study 50 patients were analysed including 28 males and 22 females. Mean age of occurrence was 38.26 years. Maximum number of cases occurred in third to fifth decade. In the present study oliguric AKI was predominant (80%). This is in concordance with study by M.A. Muthusethupathi *et al* in 1999[16]. Sepsis is the leading cause in the present study that accounts for 19 cases (38%) of the cases. This is in concordance with most of the multicentric trials[3]. Of them, 42% were treated with dialysis and 58% treated conservatively. Mortality observed in 6 cases and 32% were due to sepsis. Out of the 15 cases of ADD only one died due to arrhythmia which is very less when compared with the report from M.A.Muthusethupathi *et al* (34.7%). S. K. Agarwal *et al* study[17] showed 11% of the AKI was due to ADD in North India. Awareness due to early rehydration therapy and early referral contribute to the decline in mortality. There were 7 cases (14%) of snake bite all of which were russel's viper with hematotoxicity and one death due to snake bite which was complicated by hyperkalemia on presentation. In the study by Harshavardhan L *et al*[18] that acute kidney injury occurs in 14.6% of the victims of snake bite[19,20]. There were 4 cases of Malarial AKI. There was no death from malarial AKI as against the 42.5% mortality in the study by Zinna *et al*[21]. A study by Prakash *et al* from eastern India reported 4.2% of Malarial AKI[22]. Mortality is decreased mainly due to early diagnosis of malaria and early use of Hemo dialysis (HD). Ostermann M Chang RW 2007 study [6] showedthe following RIFLE class F has a mortality of 57%, RIFLE class I has 45%, RIFLE class R has 21% whereas in the present study mortality was 38.9%in RIFLE class F, 8.3% inRIFLE class I and 10% amongRIFLE class R.

Conclusion

The presentation of AKI is predominantly oliguric. But non-oliguric AKI should be borne in mind as lab findings help us in diagnosis, monitoring the prognosis.Sepsis is the most common cause of AKI in critically ill patients with highest mortality rate. It is highly essential to prevent the emergence of multi organ failure in any case of sepsis.

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