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Original Research Paper

Internal Medicine

SEQUELAE AND OUTCOMES OF ACUTE KIDNEY INJURY OBSERVED AT A TERTIARY CARE CENTRE

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ABSTRACT Acute kidney injury (AKI) is defined as an sudden decline in renal function resulting in the inability to excrete metabolic wastes and maintain proper fluid and electrolyte balance.

The purpose of current study is to study the post discharge long term outcome among the survivors of Acute kidney injury. The study will also see the relationship of etiology, serum creatinine, blood urea, serum electrolytes, urine routine and hemogram among the patients with acute kidney injury.

AIM: To determine the long-term outcome and sequelae in survivors of AKI.

OBJECTIVES:

1. To assess the partial and complete recovery of renal functions at discharge and further follow-up period.
2. To assess the morbidity of patients during long term follow-up.
3. To study the subsequent development of chronic kidney disease.
4. To study the progression to dialysis dependency.

PLACE OF STUDY:

Department of General Medicine, Kamineni Institute of Medical Sciences, Narketpally

Duration of the study: September 2019 – September 2020

STUDY DESIGN: Prospective study design

SAMPLE SIZE: This study included follow-up study of 47 survivors of AKI patients.

KEYWORDS : AKI; ARF; CKD; AKIN; Dialysis; Leucocytosis; Acute Tubular Necrosis; Acute Tubulo- Interstital Nephritis, Acute Glomerulonephritis, End stage /Kidney Disease

INTRODUCTION

Acute kidney injury (AKI) is a complex disorder is also known as acute renal failure and it is a syndrome characterized by the brisk loss of the kidney's excretory function and is typically diagnosed by the accumulation of end products of nitrogen metabolism (urea and creatinine) or decreased urine output, or both.[1] It is the clinical sign of several disorders that affect the kidney acutely. Acute kidney injury is common in hospital patients and very common in critically ill patients.

The term Acute Kidney Injury (AKI) was used for the first time by William Mac Nider in 1918 in a situation of acute mercury poisoning.[2] Acute kidney injury is recognized as a major public health problem affecting millions of patients worldwide and leading to decreased survival, increased progression of underlying chronic kidney disease (CKD), and sometimes to new onset of CKD. Acute kidney injury is defined as an abrupt (within 48 hours) reduction in kidney function based on an elevation in serum creatinine level, a reduction in urine output, the need for renal replacement therapy (dialysis), or a combination of these factors. Acute events involving renal arteries or veins can also lead to intrinsic acute kidney injury.[3]

Furthermore, AKI is not a single disease but rather a syndrome comprising multiple clinical conditions. Outcomes in AKI are influenced by the underlying disease causing the condition, as well as by the severity and duration of renal impairment and by the baseline condition of the patient in whom does AKI result in these outcomes is also the subject of active research and requires much speculation

Principal tools to detect AKI were consecutive measurements of sCr, serum urea (sUr), urinalysis, and measurements of UO. Urine indices such as fractional excretion of sodium (FeNa) and urea (FeUr) were also used to differentiate transient from persistent AKI.

Acute kidney injury (AKI) usually happens when your kidneys are damaged suddenly. The damage that leads to AKI may be caused by not having enough blood flowing through kidneys, sometimes an injury directly to your kidneys or a problem with your kidneys and a blockage in your ureters, the tubes that take urine from your kidneys to your bladder. problems that can cause you to have too little blood flowing through your kidneys are Low blood pressure, bleeding too much, having severe diarrhea, heart disease or heart attack, infection, liver failure using NSAIDs (non-steroidal anti-inflammatory drugs), such as aspirin, ibuprofen and naproxen, serious burns, dehydration and some severe allergic reaction.

BACKGROUND:

Acute kidney injury (AKI) is defined as an sudden decline in renal function resulting in the inability to excrete metabolic wastes and maintain proper fluid and electrolyte balance.

Pre-renal azotaemia and ischemic tubular necrosis occur in a continuum of the same pathophysiological process. These two conditions account for 75% of AKI cases.[4,5]

Acute Kidney Injury (AKI), previously called Acute Renal Failure (ARF), proposed by Acute Kidney Injury (AKIN), to represent the entire spectrum of ARF.[6]

Specific criteria exist for the diagnosis of AKI

1. Rapid time course (less than 48 hours)
2. Reduction of kidney function

- Rise in serum creatinine, defined by either:

Absolute increase in serum creatinine of ≥0.3 mg/dl (≥26.4μmol/l) Percentage increase in serum creatinine of ≥50% above baseline value

- Reduction in urine output, defined as <0.5 ml/kg/hr. for more than 6 hours.

A standard multilevel classification system was also used in defining AKI which is given below:

The RIFLE criteria, proposed by the Acute Dialysis Quality Initiative (ADQI) group, aid in the staging of patients with AKI 7**RIFLE (Risk, Injury, Failure, Loss, End Stage Renal Disease)** depending on GFR, percentage of serum creatinine and Urinary output classified as

Risk:

GFR decrease >25%, serum creatinine increased 1.5 times or urine production of <0.5 ml/kg/hr. for 6 hours.

Injury:

GFR decrease >50%, doubling of creatinine or urine production <0.5 ml/kg/hr. for 12 hours.

Failure:

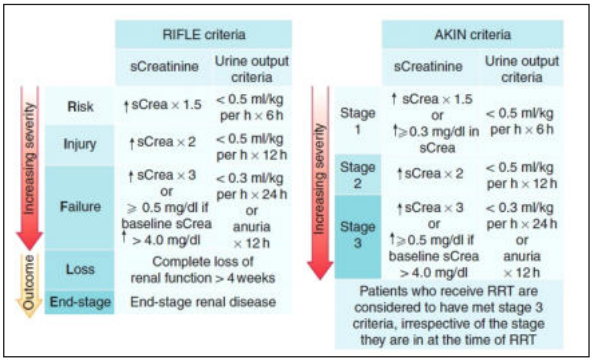
GFR decrease >75%, tripling of creatinine (>4 mg/dl) OR urine output below 0.3 ml/kg/hr. for 24 hours.

Loss:

Persistent AKI or complete loss of kidney function for more than 4 weeks

End stage-renal disease:

Complete loss of kidney function for more than 3 months



Comparison of RIFLE and AKIN criteria of Acute kidney injury [8,9] The key cause of in-hospital AKI is acute tubular necrosis resulting from multiple nephrotoxic insults such as sepsis, hypotension and the use of nephrotoxic drugs or radio contrast media. [5]

The incidence of AKI is almost 500 per million per year placing high demands on the public health system.[6,7] AKI is becoming common, occurring in almost 5% of all in-hospital patients and 6% to 23% among ICU patients.[5,6] The mortality of patients with multiple organ failure receiving renal replacement therapy is high, exceeding 70% in intensive care units (ICU).[8,9]

Mortality rates have changed little over the past decades despite significant advances in supportive care. This lack of improvement may be more apparent than real as patients have become older and have more pre-existing chronic health problems.[10,11]

There are few studies to investigate prognostic factors in infectious disease-associated AKI. The risk factors for death and the outcome of critically ill patients with AKI in ICU have been studied for several groups. The main risk factors identified were advanced age, male gender, prolonged hospital stay, hepatic, biliary tract and hematological diseases, hypotension, coma, use of vasoactive drugs, respiratory distress or the need for mechanical ventilation, sepsis, need for dialysis treatment, high levels of creatinine, oliguria and delayed nephrology consultation. AKI is an important complication seen in many infectious diseases.

Acute renal failure (ARF) is a less pleasant problem with various aetiologies. ARF is reversible when recognized and managed early and a delay in diagnosis or treatment of ARF may lead to increased morbidity and mortality.

However, risk for disease represents the interaction between susceptibility (i.e., features intrinsic to the patient) and exposure (i.e., the causative factor or factors). Exposures known to produce AKI in susceptible populations include sepsis, ischemia, heart failure, liver disease, major surgery (especially vascular and cardiac), myonecrosis, urinary tract obstruction, and various nephrotoxins. In the critically ill, sepsis is the major cause of AKI, accounting for nearly 50% of cases.[12,13]

Outcomes And Pathophysiology

There is substantial evidence from clinical studies that both shortterm and long-term outcomes are adversely affected by AKI. As discussed before, hospital mortality increases in association with AKI stage. Furthermore, survival appears to be affected for at least 1 year and maybe longer.[14]

Recovery of renal function is also a problem, with many patients failing to recover renal function. Chertow et al.[15]demonstrated in a cohort of critically ill patients with AKI who required renal replacement therapy that 33% of the survivors were still on renal replacement therapy after 12 months. The Acute Renal Failure Trials Network study enrolled 1124 patients with severe AKI, and nearly 25% of the survivors were dependent on renal replacement therapy on day 60.[16]However, an Australian study of 1508 patients with severe AKI found that only 5.4% of survivors still required renal replacement therapy by day 90.[17] Finally, there is emerging evidence showing that less severe AKI may be associated with important long-term outcomes including progression of CKD and cardiovascular disease.[18]

Unfortunately, very tiny information is known about why AKI is associated with short- and long-term adverse effects. Although some manifestations of AKI are directly linked to impaired glomerular / tubular function and recognized without difficulty at the bedside in the form of hyperkalaemia, pericarditis, or encephalopathy, pulmonary oedema, other changes are less obvious or might not become evident until sometime after the patient has discharged from the hospital. Here, the modulatory effects of AKI on the (innate) immune system and the progression from AKI to CKD have recently emerged as very critical and highly important factors.

AKI and the (innate) immune system

Current concepts about the effects of AKI on the innateimmune system largely stem from experimental studies andmostly focus on interactions between the kidneys and remoteorgans, such as the lungs and heart. Experimental AKI hassome striking effects on the heart.[19] Bilateral renal ischemiasig nificantly increases the myocardial transcription of tumourn ecrosis factor-a and interleukin (IL)-1. Moreover, renal ischemia–reperfusion also led to increases in left ventricular enddiastolic diameter and left ventricular end-systolic diameter, while decreasing fractional shortening.

Several studies have shown that bilateral ischemic AKI causes pro-inflammatory changes in the uninjured lung. In

particular, postischemic AKI down regulates the pulmonary expression of epithelial sodium channels, Na/K–ATPase, and aquaporin-5.[20]

In various experimental models, AKI also leads to altered pulmonary cytokine expression and to changes in serum cytokine concentrations. This includes changes in IL-1, IL-6, IL-12, granulocytemacrophage colony-stimulating factor, and IL-10, as well as in some neutrophil-specific chemokines.[21] However, not all mediators are up regulated in all animal models at the same time. Different models of AKI or acute loss of renal function reveal a similar, but unique, cytokine/chemokine profile.[22]

For example, only mild increase in plasma IL-6 occurred in a mouse model of folic acid-induced AKI.[23] Prophylactic administration of anti-inflammatory agents, such as IL-10 or antibodies against IL-6, can attenuate the inflammatory response and subsequent lung damage after bilateral nephrectomy or renal ischemia.[21,24]

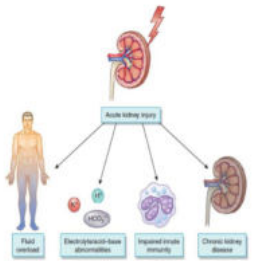
Furthermore, in another recent study, patients with septic AKI have impaired leukocyte rolling when compared with septic patients without AKI.[25]The findings when compared with patients without AKI, patients with AKI more frequently demonstrate bacteraemia and poor outcome in various clinical settings, including peritonitis, after cardiac surgery and during haematological malignancies.[26-28]

AKI and CKD

Several recent clinical studies have provided evidence for a link between AKI, CKD, and ultimately progression to end stage renal disease.[29-39] Under normal circumstances, the regeneration of the tubular epithelium after AKI occurs in a cascade-like manner, including initial de-differentiation, migration, proliferation of surviving cells, redifferentiation, and, in a last step, the full restoration of the tubular epithelium. Incomplete repair after AKI, by contrast, is characterized by persistent tubulo-interstitial fibrosis and inflammation, even in the absence of prior kidney disease.[40, 41] Persistent tubular interstitial fibrosis is the pathological correlate of loss of kidney function. The severity of AKI significantly determines the extent of recovery.[42,43]

Pre-existing kidney disease increases a patient's risk of developing AKI is well accepted; the risk for AKI is proportional to the respective stage of CKD. On the other hand, any episode of AKI in a patient with underlying CKD inflicts additional damage on already compromised kidneys and thereby substantially increases the rate of transition to endstage renal disease.

Progressive kidney disease is more likely after an episode of acute-on chronic kidney injury than after simple AKI alone.As much as inflammation is crucial for the development of AKI, it also has a crucial role in the development of interstitial fibrosis after AKI. Experimental studies have shown a delayed mononuclear cell infiltration after AKI, which is a central factor in kidney repair, regeneration, and tissue remodelling.[43,44]



Acute Kidney Injury (aki) Can Have Both Immediately Recognizable Consequences As Well As Less Noticeable Or Delayed Consequences.[8,9]

There were many causes that be able to trigger pathophysiological mechanisms leading to acute renal failure (ARF). This syndrome is characterized by a sudden decrease in kidney function, with a consequence of loss of the haemostatic equilibrium of the internal medium. The primary marker is an increase in the concentration of the nitrogenous components of blood. A second marker, oliguria, is seen in 50% to 70% of cases. In general, the causes of ARF have a dynamic behaviour as they change as a function of the economical and medical development of the community. Economic differences justify the different spectrum in the causes of ARF in developed and developing countries.

The setting where ARF appears (community versus hospital), or the place where ARF is treated (intensive care units [ICU] versus other hospital areas) also show differences in the causes of ARF. While functional outcome after ARF is usually good among the surviving patients, mortality rate is high: around 45% in general series and close to 70% in ICU series. Although it is unfortunate that these mortality rates have remained fairly constant over the past decades, it should be noted that today's patients are generally much older and display a generally much more severe condition than was true in the past. These age and severity factors, together with the more aggressive therapeutical possibilities presently available, could account for this apparent paradox.

As is true for any severe clinical condition, a prognostic estimation of ARF is of great utility for both the patients and their families, the medical specialists (for analysis of therapeutically manoeuvres and options), and for society in general (demonstrating the monetary costs of treatment).

Causes Of Pre-renal Acute Renal Failure:

- Decreased effective extracellular volume.
- Renal losses: haemorrhage, vomiting, diarrhoea, burns, diuretics.
- Redistribution: hepatopathy, nephrotic syndrome, intestinal obstruction, pancreatitis, peritonitis, malnutrition.
- Decreased cardiac output: cardiogenic shock, valvulopathy, myocarditis, myocardial infarction, arrhythmia, congestive heart failure, pulmonary emboli, cardiac tamponade.
- Peripheral vasodilation: hypotension, sepsis, hypoxemia, anaphylactic shock, treatment with interleukin L2 or interferons, ovarian hyper-stimulation syndrome
- Renal vasoconstriction: prostaglandin synthesis inhibition, alpha adrenergics, sepsis, hepatorenal syndrome, hypercalcemia.
- Efferent arteriole vasodilation: converting-enzyme inhibitors.

Causes Of Intrinsic Acute Renal Failure:

1. Acute Tubular Necrosis

- Hemodynamic: cardiovascular surgery, sepsis,pre-renal causes
- Toxic: antimicrobials, iodide contrast agents, anaesthetics, immunosuppressive or antineoplastic agents, Chinese herbs, Opiaceous, mercurials, organic solvents, venoms, heavy metals, mannitol, radiation.
- ** **most common causes among above mentioned were :** sepsis, pre-renal causes, iodide contrast agents, anaesthetics, Chinese herbs
- Intra-tubular deposits: acute uric acid nephropathy, myeloma, severe hypercalcemia, primary oxalosis, sulfadiazine, fluoride anaesthetics.
- Organic pigments (endogenous nephrotoxins):
- **Myoglobin rhabdomyolysis:** muscle trauma; infections; dermatopolymyositis; metabolic alterations; hyperosmolar coma; diabetic ketoacidosis; severe hypokalaemia; hyper- or hyponatremia; hypophosphatemia; severe hypothyroidism;

malignant hyperthermia; toxins such as ethylene glycol, carbon monoxide, mercurial chloride, stings; drugs such as fibrates, statins, opioids and amphetamines; Hereditary diseases such as muscular dystrophy, Metabolopathies, McArdle disease and Carnitine deficit.

- **Haemoglobinuria:** malaria; mechanical destruction of erythrocytes with extracorporeal circulation or metallic prosthesis, transfusion reactions, or other haemolysis; heat stroke; burns; glucose-6-phosphate dehydrogenase; nocturnal paroxysmal Haemoglobinuria; chemicals such as aniline, quinine, glycerol, benzene, phenol, hydralazine; insect venoms.

1. Acute Tubulointerstitial Nephritis:
- **Antimicrobials -**
- Penicillin, Ampicillin, Rifampicin
- Sulphonamides
- **Analgesics and anti-inflammatories** Fenoprofen,
- Ibuprofen , Naproxen, Amidopyrine
- **other drugs** – Cimetidine, Allopurinol
- **Immunological -** Systemic lupus erythematosus, Rejection
- **Infections**
- **Neoplasia** – Myeloma, Lymphoma, Acute leukaemia
- **Idiopathic** – Isolated, Associated with uveitis

3. Vascular Occlusion
Principal vessels: bilateral (unilateral in solitary functioning kidney) renal artery thrombosis or embolism, bilateral renal vein thrombosis
Small vessels:athero-embolic disease, thrombotic microangiopathy, haemolytic-uremic syndrome or thrombotic thrombocytopenic purpura, postpartum acute renal failure, antiphospholipid syndrome, disseminated intravascular coagulation, scleroderma, malignant arterial hypertension, radiation nephritis, vasculitis.

4. Acute Glomerulonephritis
Post-infectious:
- Streptococcal or other pathogen associated with visceral abscess, endocarditis, or shunt
- Henoch-Schonlein purpura
- Essential mixed cryoglobulinemia
- Systemic lupus erythematosus
- Immunoglobulin A nephropathy
- Mesangio-capillary
- With anti-glomerular basement membrane antibodies with lung disease (Good pasture is syndrome) or without it
- Idiopathic, rapidly progressive, without immune deposits

5. Miscellaneous
Cortical necrosis, abruptio-placentae, septic abortion, disseminated intravascular coagulation.

Causes Of Obstructive Acute Renal Failure
1. Congenital Anomalies
Ureterocele
Bladder diverticula
Posterior urethral valves
Neurogenic bladder

2. Acquired Uropathies
Benign prostatic hypertrophy
Urolithiasis
Papillary necrosis
Iatrogenic ureteral ligation

3. Malignant Diseases
Prostate; Bladder; Urethra; Cervix; Colon; Breast (metastasis)

4. Retroperitoneal Fibrosis
Idiopathic
Associated with aortic aneurysm
Trauma
Iatrogenic
Drug-induced

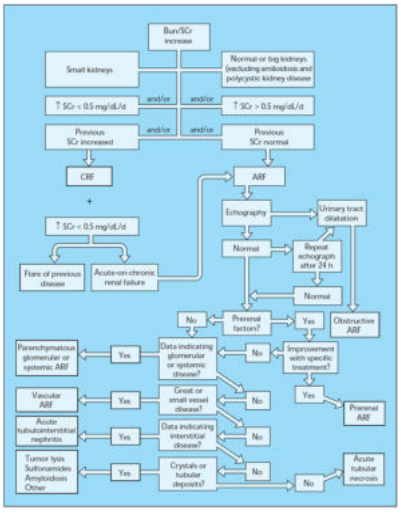
5. Gynecologic Non-neoplastic
Pregnancy-related
Uterine prolapse
Endometriosis

6. Acute Uric Acid Nephropathy
- **Drugs**

€-aminocaproic acid
Sulphonamides

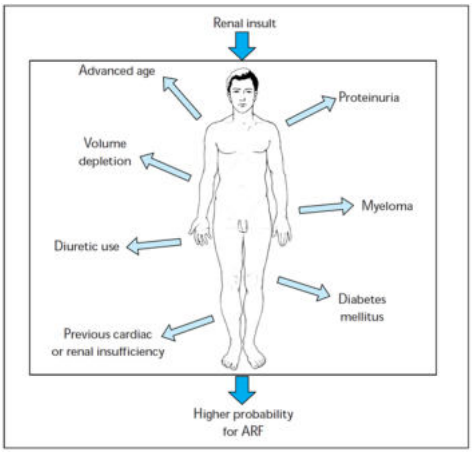
• Infections
Schistosomiasis
Tuberculosis
Candidiasis ; Aspergillosis; Actinomycosis

7. Others
Accidental urethral catheter occlusion
As acute kidney injury is multifactorial in aetiology as mentioned above it is very difficult to diagnose the cause of AKI. Hence here is the simple diagnostic algorithm which guides us towards the cause of AKI



DIAGNOSTIC ALGORITHM IN AKI[6]

There are numerous predisposing conditions that have the capacity to precipitate and fasten the development of AKI. Among these, age factor especially the vulnerable age groups and volume status of the patient has highest potential to cause AKI.



Factors Predisposing Acute Kidney Injury[6]

Inclusion Criteria

1. Patients who were diagnosed with AKI according to AKIN

Exclusion Criteria

1. Patients with acute worsening of chronic kidney disease.
2. Patients who are already diagnosed with chronic kidney disease and on treatment.

Patients with co-morbid conditions like diabetes mellitus, essential hypertension and structural kidney diseases like polycystic kidney disease, medullary sponge kidney etc. are excluded.

Place Of Study:

Department of General Medicine, Kamineni Institute of Medical Sciences, Narketpally

Duration of the study: September 2019 – September 2021

Study Design:

Prospective study design

Sample Size:

This study included follow-up study of 47 survivors of AKI patients with serum urea, serum creatinine, serum electrolytes (hyperkalemia, hyponatremia), Haemogram (abnormal haemoglobin, leukocytosis, thrombocytopenia), Urine routine examination (pyuria, hematuria and proteinuria),), Ultrasonography of abdomen and pelvis (as required), at admission, at discharge, at three months, at six months and at one year. Importance of the study was explained and an informed consent was taken from all the study participants before collecting the data.

OBSERVATION AND RESULTS

Table 1: Gender wise Distribution of study participants

Gender	Frequency	Percentage (%)
Male	28	59.57
Female	19	40.43
Total	47	100

From table 1, major proportion of the study population were males i.e., 59.57 % and the remaining proportion were females.

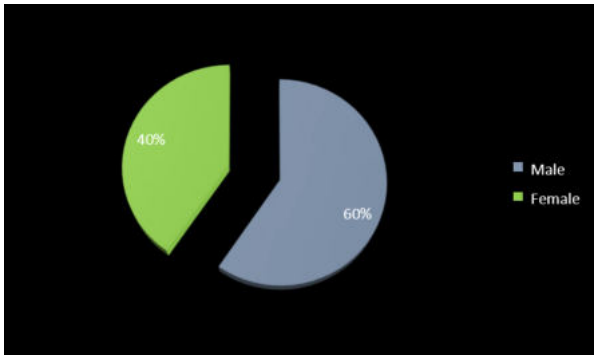


Figure 1 : Showing genderwise distribution of study population

Table 2: Showing distribution of study participants according to age

	Age group	Frequency (n)	Percent (%)
≤ 20		3	6.38
21 – 30		6	12.77
31 – 40		7	14.89
41 – 50		8	17.02
51 – 60		13	27.66
> 60		10	21.28
Total		47	100

Majority (i.e., 27.66%) of the patients with AKI belong to age group between 51 to 60 years. Therefore incidence of AKI is more during 6th decade of life in the current study. Mean age of study population was 48.23 with standard deviation of 15.65.

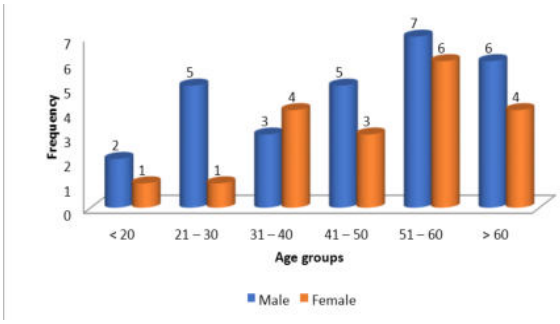


Figure 2: Showing genderwise distribution of study subjects with respect to age

ETIOLOGY OF AKI:

Table 3: Showing incidence of AKI based on etiology

DIAGNOSIS	FREQUENCY	PERCENT
Acute Gastroenteritis	14	29.78
Acute Pancreatitis	3	6.38
Dengue	3	6.38
Malaria	1	2.13
Sepsis	22	46.81
Snake bite	2	4.26
Heart failure	2	4.26
Total	47	100

** UTI – Urinary tract infections

From the above table it is evident that, sepsis contributes as a cause in majority i.e., 46.81% of patients with AKI by different mechanisms (either direct or indirect). Followed by acute gastroenteritis, acute pancreatitis and dengue accounting for second and third major cause of AKI.

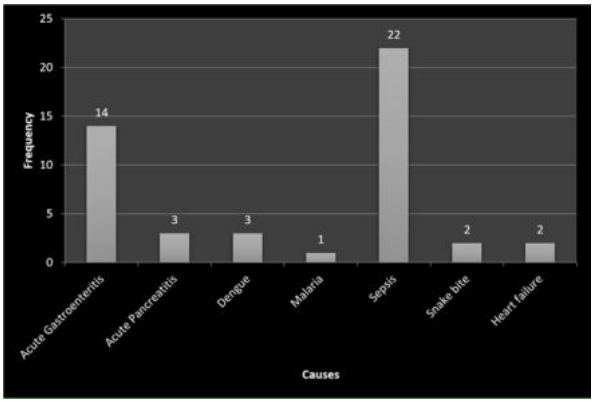


Figure 3. Causes of Acute kidney injury

Serum Creatinine:

Table 4: Showing Mean, Standard deviation and p value of S.creatinine during study

S. Creatinine	N	Minimum	Maximum	Mean	Std. Deviation	P value
At admission	47	1.8	8.1	3.89	1.56	<0.001
At discharge	47	0.7	4.2	1.68	0.78	
At 3 months	47	0.7	3.1	1.15	0.53	
At 6 months	47	0.5	2.5	1.04	0.40	
At 1 year	47	0.6	2.1	0.93	0.27	

Above table 4 represent the change in serum creatinine levels during follow-up period suggesting that there was significant drop in serum creatinine levels from admission till the end of 1 year i.e., in every follow-up till end of study period) with P value <0.001(<0.05).

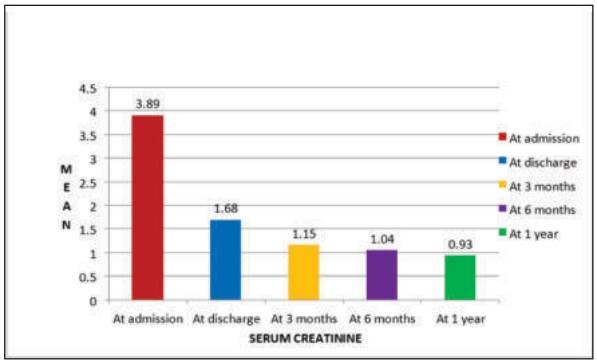


Figure 4: Mean serum creatinine levels during follow-up

Table 5: Showing study population with normal and abnormal creatinine during study period

Serum Creatinine	Normal		Abnormal		Total	
	No. Of Patients	%	No. Of Patients	%	No. Of Patients	%
At admission	0	0	47	100	47	100
At discharge	24	51.06	23	48.94	47	100
At 3 month	42	89.36	5	10.64	47	100
At 6 months	45	95.74	2	4.26	47	100
At 1year	45	95.74	2	4.26	47	100

Table 6: Showing McNemer test analysis in study population during study period

Parameter Creatinine)	(Serum	P value	Significance
At Discharge Admission	– At	<0.001	Hs
At 3months Admission	– At	<0.001	Hs
At 6 Months Admission	– At	<0.001	Hs
At 1 Year – At Admission		<0.001	Hs
At 3 Months – At Discharge		<0.001	Hs
At 6 Months – At Discharge		<0.001	Hs
At 1 Year – At Discharge		<0.001	Hs
At 6 Months – At 3months		0.239	Ns
At 1 Year – At 3months		0.239	Ns
At 1 Year – At 6 Months		1.000	NS

From the above tables 5, 6 and figure 4, it is evident that

1. At time of admission all patients had abnormal creatinine and at the end of 1year only 4.26 % of patients had abnormal serum creatinine values.
2. Improvement of S.creatinine to normal level during follow-up period was significant till end of study period i.e., 1 year (which is evident by P value < 0.001 from McNemer test).

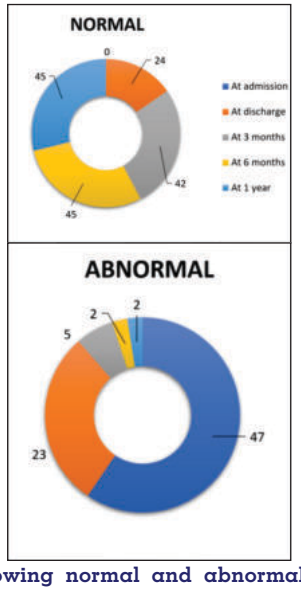


Figure 5. Showing normal and abnormal S.creatinine during study period

Table 7: Showing percentage and no. of subjects with CKD at end of 1 year.

CKD	NO.OF SUBJECTS	PERCENTAGE (%)
Absent	45	95.75
Present	2	4.25
Total	47	100

****CKD – chronic kidney disease**

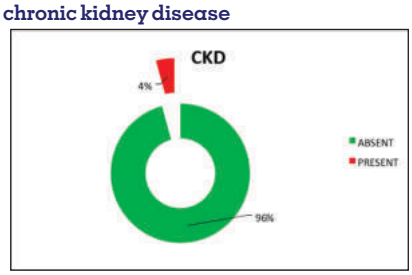


Figure 6: Percentage of population progressed to CKD in 1 year.

eGFR calculated at the end of 1 year for all study population as per MDRD eGFR formula (according to KDOQI CKD criteria [61]) showed that only 2 individuals (4.25%) had eGFR less than 60 ml/min/1.73m^2 and are labelled as chronic kidney disease according to KDOQI guidelines. Remaining 45 individuals (95.75%) had eGFR above 60 ml/min/1.73m^2.

Blood Urea:

Table 8: Showing Mean and Standard deviation of Blood urea during study

Blood Urea	N	Min	Maximum	Mean	S. Deviation	P Value
At Admission	47	52	212	96.93	37.17	<0.001
At Discharge	47	32	74	52.04	10.54	
At 3 Months	47	27	93	43.76	12.03	
At 6 Months	47	18	76	31.12	12.26	
At 1 Year	47	17	60	27.59	9.68	

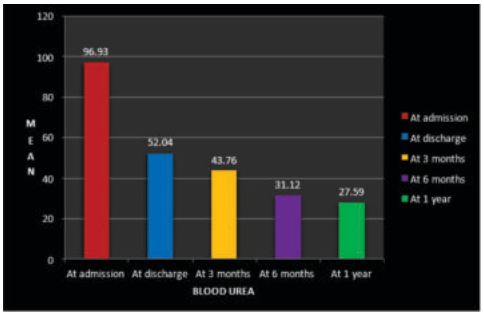


Figure 7. Mean Blood urea levels during follow-up

From the above table 8 and its corresponding figure 5, the drop in blood urea levels are analyzed during follow-up period by ANOVA and an statistically significant association was observed between blood urea levels and during follow up with a p value of <0.001

Table 9: Showing McNemer test analysis in study population during study period

Parameter (Blood Urea)	P Value	Significance
At Discharge – At Admission	<0.001	Hs
At 3months – At Admission	<0.001	Hs
At 6 Months – At Admission	<0.001	Hs
At 1 Year – At Admission	<0.001	Hs
At 3 Months – At Discharge	<0.001	Hs

At 6 Months – At Discharge	<0.001	Hs
At 1 Year – At Discharge	<0.001	Hs
At 6 Months – At 3months	0.293	Ns
At 1 Year – At 3months	0.293	Ns
At 1 Year – At 6 Months	1.000	Ns

It is clear that there was significant drop in mean blood urea level from admission to 6 months (about 65.81) with P value <0.001 which is statistically highly significant whereas from 6 months to the end of 1 year, there was slight significant drop in mean blood urea levels (about 3.53) with P value of 0.013 (<0.05) which is just statistically significant.

Table 10: Showing Study Population With Normal And Abnormal Blood Urea During Study Period

Blood Urea	Normal		Abnormal		Total	
	No. Of Patients	%	No. Of Patients	%	No. Of Patien ts	%
At Admission	0	0	47	100	47	100
At Discharge	22	46.80	25	53.2	47	100
At 3 Month	41	87.23	6	12.77	47	100
At 6 Months	44	93.61	3	6.39	47	100
At 1year	44	93.61	3	6.39	47	100

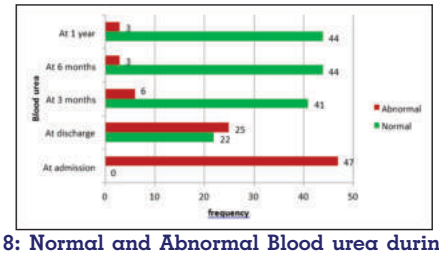


Figure 8: Normal and Abnormal Blood urea during study period

From the above tables 9, 10 and figure 8 it is evident that

1. At admission 100% of patients had abnormal blood urea and at the end of 1 year 6.39% of patients had abnormal blood urea.
2. Improvement of blood urea to normal level during follow-up period was significant till 6months (which is evident by P values <0.001) and after 6months it is statistically insignificant (which is evident by P value of 0.293 and 1.000 i.e., > 0.05 from McNemer test)

Serum Electrolytes:

Table 11: Showing study population with normal and abnormal S.electrolytes during study period.

Serum Electrolytes	Normal		Abnormal		Total	
	No. Of Patients	%	No. Of Patients	%	No. Of Patients	%
At Admission	10	21.27	37	78.73	47	100
At Discharge	41	87.23	6	12.77	47	100
At 3 Month	46	97.87	1	2.13	47	100
At 6 Months	47	100	0	0	47	100
At 1year	47	100	0	0	47	100

Table 12: Showing McNemer test analysis in study population during study period.

Parameter (Serum Electrolytes)	P Value	Significance
At Discharge – At Admission	<0.001	Hs
At 3months – At Admission	<0.001	Hs
At 6 Months – At Admission	<0.001	Hs
At 1 Year – At Admission	<0.001	Hs
At 3 Months – At Discharge	0.049	Hs
At 6 Months – At Discharge	0.011	Hs
At 1 Year – At Discharge	0.011	Hs
At 6 Months – At 3months	0.314	Ns
At 1 Year – At 3months	0.314	Ns

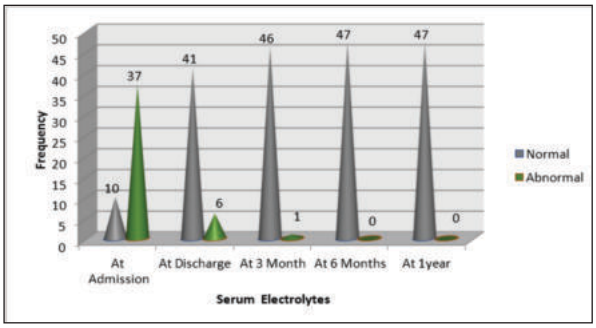


Figure 9: Norm al and Abnormal serum electrolytes during study period.

From the above table 11, 12 and figure 9 it is evident that

- About 78.73% of study population had abnormal serum electrolytes at the time of admission and all the study participants were having normal serum electrolytes at 6th month and end of study period (1year).
- Serum electrolytes took about 3 months duration to get normalised which is statistically significant with P value <0.05.
- After 3 months there was no significant percentage of patients becoming normal which is statistically insignificant with P value >0.05.

Urine Examination:

Table 13: Showing study population with normal and abnormal urine examination duringstudy period

Urine Routine Examination	Normal		Abnormal		Total	
	No. Of Patients	%	No. Of Patients	%	No. Of Patients	%
At Admission	20	42.55	27	57.45	47	100
At Discharge	36	76.59	11	23.41	47	100
At 3 Month	44	93.61	3	6.39	47	100
At 6 Months	43	91.48	4	8.52	47	100
At 1year	46	97.87	1	2.13	47	100

Table 14: Showing Mcnemer Test Analysis In Study Population During Study Period.

Parameter (Urine Routine Examination)	P Value	Significance
At Discharge – At Admission	<0.001	Hs
At 3months – At Admission	<0.001	Hs
At 6 Months – At Admission	<0.001	Hs
At 1 Year – At Admission	<0.001	Hs
At 3 Months – At Discharge	0.020	Hs
At 6 Months – At Discharge	0.048	Hs
At 1 Year – At Discharge	0.001	Hs
At 6 Months – At 3months	0.694	Ns
At 1 Year – At 3months	0.306	Ns
At 1 Year – At 6 Months	0.167	Ns

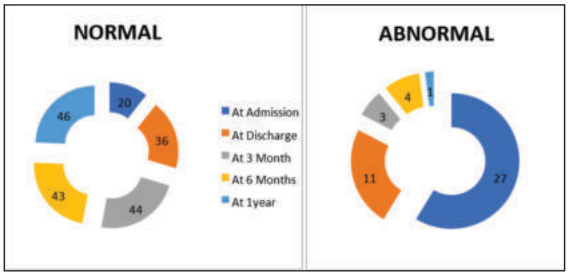


Figure 10. Normal and Abnormal urine examination during study period.

From the above tables 13, 14 and figure 10:

- About 57.45 % patients had abnormal urine analysis at the time of admission and only 23.41% of study population

had abnormal urine analysis at time of discharge.
- This implies that the study population had recovered without developing abnormalities during the course of the disease (in hospital stay) and that lead to the clinical improvement by the time of discharge. And it is found to be statistically highly significant with P value <0.001(<0.05).
- About 93.61% patients got normalised by the end of 3rd month follow up from time of discharge which is statistically highly significant with McNemer test P value 0.020 (<0.05).
- From the end of 3 months to end of 1 year and from the end of 6 months to 1 year, study population who got normalised was found to be statistically insignificant with McNemer test P value 0.307 and 0.617 (>0.05).

Hemogram:

Table 15: Showing study population with normal and abnormal hemogram during study period

Hemogram	Normal		Abnormal		Total	
	No. Of Patients	%	No. Of Patients	%	No. Of Patients	%
At Admission	6	12.76	41	87.24	47	100
At Discharge	32	68.08	15	31.92	47	100
At 3 Month	41	87.24	6	12.76	47	100
At 6 Months	43	91.48	4	8.52	47	100
At 1year	42	89.36	5	10.64	47	100

Table 16: Showing Mcnemer Test Analysis In Study Population During Study Period.

Parameter (Hemogram)	P Value	Significance
At Discharge – At Admission	<0.001	Hs
At 3months – At Admission	<0.001	Hs
At 6 Months – At Admission	<0.001	Hs
At 1 Year – At Admission	<0.001	Hs
At 3 Months – At Discharge	0.025	Sig
At 6 Months – At Discharge	0.004	Sig
At 1 Year – At Discharge	0.011	Sig
At 6 Months – At 3months	0.503	Ns
At 1 Year – At 3months	0.748	Ns
At 1 Year – At 6 Months	0.725	Ns

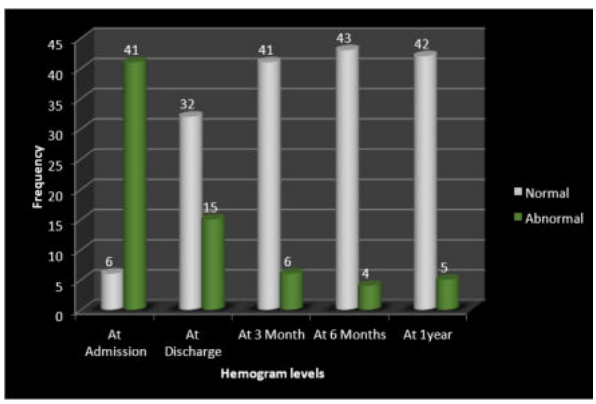


Figure 11 : Normal and Abnormal hemogram during study period.

From the above tables 15, 16 and figure 11:
- Majority of the patients with AKI had abnormal hemogram i.e., 87.24% at time of presentation and by the time of discharge only 31.24% of the study population were found to have abnormal hemogram.
- Around 87.2% and 91.5% of study population had normal hemogram at the end of 3 and 6 months respectively. But the proportion of study participants having normal hemogram levels has decreased to 89.4% at end of 1 year.
- It is obvious from the above data that haematological manifestations related to AKI took around 6 months to get normalised and was found statistically significant with McNemer test P value 0.004 (<0.05).

DISCUSSION

In current study, the pattern of recovery and time duration required for recovery of renal function after AKI was studied in 47 patients with acute kidney injury admitted in General medicine ward at an tertiary care hospital, Narketpally. Also studied the recovery of other parameters like urine analysis, serum electrolytes and complete hemogram to the normal limits following AKI. This study also analyzed the percentage of survivors of AKI progressed into the chronic kidney disease and dialysis dependency.

Gender

Among a total of 47 study subjects' prevalence of AKI is observed to be high in males i.e., 59.57% and remaining comprised of females.

Jose´e Bouchard et al (2009)47 conducted a Fluid accumulation; survival and recovery of kidney function in critically ill patients with acute kidney injury and reported that 59% of the study population consisted of males and remaining 41% were females.

A similar preponderance towards male was observed in the table given below.

Table no.17: Showing comparison of different studies based on gender

Authors	Male (%)	Female (%)
Jose´e Bouchard et al[47]	59	41
Jean-Philippe Lafrance and Donald R. Miller[50]	96.8	3.2
Sean M. Bagshaw[51]	64	36
Guadalupe Garcia-Tsao et al60	68	32
Lakhmir S Chawl et al[61]	98	2

Similar findings to that of present study were reported by Sean M. Bagshaw6 and Guadalupe Garcia-Tsao et al[60] in their respective studies with an male preponderance of 64% and 68%.

Age

In the present study major proportion (i.e., 27.66%) of the patients with AKI belong to age group between 51 to 60 years. Therefore incidence of AKI is more during 6th decade oflife followed by age group >60 years comprising of 21.28%. Among the total of 47 study subjects a mean of 48.23 with standard deviation of 15.65 was observed.

Table no.18: Comparison of studies done by other authors based on age

Authors	Mean age (in years)
Current study	48.23
Lo LJ et al (2009)[35]	63.5
Weiss AS (2006)[62]	54
Jean-Philippe Lafrance and Donald R. Miller(2010)[50]	66.3

In a study done by Lo LJ et al (2009)35, the mean age in years was reported as 63.5 years and in another study done by Weiss AS (2006)62 the mean age was reported as 54 years.

Jean-Philippe Lafrance and Donald R. Miller(2010)50 reported a mean age of 66.3 + 12.4 and prevalence of AKI was highest in the age group 70-79 years i.e., 29.2%.

Etiology

Based on the above study and data analysis,

sepsiscontributes as a cause for majority of patients with AKI i.e., 46.81% by different mechanisms (either direct or indirect). Following sepsis, Acute gastroenteritis, dengue and acute pancreatitis consisting of 29.78% and 6.38%. Least contribution to the cause of AKI in this study is by heart failure and snake bike with 4.26% each.

A study on Septic Acute Kidney Injury in Critically ill patients clinical characteristics and outcomes done by Sean M. Bagshaw6(2007)[51] reported that sepsis was a contributing factor to AKI in 47.5% patients among a total of 1178 study population. Similarly major cause of AKI was reported as Sepsis (36.1%) followed by gastroenteritis and heart failure (15%) in a study done by AlalehGheissari et al(2012)[71].

Table no.19: Showing results of various studies based on etiology

CAUSES	Current study	Sean M.Bagshaw et al51	ZAlalehGheissari et al (2012)71	Srira m Krishna murthy et al (2013)70	Ali Duzova et al (2010)72
Sepsis	46.81 %	47.5 %	36.1 %	55.4 %	18.2 %
Acute Gastro enteritis	29.78 %	-	15%	-	8.3%
Dengue	6.38%	-	-	15.6 %	-
Heart failure	4.26%	-	15%	4.8%	-
Envenomations /toxins	4.26%	-	-	-	6.4%

Sriram Krishnamurthy et al(2013)[70] done a study on Incidence and Etiology of Acute Kidney Injury in Southern India reported that AKI occurred in association with infections/sepsis (55.4 %), acute glomerulonephritis (16.9 %), cardiac disease (4.8 %), envenomations (4.2 %) and hemolytic uremic syndrome (3.6 %). Tropical febrile illnesses (dengue, scrub typhus, enteric fever, cholera, tuberculosis, malaria and leptospirosis) constituted 15.6 %.

In a study by Ali Duzova et al (2010)[72], among a total of 472 study population the cause for AKI was reported as 18.2% had sepsis, 8.3 % has acure gastroenteritis and 6.4%.

Serum creatinine

In the present study, recovery of renal function with serum creatinine as a determinant it is evident from the analysis that, at admission 100% of patients had abnormal creatinine and at the end of 1 year only 4.26% of patients had abnormal creatinine levels.

The mean creatinine level at admission was 3.89 ± 1.56 with a maximum of 8.1mg/dl and by the end of follow up the mean creatinine value was observed to be 0.93 ± 0.27.

Table no.20: Comparison of mean and SD with study done by Daniela Ponce et al.

Authors	Maximum (mg/dl)	Mean and SD
Current study	8.1	3.89 ± 1.56
Daniela Ponce et al (2011)[77]	9	3.46 ± 1.44

The improvement in serum creatinine levels during follow-up period suggesting that there was significant drop in serum creatinine levels from admission till the end of 1 year i.e., in every follow-up till end of study period with P value $<0.001(<0.05)$.

Table no.21: Showing patients with normal creatinine values at discharge and end of follow among various studies

Authors	Normal at discharge (%)	Normal at end of follow up (%)
Current study	52	95.7
Jean-Philippe Lafrance and Donald R. Miller(2010)[50]	89.8	100
Daniela Ponce et al (2011)[77]	56	-

In the present study 52 % of the study population had normal creatinine values at the time of discharge and an significant improvement was observed by the end of follow up with 95.7% of the study population has normal serum creatinine values.

Jean-Philippe Lafrance and Donald R. Miller(2010)[50] conducted a study on Acute Kidney Injury Associates with Increased Long-Term Mortality reported that 57.2% of 87211 study population had normal creatinine values. Significant improvement in levels of creatinine was observed at the time of discharge (89.8%) and 100% normal levels were reported post discharge.

Daniela Ponce et al[77] in 2011 conducted a study and reported that 44% of the study population had serum creatine value of >1.5 mg/dL.

There is collective evidence that small increments in serum creatinine are associated, in a variety of settings, with adverse outcomes and also decrement in creatinine levels helps in better long term outcome[65], and they manifest in short-term morbidity and mortality and in longer-term outcomes, including 1-year mortality.[66]

Chronic Kidney Disease

Progression of AKI to CKD is assessed by calculating the reduced effective glomerular filtration rate (to less than 60 ml/min/1.73m^2)according to KDOQI CKD guidelines.[63]

eGFR calculated at the end of 1 year for all study population as per MDRD eGFR formula showed that only 2 individuals (4.25%) had eGFR less than 60 ml/min/1.73m^2 and are labelled as chronic kidney disease. Remaining 45 individuals (95.75%) had eGFR above 60 ml/min/1.73m^2.

Table no.22: Showing eGFR values among various studies

Authors	eGFR<60 ml/min/1.73m^2 (in percentage)
Current study	4.25
Hiroshi W et al(2009)[75]	3.3
Jaime Lucove et al (2008)[74]	7.8

A report stating that 12% of the participants had an eGFR<60 mL/min/1.73 m^2 among a total of 7,839 study subjects by Helmer C et al(2011).[73]

Jaime Lucove et al (2008)[75], in their study the observed prevalence of 7.8% with eGFR less than 60 mL/min/1.73 m^2.

James M T et al[64] showed in a cohort of over 920,000 patients that the level of proteinuria and diminished baseline e GFR were independent risk factors for developing AKI.

Almost every multivariate analysis has revealed that CKD is an independent risk predictor for AKI.[68,69] The risk of AKI is increased in patients with an e GFR <60ml/min/1.73 m (stage 3 to 5 CKD), and special precautions should be taken in these patients.[59]

Blood urea

In this study analysis of blood urea levels showed that, at

admission 100% of patients had abnormal blood urea and at the end of 1 year 6.39% of patients had abnormal blood urea. Improvement of blood urea to normal level during follow-up period were significant till 1 year (which is evident by P values <0.001 from McNemer test).

Mean serum urea value was observed to be 96.93 with SD 37.17 at admission with a maximum of 212 and by the end of 12months the mean value was 27.59 with an standard deviation of 9.68 with a maximum value of 60.

Table no.23: Showing mean and SD values of urea at admission and end of follow up among various studies

	At admission		At end of follow up	
	Maximu	Mean	Maximu	Mean
Authors	**m** (mg/dl)	**and SD**	**m** (mg/dl)	**and SD**
Current study	212	96.93 ±37.17	60	27.59 ± 9.68
Daniela Ponce et al (2011)[77]	-	127.6 ± 43.8	-	-
MarliesOstermann and René WS Chang(2009) 76	-	-	-	24.23 ± 8.26

MarliesOstermann and René WS Chang(2009)[76] done a study on Correlation between parameters at initiation of renal replacement therapy and outcome in patients with acute kidney injury, their results showed that the mean serum value was 24.23 at the end of follow up.

Daniela Ponce et al[77] conducted a study in 2011 and reported a mean of 127.6 with a standard deviation of 43.8.

Serum electrolytes

In the present study about 78.73% of study population had abnormal serum electrolytes at the time of admission and 2.13% had abnormal at the end of 3 months. All the study subjects had normal serum electrolytes values by the end of study period (1year).

Similar results were reported in a study done by Biagioni Santos M.S et al[81] in the year 2010, where they observed a proportion of 87% with abnormal serum electrolyte values at the time of admission.

Serum electrolytes took about 3 months duration to get normalised which is also statistically significant with P value <0.05. After 3 months there was no abnormal study population observed as all patients becoming normal which is statistically significant with P value <0.05.

In the present study, at time of admission major proportion i.e., 42.5% of the study subjects had hyperkalemia followed by hypokalemia and hyponatremia in 21.3% and 12.8%. Least proportion of imbalance in electrolytes was observed in hypernatremia with 2.1%.

Table no.24: showing results of various studies with respect to hyperkalemia

Authors	Hyperkalemia at admission (in %)
Current study	42.5
JagadishKhanagavi et al (2013)[78]	69.8
Lisa M. Einhorn et al (2009)79	52.7
Anna Grodzinsky et al (2016)80	66.8

Table no.25: Showing results of various studies with respect to hypokalemia

Authors		Hypokalemia admission (in %)
Current study		21.3
Biagioni Santos M.S al(2010)[81]	et	46
Barrett C. Bowling (2010)[82]		18.86

Table no.26: Showing results of various studies with respect to hyponatremia

Authors		Hyponatremia at admission (in %)
Current study		12.8
Biagioni Santos M.S al(2010)[81]	et	59

Urine examination

In this study, only 57.45% of study subjects had abnormal urine analysis at the time of presentation and about 23.41% and 2.13% of study population had abnormal urine analysis at time of discharge and at the end of study period (i.e., 1 year).

This implies that there is only a little drop in urine abnormalities during the course of the disease (in hospital stay) and the abnormalities in urine still persists in about 23.41% of study population even at time of discharge which lags behind the clinical improvement. This is statistically highly significant with P value <0.001(<0.05).

Table no.27: Showing results of various studies in the presence of Albumin

Authors	Presence Albuminuria admission (in %)	
Current study	14.9	
Morgan E. Grams et al(2010)[83]	16.9	
Ferdau L. Nauta (2011)[84]	56.4	

In the present study, at time of admission major proportion i.e., 46.8% of the study subjects had pyuria followed by albuminuria and hematuria in 14.9% and 2.12%. And 57.4% of the study subjects were found serum electrolytes within normal limits.

Table no.28: Showing results of various studies in the presence of pyuria Hemogram

Authors	Presence pyuria at time of admission (in %)
Current study	46.8
Abdul Chaudhryet al(1993)[85]	16.9
Frank B.Cortazar (2016)[86]	8.8

Majority of the patients with AKI had abnormal hemogram i.e., 87.24% at time of presentation and by the time of discharge only 31.24% of the study population were found to have abnormal hemogram.

From the current study it was observed that majority of the patients with AKI had abnormal hemogram at time of presentation but had drastically decreased at time of discharge. This coincides with clinical improvement of survivor of AKI patients.

Around 87% and 91% of study population had normal haemogram at the end of 3 and 6 months respectively.

In the present study, it was observed that 19.1% of study population had anemia at the time of admission and 70.2% of study population had leukocytosis during admission.

Table no.29: Showing results of various studies in the presence of anemia in patients with AKI

Authors	Presence of anemia at time of admission (in %)
Current study	19.1
Luca De Santoet al(2009)[87]	28
KeyvanKarkouti (2011)[88]	4.1

It is evident that haematological manifestations related to AKI took around 3 months in majority of study population to get normalised which is statistically highly significant with McNemer test P value <0.001 (<0.05).

Serum creatinine levels and urine output are two common measures reflecting renal function; however, they are each influenced by factors other than the glomerular filtration rate and do not provide information on the nature and site of kidney injury. Currently, there is lack of sensitive and specific markers for kidney injury available in clinical practice, although several kidney- specific biomarkers are under development.[67]

Coming to the morbidity pattern only 2 individuals had eGFR below 60 ml/min/1.73m^2 at the end of the study leading to chronic kidney disease. Hence majority of the study population (95.75%) got completely recovered from AKI and only 4.25% had progressed to CKD which is statistically insignificant.

None of the study population had gone into dialysis dependency. And there were no mortalities observed during the follow up for a period of 12 months.

Limitations

- The sample size was small so it cannot be projected on to a large population.
- Shorter duration of study period.
- Individuals without any prior history of CKD or without any baseline values are assumed to have normal kidney function.
- Non randomised and purposive sampling technique was used
- for subject selection.

Recommendations

- As acute kidney injury is a leading cause of mortality in hospital further studies are required ,for its early detection.
- S.creatinine acts as one of the markers of acute kidney injury .
- Studies on new kidney injury molecules like kidney injury molecule 1 (KIM – 1) ,Neutrophil Gelatinase Assosciated Lipocalin (NGAL), urinary interleukin 18 are being currently studied and can be helpful for early detection of acute renal failure which can improve the prognosis in cases of reversible renal failure .

SUMMARY AND CONCLUSIONS

1. This study was designed to evaluate the sequelae and outcomes of acute kidney injury.
2. A total of 47 survivors of Acute kidney injury aged 15 years and above were followed up for one year
3. The age of patient varied from 15 to 71 years and the mean age was 48.23 years .There were 28 males and 19 females included in the study.
4. All patients underwent complete blood count, complete urine examination, blood urea, serum creatinine, serum electrolytes at admission and further follow up period and ultrasound abdomen and pelvis was done once during admission
5. In the study Majority (i.e., 27.66%) of the patients with AKI belong to age group between 51 to 60 years. Therefore incidence of AKI is more during 6th decade of life in the current study.
6. Sepsis contributes as a cause in majority i.e., 46.81% of patients with AKI by different mechanisms (either direct or indirect).
   Followed by acute gastroenteritis, acute pancreatitis and dengue accounting for second and third major cause of AKI.
7. Change in serum creatinine levels during follow-up periods was significant from admission till the end of 1 year i.e., in every followup till end of study period) with P value <0.001(<0.05). (Mcnemer test)
8. At time of admission all patients had abnormal creatinine and eGFR calculated at the end of 1 year for all study population as per MDRD eGFR formula (according to KDOQI CKD criteria [61]) showed that only 2 individuals (4.25%) had eGFR less than 60 ml/min/1.73m^2 and are labelled as chronic kidney disease according to KDOQI guidelines. Remaining 45 individuals (95.75%) had eGFR above 60 ml/min/1.73m^2.
9. Other parameters like urine analysis, routine hemogram and serum electrolytes took about 3 months to become normal.
10. The most common electrolyte abnormality found in the study population was hyperkalemia.
11. The most common hemogram abnormality was found to be
    Leucocytosis
12. None of them progressed into dialysis dependency at the end of the study period.

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