A STUDY ON ACUTE KIDNEY INJURY IN INTENSIVE CARE SETTING

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CERTIFICATE

This is to certify that this dissertation titled **"A STUDY ON ACUTE KIDNEY INJURY IN INTENSIVE CARE SETTING"** is the bonafide work done by **Dr. ELAVAZHAGAN.B,** Post Graduate Student (2010 – 2013) in the Department of General Medicine, Govt. Stanley Medical College and Hospital, Chennai under the direct guidance and supervision and in partial fulfillment of the regulations laid down by The Tamil Nadu Dr. M.G.R. Medical University, Chennai for M.D. Branch I, General Medicine Degree Examination to be held in April 2013.

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DECLARATION

I, **Dr. ELAVAZHAGAN.B.,** solemnly declare that the dissertation titled **"A STUDY ON ACUTE KIDNEY INJURY IN INTENSIVE CARE SETTING"** is a bonafide work done by me at Govt. Stanley Medical College and Hospital from May 2012 to Oct 2012 under the guidance and supervision of my unit chief, **Dr. P. VIJAYARAGHAVAN. M. D., Professor of Medicine.**

This dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University towards the partial fulfillment of the requirement of M.D. Branch I, General Medicine degree examination.

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LIST OF ABBREVIATIONS

1.	**AKI**	**Acute Kidney Injury**
2.	**ICU**	**Intensive Care Unit**
3.	**ACE**	**Angiotensin Converting Enzyme**
4.	**ADH**	**Anti Diuretic Hormone**
5.	**COX**	**Cyclooxygenase**
6.	**GFR**	**Glomerular Filtration Rate**
7.	**MDRD**	**Modification Of Diet In Renal Disease**
8.	**CKD**	**Chronic Kidney Disease**
9.	**FENA**	**Fractional Excretion Of Sodium**
10.	**BUN**	**Blood Urea Nitrogen**
11.	**ATN**	**Acute Tubular Necrosis**
12.	**HRS**	**Hepato Renal Syndrome**
13.	**DCLD**	**Decompensated Liver Disease**

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INTRODUCTION

Acute kidney injury is not a single disease but a terminology for a group of conditions that have similar diagnostic features, importantly, an elevation in the blood urea nitrogen (BUN) level and / or an elevation in the plasma or serum creatinine (S.Cr) concentration, often associated with a decrease in urine volume.

AKI can vary in severity from asymptomatic and transient changes in laboratory measures of glomerular filtration rate (GFR), to exaggerated and rapidly fatal derangements in effective circulating blood volume, electrolyte and acid-base composition of the plasma.

AKI is the cause for 5–7% of acute care hospital admissions and 30% of intensive care admissions. The epidemiology of AKI varies enormously between developed and developing regions, because of differences in demographics, social and cultural factors. But recent change in cultural habits, life style changes and social values in developing regions produce the near similar picture as developed countries.

The incidence of AKI has increased by more than fourfold in the United States from 1988 and is calculated to have a yearly incidence of 500 per 100,000 persons, more than the yearly incidence of cerebrovascular accidents. AKI causes a markedly increased risk of death in hospitalized persons, especially in those admitted to the ICU where in patient death rates may be more than 50%.

The term acute renal failure was changed to "acute kidney injury." The term *failure* denotes only portion of the spectrum of damage to the kidney that occurs clinically. Also the term *renal* is not well understood in the general population and this makes understanding with patients and their caretakers more difficult; so the term renal failure has been changed to acute kidney injury.

Western literature has lot of data regarding the occurrence and nature of acute kidney injury both in the community and inpatient setting. Sadly we are lagging behind in this regard as there are not many records or reports on this topic .This prompted me to take up this study which would throw light on the present scenario of acute kidney injury in intensive care unit. I sincerely believe in the relevance of this topic in our set up and hence chose this topic as my dissertation.

REVIEW OF LITERATURE

Kidney is the major organ involved in our body homeostasis. It maintains equilibrium between intracellular and extracellular compartments. It also protects against various insults occurring to the body which can be exogenous or endogenous. The kidneys functions can be excretory, synthetic, absorptive and it can operate as a paracrine or endocrine organ secreting hormones.

RENAL PHYSIOLOGY:

Nephron is the functional unit of the kidney. This functional unit is grossly divided into glomerulus and tubules. The glomerulus consists of afferent arterioles, efferent arterioles, tuft of capillaries, and Bowman's capsule. Podocytes covering the capillary endothelium play a significant role in forming the filtration barrier. Tubules can be divided into proximal convoluted tubule, distal convoluted tubule, loop of Henle and collecting duct.

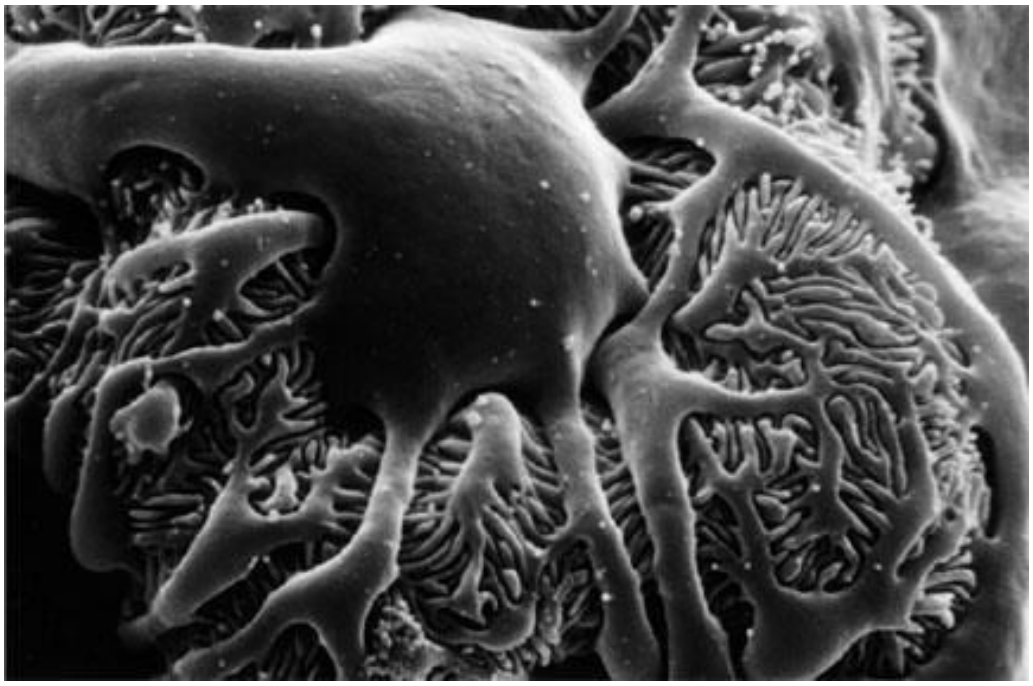
The blood flowing through the glomerulus gets filtered into the renal tubules as a plasma like fluid. As the filtered fluid passes further downward glomerulus, most of which gets absorbed. Only 1.2 litres of urine is excreted per day with nitrogenous waste products and acids arising from metabolism. Various regulatory processes have been involved in this mechanism. REGULATORY PROCESSES:

AUTOREGULATION:

Even though the mean arterial pressure of our body can vary from 90mm to 180 mm hg, the glomerular filtration is remarkably and reasonably kept at a constant rate by a process called – **auto regulation** –.

When there is reduced renal perfusion the afferent arteriole dilates and efferent arteriole constricts thereby increasing the filtration fraction and preserving the renal function. Prostacyclin is involved in afferent arteriole dilatation and angiotensin II in efferent arteriole constriction.

The **myogenic reflex**[1] is a defence mechanism against variations in glomerular blood flow. Acute changes in renal perfusion pressure causes reflex constriction or dilatation of the afferent arteriole in order to increase or decrease pressure. This mechanism helps to protect the glomerular capillary pressure from abrupt changes in mean arterial pressure.



This picture shows the glomerulus, and the podocytes which engulf the capillaries to form the filtration barrier.

TUBULO GLOMERULAR FEEDBACK

Whenever there is increased tubular flow, thereby indirectly indicating an increased delivery of sodium and chloride, the macula densa, which is present in the distal tubule senses the increased load and sends a signal which has been found to be probably adenosine, thus constricting the afferent arterioles and reducing the glomerular filtration.

GLOMERULOTUBULAR BALANCE:

Whenever there is increased glomerular filtration there will be an increased absorption of solutes along with an increased absorption of water. Indirectly this means the efferent arteriole, and the subsequently emerging peritubular capillaries carry less water and have a high oncotic pressure .This reflects in the interstitium too and following the Starling‘s forces, there is increased reabsorption of solutes and water from the tubules thereby maintaining constancy.

RENIN ANGIOTENSIN SYSTEM:

Whenever there is decreased sodium delivery to the distal tubules, the macula densa causes secretion of renin from the Juxta Glomerular cells via an ATP mediated mechanism. The renin converts angiotensinogen to angiotensin I which is converted to angiotensin II by ACE. This angiotensin II causes sodium retention by aldosterone mediated pathway.

WATER REABSORBTION

Antidiuretic hormone (ADH) plays an important role in producing concentrated or diluted urine by inserting aquaporin 2 channels in the luminal side of the collecting duct. The receptor for ADH action is the V2 receptor family. Whenever there is a dysregulation in this mechanism hyponatremia may occur due to the relative increase in the water content.

ACID BASE BALANCE:

Most of the hydrogen ions get secreted in the proximal convoluted tubule via Na^+H^+ antiport mechanism. Carbonic anhydrase mediates the production of H^+ ions in the renal tubular cells .The secreted H^+ ions are buffered by ammonium and diphosphate ions to maintain the ph of the tubular fluid. This is called urinary titrable acidity. H^+ ions also get secreted in the distal tubule by aldosterone mediated pathway.

POTASSIUM REGULATION:

Most of the potassium gets absorbed in the proximal convoluted bule. Potassium is also secreted in the collecting tubules by aldosterone mediated pathway.

COUNTERCURRENT MECHANISM

The Loop of Henle acts as a counter current multiplier which makes the medullary interstitium more hyper tonic compared to the cortex and the tubular lumen. This enables the production of more concentrated urine. The vasa recta acts as a counter current exchanger which also helps in making the medullary interstitium hypertonic by retaining urea and other solutes in the interstitium.

ACUTE KIDNEY INJURY PATHOPHYSIOLOGY:

The glomerulus and the tubules can get injured due to various causes. The glomerular filtration barrier is more susceptible to immune mediated injury which causes disruption of the barrier resulting in proteinuria and hematuria. It also gets affected by chronic diseases like diabetes and hypertension and diseases affecting renal vascular system like atherosclerosis and vasculitis.

Tubules get affected by ischemia particularly the S 3 segment [3] of the proximal convoluted tubule and thick ascending limb of the loop of Henle. The renal medulla is also more prone to ischemia due to vascular arrangement. The renal tubules are also affected by endogenous and exogenous toxins which cause direct injury to the tubular epithelium.

Any obstruction in the urinary outflow builds up a back pressure which increases the hydrostatic pressure in the Bowman‘s capsule resulting in decreased glomerular filtration.

By definition acute kidney injury is characterized by an abrupt decline of renal function which leads to an accumulation of nitrogenous waste products. It can be symptomless with subtle changes in the levels of urea; creatinine or it can be rapidly fatal.

APPROACH TO ACUTE KIDNEY INJURY:

First step is to identify

- the elevation in the blood urea nitrogen and creatinine
- any reduction in the urine output
- any alteration in the acid base changes
- accumulation of uremic toxins

Next is to find out whether it is reversible, either partially or fully with the aid of the clinical scenario.

A meticulous history regarding the fluid intake, drug intake, associated comorbid factors, associated infections and previous illnesses is crucial.

Look for anaemia, jaundice, rashes, patency of peripheral vessels and hydration status.

Identify the patients who need emergency intervention like renal replacement therapy which can be intermittent or continuous.

Identify the patients who are at risk of further progression.

CATEGORISATION

Categorise the patient into either pre-renal, intrinsic renal or post renal pathology.

Identify the site of the lesion whether it is in the glomerulus or tubules by urine microscopy.

PRE RENAL AZOTEMIA

Prerenal azotemia can occur in the following clinical scenario.
When there is reduced effective circulatory volume due to

- Dehydration
- Decreased stroke volume due to cardiac diseases
- Peripheral vaso dilation due to liver cell failure
- Sepsis

When there is defective renal auto regulation by

- ACE inhibitors
- COX inhibitors
- Cyclosporine

INTRINSIC AKI

Any event causing direct injury to the glomerulus, tubules, interstitium or renal vasculature leading to compromised renal function can cause this type of AKI. Causes include the following.

Glomerulonephritis by

i) immune mechanism

ii) viral infections(HBV, HCV, HIV)

iii) others(malaria, leprosy, leptospirosis, rickettsial infection)

iv) endocarditis

v) vasculitis

vi) storage disorders

Diseases affecting tubules-interstitium

i) ischemia

ii) sepsis

iii) exogenous toxins(drugs, contrast)

iv) endogenous toxins(hemolysis, rhabdomyolysis)

POST RENAL

- urethral obstruction
- Retro peritoneal fibrosis
- Bladder outlet obstruction

CLINICAL EVALUATION:

A patient with acute kidney injury may be oliguric or non oliguric. In oliguric AKI reduced urine output occurs before the elevation of creatinine, so monitoring the urine output will identify the AKI much earlier than the creatinine measurement.

In non oliguric AKI, we have to rely on urea, creatinine measurements to guide us. It takes around 24 hours for urea and creatinine to rise after GFR has reduced. Recent biomarkers may be helpful in early detection of AKI.

PITFALLS IN CREATININE AS A MARKER OF AKI[4]

- It varies with the muscle mass.
- In a wasted patient the creatinine may be inappropriately low. On the other hand in a muscular patient it may be spuriously high.
- Certain drugs can interfere with creatinine secretion. Eg. trimethoprim, cimetidine.
- Creatinine measurement by Jaffe's assay which is more commonly used may detect other chromogens as creatinine and show false elevation.
- In a non-steady state like AKI, creatinine cannot be used in GFR measuring formulas.

GFR MEASURING FORMULAS

CockGroft-Gault Formula:

GFR=(140-Age)*lean body weight/Serum creatinine *72

Multiplied by 0.85 in females

Modified MDRD formula:

GFR, in mL per minute per 1.73 m^2 = 186.3 × (serum $Cr^{-1.154}$)

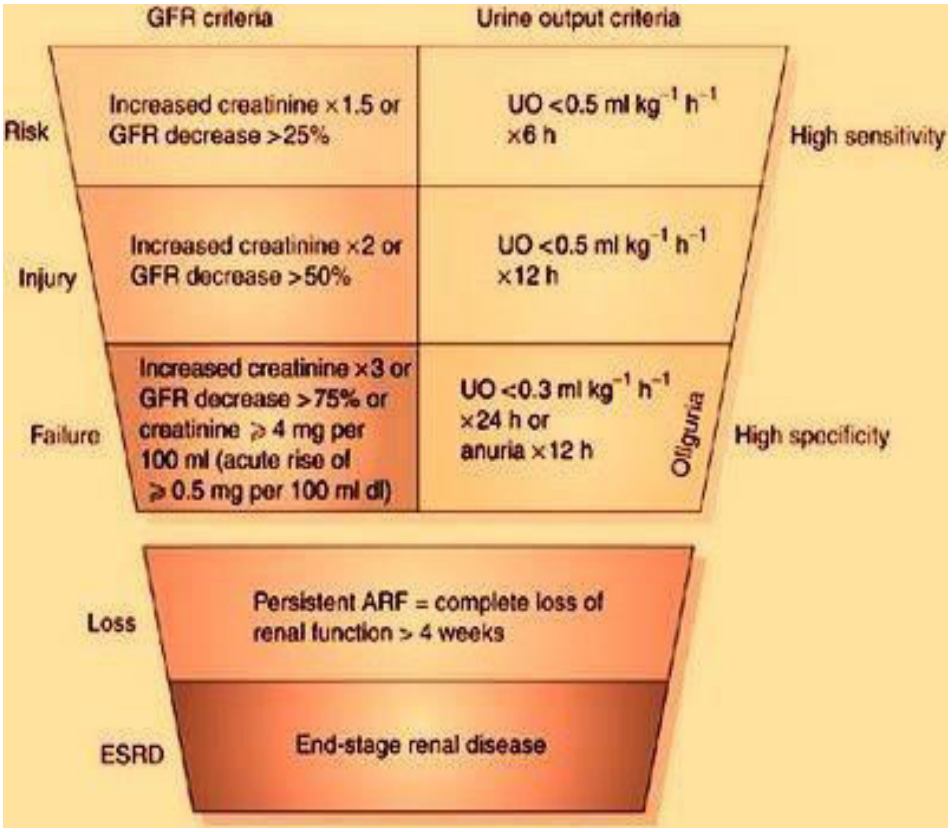
× ($age^{-0.203}$) × (0.742 if female)× (1.21 if black).

In case of AKI due to fluctuations in creatinine levels above said formulas will not be helpful. In these situations creatinine clearance serves as a better marker of GFR.

Creatinine clearance= urine creatinine x urine volume /serum creatinine

In order to avoid delay in diagnosis and assess the severity, a criteria[5] has been formed in 2004, by **the Acute Dialysis Quality Initiative workgroup**. This is a multilevel classification system for acute kidney injury (AKI) identified by the **acronym RIFLE**. It is based on creatinine and urine output. It is easily applicable in clinical setting.

RIFLE criteria has been validated by various studies in predicting the mortality of patients with AKI. Still further studies are going on. Some studies fail to show the utility of RIFLE criteria in assessing the severity of AKI, but most of the studies confirmed the significance of RIFLE criteria in AKI.



If a patient presents with increased urea and creatinine it may be due to acute kidney injury or pre- existing chronic kidney disease. Although it is difficult to differentiate the two conclusively at the initial presentation, certain variables may prove helpful.

In a patient with CKD and a GFR of less than 30 ml /min there is usually normocytic normochromic anaemia[4]. If a patient with GFR less than 30 ml/minand he is not anaemic it suggests recent onset of kidney injury.

On the other hand acute kidney injury can occur with anaemia in conditions like haemolytic uremic syndrome, thrombotic thrombocytopenic purpura. Thus it is understood that such approximations cannot be taken as a rule and decisions regarding diagnosis and management need to be individualised.

Another parameter of help is the kidney size. A kidney size of less than 10cm i.e a shrunken, fibrosed kidney with loss of cortico-medullary differentiation denotes chronic kidney disease.

Last but not the least meticulous history and previous records play a significant role in determining the disease onset.

CYSTATIN C

It is used as a marker of acute kidney injury. It can detect decrease in renal function earlier than creatinine elevation. It is not affected by the factors which interfere with the creatinine measurement. These are equivalent to cardiac troponins.

RECENT BIOMARKERS: [21, 22]

- β2 microglobulin
- Kidney injury molecule(KIM)
- Neutrophil gelatinase associated lipocalin
- Interleukin- 18
- Feteuin A.

AKI has been classified into

- Prerenal,
- Intrinsic
- Postrenal.

PRERENAL AKI

It is due to impaired renal perfusion by the local causes and systemic causes. Pathologically no injury or necrosis occurs to the renal tissue.

The main criteria to define the pre renal AKI is the return of urea, creatinine values to the baseline within 72 hours of correction of the hypoperfused state. The following variables will be of help in identifying the prerenal AKI.[4]

- Input-output chart
- Drug history like diuretic, NSAIDS
- Volume assessment by skin turgor, JVP.
- History of vomiting, diarrhoea, fever, burns.
- Any cardiac failure, shock, sepsis, chronic liver disease.
- Urine microscopy will be normal. No abnormal cast seen. Urine osmolality > 500 m Osm.
- Spot urine sodium less than 20 mEq.
- FeNa < 1
- BUN/Creatinine > 20

In a hypoperfused state the tubular absorption of sodium will be more, so the sodium excretion will be less in the urine. But associated diuretic usage will increases the sodium excretion by their inherent action.

TABLE 1. URINE ANALYSIS IN AKI

Diagnosis	Urinalysis	Urine-to-Plasma Osmolality	U_{Na} (mEq/L)	Fractional Excretion of Na
Prerenal	Normal	>1.0	<20	<1.0
Acute tubular necrosis	Granular casts, epithelial cells	≤1.0	>20	>1.0
Interstitial nephritis	RBCs, WBCs, ± eosinophils, granular casts	≤1.0	>20	>1.0
Glomerulonephritis	RBCs, RBC casts, marked proteinuria	>1.0	<20	<1.0
Vascular disorders	Normal or RBCs, proteinuria	>1.0	<20	<1.0
Postrenal	Normal or RBCs, casts, pyuria	<1.0	>20	>1.0

To overcome this problem **Fractional excretion of sodium (FeNa)** will be helpful. It is not affected by diuretic usage.[19]

FeNa =Urine sodium x plasma Creatinine x100/Plasma sodium x urine creatinine.

In case of reduced renal perfusion there will be more tubular absorption of urea in relation to the creatinine so the urea level will be disproportinately more than the creatinine levels. So the BUN:Creatinine ratio will be high.

In contrast, the BUN/Cr ratio may be decreased in decompensated liver failure, malnutrition, and rhabdomyolysis. In these conditions, low BUN/Cr ratio will occur as a result of a relative reduction in urea production, an increase in Creatinine production, or both.

POST RENAL AKI

Commonly occurs in old age.

Usually associated with

- Prostatic hypertrophy,
- Pelvic malignancy,
- Prostatic carcinoma
- Renal stone.

PREDISPOSING FACTORS:

- Diabetes mellitus
- Sickle cell anaemia
- Analgesic nephropathy
- Hypercalciuria.

Patient may have anuria or polyuria, urinary hesitancy, urgency, colicky abdominal pain.

Urine analysis will show RBCs with absent protein. In case of infection urine may be positive for pus cells and WBCs. USG might show hydronephrosis which it can occur in pregnancy as well as a normal phenomenon.

In retroperitonial fibrosis and early stages of other post renal diseases there will be no dilatation. CT abdomen and cystoscopy and retrograde pyelography will find out the level of lesion.

INTRINSIC RENAL AKI:

The pathology may be in the glomerulus, tubules, renal vasculature or interstitial tissue. Urinalysis forms the corner stone[1,23] in the evaluation of AKI and should be performed by the nephrologist. Abnormal urinary sediment strongly denotes an intrarenal cause for renal failure. Gross color changes in the urine may be seen with various intrinsic renal diseases.

For example, the urine of a patient with ATN usuallyappears **"dirty"** brown and opaque on gross examination due to the tubular casts. **Reddish-brown urine or "Coca-Cola" urine**[1] is diagnostic of some patients with acute glomerulonephritis and of those with pigment-induced tubular necrosis, including myoglobinuria .

- In glomerulonephritis granular cast, WBC cast, RBC cast can be seen.
- In acute tubular necrosis muddy brown granular cast can be seen.
- In interstitial nephritis WBC cast and eosinophiluria will be present.
- Crystalluria is usually seen in uric acid nephropathy, drug induced AKI and ethylene glycol intoxication.

Next to the urine analysis **renal biopsy** play a significant role in undiagnosed glomerular disorders, ATN, interstitial nephritis. When clinical, biochemical, and imaging studies are not adequate to arrive at a conclusion, a renal biopsy should be considered. Some studies show that biopsy in the setting of AKI often has unexpected findings.[24] Inspite of that **renal biopsy** is considered the **–gold standard‖** for diagnostic accuracy in AKI.

GLOMERULAR DISEASE:

Mostly it is immune mediated. Linear immune deposits along the glomerular basement membrane are seen in Good pastures disease.

Granular immune complex deposition is seen in postinfectious glomerulonephritis, lupus nephritis, infective endocarditis, IgA nephropathy, Henoch Scholein purpura, membranoproliferative glomerulonephritis.

Certain glomerular diseases do not have any immune complex deposition. Eg.Wegeners granulomatosis, Churg strauss, and microscopic polyangitis which are called as pauci immune glomerulonephritis.

ACUTE TUBULAR NECROSIS

Ischemia or toxin mediated direct damage results in acute tubular necrosis.

ISCHEMIC ATN

Ischemic injury to the renal tubules can occur due to the prolonged hypoperfusion which causes significant damage to the tubular epithelium. Normally the medullary interstitium is relatively hypoxic due to its vascular arrangements.

The S3 segment of the proximal convoluted tubule and the thick ascending limb are more prone for the ischemic injury.

Causes:

- Shock
- Haemorrhage

TOXIC ATN:

- Trauma
- Gram negative sepsis
- Pancreatitis

It can be due to any exogenous or endogenous substance. Exogenous causes are predominantly drugs and contrast media.

Drugs:

- Acyclovir,
- Amphotericin,
- Aminoglycoside,
- Fluorinated anaesthetic agents,
- Platinum compounds.

Aminoglycosides cause acute tubular necrosis. They get significantly concentrated in renal cortex .AKI develops five to seven days after the therapy and it may persist even after the discontinuation of the drug.

Amphotericin B causes increase in the tubulo-glomerular feedback, which promotes intense renal vasoconstriction. It is mainly dose and duration dependent. It is directly toxic to the tubules and also causes injury by the free radicals.

Acyclovir gets precipitated in the renal tubules and causes crystalluria and also causes direct tubular toxicity.

CONTRAST NEPHROPATHY:

Contrast agents which are predominantly iodinated can cause this type of renal injury. Rise in creatinine occurs after 48 hours, peaks around 5days and resolves after one week. Severe renal injury requiring dialysis is rare. Injury occurs mainly due to hypoxia in the medullary region , cyto toxic injury to the tubules, and tubule obstruction by the contrast media.

ENDOGENOUS TOXINS:

In case of rhabdomyolysis release of myoglobulins cause injury to the tubules. The causes of muscle injury include crush injury, compression fractures, excessive exercise, heat stroke, hypothyroidism, snake bite.

In case of hemolysis release of heme and globulins injure the tubular

epithelium. In multiple myeloma, the light chains injure the tubules.

If the uric acid level is more than 15 mg/dl uric acid gets precipitated in the tubules and results in tubular dysfunction.

The basic problem is due to intra renal vasoconstriction, direct toxicity, precipitation of molecules in the tubules. These solutes get precipitated in the tubules along with the Tamm Horsfall protein.

INTERSTITIAL NEPHRITIS:

Many drugs can produce an idiosyncratic reaction as an allergic response and injure the glomerular interstitium. It also can present acutely. The drugs commonly causing this include methicillin, rifampicin, sulfadrugs, nsaids.

Pathogenesis:

Lymphocytic and eosinophilic infiltration of the renal interstitium and edema of the interstitium.[6]

Certain infections may cause the same including bacteria like staphylococcus, streptococcus, mycobacteria and viruses like cytomegalovirus, Ebstein Barr virus.

Systemic non infectious diseases like systemic lupus erythematosis may also cause such a disease via immune mediated reaction.

VESSEL WALL DISORDERS:

Athero embolic AKI:

Patient may present with progressive renal failure in post angiography, post thrombolysis, post cardiac surgery.

Atherosclerotic plaques detach from the vessel wall and occlude the distal renal vessels. Urine analysis may show eosinophiluria, or may be bland. Extrarenal features include skin necrosis, livedo reticularis. Investigations reveal hypocomplementemia especially a low C 3 level.

Thrombotic micro angiopathies:

Endothelial injury causes activation of coagulation cascade and formation of platelet thrombi in small vessels leading on to haemolysis, anaemia, thrombocytopenia along with AKI.

Patient may have associated retinal haemorrhages, papilledema, CNS manifestations, malignant hypertension.

Two diseases with this same pathologic basis are haemolytic uremic syndrome and thrombotic thrombocytopenic purpura.

ACUTE KIDNEY INJURY IN SPECIAL SETTINGS:

AKI in sepsis:

The hemodynamic role of sepsis [1] is evident from the diffuse arterial vasodilatation, caused by cytokines which increase the expression of inducible NO synthase in the vasculature. This causes a decrease

The underlying mechanisms are

- Exaggerated efferent arteriole vasodilatation- especially early in the course of sepsis,
- Renal vasoconstriction from activation of the sympathetic nervous system,
- The renin-angiotensin-aldosterone system,
- Vasopressin, endothelin mediated.

Sepsis may lead to endothelial injury, which causes small vessel thrombosis, activation of reactive free radicals, and leukocyte adhesion and migration, all of which may damage renal tubular cells.

Though the idea of sepsis has been always associated with infection, there is an entity called systemic inflammatory response syndrome which is basically a dysregulated cytokine response and uncontrolled activation of inflammatory mediators which itself can cause significant renal morbidity. The various processes contributing to kidney injury in sepsis are as follows[7,8,9]

- Hypotension
- Inflammatory injury to the tubules
- Altered surface molecules in endothelium
- Activation of rennin angiotensin system
- Increased nitric oxide production
- Occlusion of the small vessels by the thrombus

Hypotension is not a prerequisite factor for development of AKI in sepsis.

ACUTE KIDNEY INJURY AFTER SURGERY

Several factors may play a role in causing AKI in the immediate post-surgical period.

The **fluorinated agents** used in anaesthesia sometimes produce nephrotoxic molecules which injure the renal tubules.

Post-operative and intraoperative **fluid imbalance** may cause prerenal azotemia.

Systemic inflammatory response syndrome occurs as a complication of surgery also produces renal shutdown.

Patients who undergo cardiopulmonary bypass surgery are more prone to the development of AKI because the non-pulsatile blood circulation and prolonged blood flow through the extra vascular circuits cause the activation of the inflammatory cascade and endothelial injury[10] Several risk stratification scoring systems for AKI after cardiac surgery, vascular surgery, general surgery, contrast-induced nephropathy, trauma have been developed .

Acute Physiology and Chronic Health Evaluation (**APACHE**) **I or II score,** though not specifically made for renal dysfunction, it is a helpful measure of severity of any illness and also a predictor of mortality.

The Cleveland Clinic Foundation (CCF) score is a preoperative[10] AKI risk score containing

The major risk factors are in postoperative AKI include

- Age more than 65
- Gender
- Uncontrolled hyperglycemia
- Refractory cardiac failure
- Chronic renal failure
- Surgeries which are done as emergency procedures.

PULMONARY RENAL SYNDROMES:

This term denotes the presence of lung involvement in a patient with renal failure in the form of hemoptysis. The common causes are

- Goodpasture‘s syndrome
- Wegener‘s granulomatosis
- Lupus nephritis

Some conditions mimic this entity called as _pseudo‘ pulmonary renal syndrome. These are:

- Buerger‘s disease with upper respiratory infections.
- Lower respiratory tract infection associated with post streptococcal glomerulo nephritis.
- Legionella infection with muscle injury.

CARDIORENAL SYNDROMES [12]

This is a far more common and worrisome problem than many kidney diseases in the cardiac ICU, that the nephrologist has to tackle

DEFINITION:

It is basically an altered hemodynamic state of cardiac and renal function in which acute or chronic problem in one organ will produce acute or chronic dysfunction in other organ. It has been classified into five types
Type 1: ***acute cardiorenal syndrome***:

- sudden dysfunction of heart causing acute renal injury.

Type 2: ***chronic cardiorenal syndrome*** :

- chronic dysfunction of heart causing acute kidney injury.

Type 3: ***acute reno cardiac syndrome*** :

- acute kidney injury causing acute heart failure.

Type 4: ***chronic renal cardiac syndrome***:

- chronic renal failure leads to heart failure and cardiac

remodulation.

Type5***: secondary cardiorenal syndrome***:

- systemic diseases results in both heart failure and kidney injury.

Pathopysiology underlying these syndromes include

- Hypoperfusion of the kidney due to low stroke volume
- Up-regulation of renin angiotensin system causing sodium and water accumulation.
- Inappropriate tubulo glomerular feedback.
- Secondary hyperaldosteronism
- Increased afterload to the heart.
- activation of the adrenergic system.

Treatment includes diuretics at increased dosage, ACE inhibitors, conivapten, tolvapten, paracentesis, peritoneal dialysis, extracorporeal ultrafiltration.

HEPATORENAL SYNDROME:

It is defined as a functional renal disease in patients with decompensated liver disease patients and portal hypertension. There is no structural damage to the glomerulus, tubules, or the interstitium.

There are two types.

Type 1 HRS:

Doubling of serum creatinine more than 2.5 mgs% or reduction in creatinine clearance <20 ml /min. It usually happens after an inciting event like infection. It has a grave prognosis. Death occurs within two weeks.

Type 2 HRS:

Less severe disease, patient life can be prolonged for six months. Rate of rise in serum creatinine less than the type one. It usually follows intractable diuretic resistant ascites.

Pathogenesis:

Dilatation of vessels in the splanchnic circulation caused by dilatory molecules released in the circulation. This decreases the peripheral resistance in the circulation and results in arterial under filling of glomerular capillaries.

As a compensation the renin angio tensin system gets activated leading to retention of sodium. The increased activation of the adrenergic system and endogenous vasoconstrictors produce intense glomerular vasoconstriction resulting in a reduced GFR.

DIAGNOSTIC CRITERIA:

In 1996 the international ascites club[13] had made a consensus and formed a criteria to diagnose HRS which included major and additional criteria. This has been revised recently to avert some confusions.

- Chronic liver disease with ascites
- Plasma creatinine above 1.5mg/dl
- No evidence of other cause of renal failure
- No evidence for continuous fluid loss
- Absence of shock
- No regression in renal failure after withholding diuretics for 2 days and infusion of albumin. Each one of the points above should be present to diagnose the hepatorenal syndrome.

Pseudo hepato renal syndrome:

Some systemic infections or conditions affect the liver and the kidney separately mimicking hepato renal syndrome. The causes are

- Sepsis, leptospirosis, tuberculosis, brucellosis
- Hepatitis B, C, HIV, liver abscess.
- SLE, vasculitis, sjogren syndrome, sacoidosis.

Treatment of hepato renal syndrome:

Treatment includes avoidance of diuretics, albumin infusion, vasopressors of the splanchnic circulation like terlipressin, vasopressin, midodrine and norepinephrine.[14,15] Octreotide can also be used.

In refractory cases intermittent hemodialysis can be used. All these are merely bridging measures to sustain life. The orthotopic liver transplantation is the definitive treatment.

COMPLICATIONS OF AKI:

Uremia :

Accumulation of nitrogen products in our body and uremic toxins causing cellular dysfunction and altered mental status.

Volume over load:

Patient may present with weight gain, dependent edema. Resolution of kidney injury maybe associated with increased urine output and volume depletion which is due to osmotic diuresis and incomplete recovery of tubular function.

Hyponatremia:

Iatrogenic administration of hypotonic solutions and decreased tubular sodium absorption and also decreased water excretion.

Metabolic acidosis:

Retention of organic and other acids and consumption of bicarbonate results in acidosis.

Hyperphosphatemia:

AKI is basically a catabolic state; Also seen in muscle injury; RBC destruction too results in increased phosphate levels.

Infections :

Many infections may result in AKI and vice versa an immuno compromised state resulting from renal failure makes the patient more prone for infections.

Cardiac problems:

- Pericarditis
- Arrhythmias
- Pericardial effusion

TREATMENT :

PRERENAL :

As it is a reversible state diagnosing the cause of under perfusion and correction of the cause is the primary treatment. It may be difficult to assess the volume status in AKI patient.

Fluid challenge of one litre over 1 hour will elevate the central venous pressure. If the elevation is more than 5cm there may be underlying cardiac failure. So cautious fluid replacement is necessary[4]

The central venous pressure cannot accurately reflect the volume status in left ventricular dysfunction. Pulmonary artery wedge pressure plays a main role in assessing the LV diastolic over load.

In cardiac failure digoxin along with diuretics will relieve the congestion. In liver disease intravenous albumin and vasopressors might be helpful.

INTRINSIC AKI:

- Avoidance of offending drugs,
- Adequate hydration in pigment induced nephropathies.
- Treating any infection appropriately , promptly and adequately
- Immunosuppressive drugs, steroids, plasmaphresis have been found to be useful.

Interventions:

Slow continous ultra filtration, continuous veno venous ultrafiltration, continuous venovenous hemodialysis, continuous veno venous dia filtration are the continuous renal replacement therapies.

Each one has its own merits and demerits.

Intermittent versus continous hemo dialysis:

Various studies are going on comparing the efficacy of both the modalities and assessing the superiority of one over other. Till now both have been proved to be equal in efficacy, provided they are used in appropriate clinical settings.[18]

Peritoneal hemodialysis:

Unlike the developed countries where the proportion of patients on peritoneal dialysis is far less than those on hemodialysis, the reasons for which are the subject matter of various studies, it is still widely prescribed to kidney disease patients in developing countries like India, especially in hemodynamically unstable patients. It has been found to have equal if not less efficacy to continuous renal replacement therapy.

POST RENAL:

Relieving the obstruction by Foleys or by any other means is the foremost thing in the treatment.

EPIDEMIOLOGY OF AKI: [16]

A. Community-acquired AKI.

The initial presentation itself is one of AKI in one percent of cases. Around 50 % of the AKI cases occur in patients with CKD. The most common causes of community-acquired AKI are follows;

- Prerenal azotemia (70%).
- postrenal (17%).

The death rate in community-acquired AKI is 15%.

B. Hospital-acquired AKI.[17]

The occurence of AKI in admitted patients is common. Using the RIFLE criteria, up to 20% of hospitalized patients may develop AKI.

The most common causes of AKI in hospitalized patients include ischemia, sepsis, medications, and radiocontrast dye.

Prerenal azotemia is one of the major forms of acute kidney injury in ward patients.

But ATN is responsible for the majority of causes of acute renal failure in ICU patients. ATN in the ICU is usually multifactorial and is frequently part of multisystem organ failure syndrome.

Prevention of AKI:

Many factors predispose hospitalized patients to the development of AKI: volume depletion, drugs which affect renal blood flow (e.g., NSAIDs and Cox-2 inhibitors), and the use of nephrotoxic medications and contrast dye.

Although data are limited on treatments to prevent AKI[20], it is prudent to carefully monitor volume status and maintain adequate hydration; discontinue (if possible) medications that are potentially nephrotoxic; choose alternate nonradiocontrast imaging techniques and use less nephrotoxic drugs.

Morbidity and mortality associated with AKI.

It is commonly thought that AKI from ATN is a completely reversible disorder. Recent data suggest that among patients who develop AKI in the ICU and require dialysis, 10% to 30% may require maintenance dialysis after discharge from the hospital.

Another widely held opinion is that patients die with AKI, not from AKI. Numerous well-controlled studies have challenged this hypothesis and declared that after adjusting for comorbidities, the development of AKI in hospitalized patients is an independent and significant predictor of in-hospital mortality.

TABLE 2. MORTALITY IN ACUTE KIDNEY INJURY (AKI)

Type of AKI	Mortality
AKI in the ICU associated with respiratory failure and the requirement of dialysis	>90%
AKI in the ICU	72%
AKI in hospitalized patients, not in the ICU	32%
AKI following intravenous contrast	34% (compared to 7% in controls) Adjusted odds ratio of death: 5.5
AKI following cardiac surgery	64% (compared to 4.3% in controls) Adjusted odds ratio of death: 7.9
AKI following administration of amphotericin B	Adjusted odds ratio of death: 6.6

So further studies are needed to understand the changing epidemiology of AKI, and also to find out the stage where we can intervene and reduce mortality

AIMS AND OBJECTIVES

1. To identify the incidence of acute kidney injury, their etiological factors, associated comorbid factors, interventions, and outcome in intensive care setting.
2. To address the factors which predict the mortality in acute kidney injury.

MATERIALS AND METHODS

STUDY DESIGN: Prospective observational study.

STUDY PLACE: Intensive medical care ward (IMCW) in Stanley Medical College and hospital, Chennai.

STUDY DURATION: May 2012 to October 2012 (6 months).

STUDY POPULATION: Those who were admitted in IMCU in that period, and also having acute kidney injury.

INCLUSION CRITERIA:

According to RIFLE criteria

- Patients who developed acute kidney injury during the hospital stay.
- Patients who developed acute kidney injury in the community.
- Patients who developed newer insult to a pre existing disease.

EXCLUSION CRITERIA:

- CKD patients who are in maintenance hemodialysis.
- Patients who got admitted and expired within 24 hours.
- Those who are not willing for the study.

After getting approval from institutional ethical committee, the study was started in IMCW. Patients were given the consent form, and explanation was given. Those who were willing to participate were included in the study.

HOW WAS THE STUDY CONDUCTED?

In the 6 months patients who got admitted in IMCU were monitored for development of AKI, and those who admitted with AKI also included in the study.

AKI was diagnosed based on RIFLE criteria.

- We mainly consider the creatinine values for the diagnosis. But urine output was also taken into the data.
- To find out AKI and differentiate acute from acute on renal disease by old records, ultrasonogram, other comorbid factors.
- Elevation of creatinine from baseline values for each patient was demonstrated.
- To differentiate the prerenal from intrinsic renal, the clinical scenario, BUN:Cr ratio, FeNa were taken into consideration.
- The associated comorbid factors, their course of stay, any significant events, the interventions they underwent were also documented.
- In hospital mortality or improvement has been set as a final point. Attempts were made to find out the etiology in every case.
- Those who were labelled with sepsis include sepsis due to urinary tract infection, soft tissue infection, pneumonia, CNS infections, and sepsis of unknown etiology.
- Only medical cases were included in the study, the surgical, trauma cases, post operative cases were not included in the study.

STATISTICAL ANALYSIS:

Statistical analysis was performed using IBM SPSS version 20. All categorical data were expressed as percentage of the whole. The continuous variables were expressed as Mean ± Standard Deviation.

Univariate analysis was performed using Chi Square test for categorical data and Mann Whitney U test was used for the continuous variables. The significance level was fixed at $p<0.05$. Adjusted Odds ratio with 95% Confidence interval was calculated as an estimate of the risk in those variables with statistically significant differences between the groups. Those variables which had p values less than 0.15 in the univariate model entered the multivariate logistic regression in backward conditional method. The odds ratio (Exp[B]) and level of significance (p) were obtained in the regression analysis. Variables with $p<0.05$ were taken as significant.

RESULTS

The study was conducted in our IMCW for 6 months. The study results were

as follows:

During the six month period total number of IMCU admissions were 700. The total no patients who developed AKI were 83.

The incidence of acute kidney injury was 118 per 1000 admissions. About 11.9% of the admissions had AKI in our IMCW .

Among the 83 cases, 43 cases were expired and 40 were discharged from ICU. The mortality rate was 51.8%.

TABLE 3. MORTALITY RATE:

TOTAL CASES	DISCHARGED	EXPIRED	MORTALITY
83	40	43	51.8%

TABLE 4. SEX DISTRIBUTION AND THEIR OUTCOME

SEX	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
Female	31	37.3%	15	37.5%	16	37.2%
Male	52	62.7%	25	62.5%	27	62.8%
			Chi square $(X)^2$=0.001		p=0.978	

In our study group, among the patients who developed AKI 52 were males and 31 were females. The percentage was 62.65 for males, 37.34 for females.

The percentage of patients developing AKI is more in males. Among the expired patients 27 were males and 16 were females with a percentage of 62.8 for males and 37.2 for females respectively.

But this had no statistical significance to predict that male gender is a risk factor for mortality in patients with AKI.

TABLE 5. AGE DISTRIBUTION IN AKI.

AGE GROUP	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
<30	8	9.6%	6	15.0%	2	4.7%
30-39	9	10.8%	1	2.5%	8	18.6%
40-49	19	22.9%	7	17.5%	12	27.9%
50-59	25	30.1%	16	40.0%	9	20.9%
>60	22	26.5%	10	25.0%	12	27.9%

Among the AKI patients, 25 were in the age group of 50-59. 22 were in the age group of more than 60. Among the expired those who were more than 60 and those between 40 -49 had increased percentage of mortality.

TABLE 6. PRIMARY CAUSE FOR ADMISSION

ADMITTED FOR	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
ADD	3	3.6%	3	7.5%	0	
CVD	7	8.4%	3	7.5%	4	9.3%
CNS	8	9.6%	5	12.5%	3	7%
MALARIA	1	1.2%	1	2.5%	0	
DCLD	13	15.6%	4	10%	9	20.9%
FULMINANT HEPATITIS	4	4.8%	1	2.5%	3	7%
RENAL	10	12%	4	10%	6	14%
SEPSIS	31	37.2%	15	37.5%	16	37.2%
CuSO4	2	2.4%	2	5%	0	
SOLANINE	1	1.2%	0		1	2.3
PANCREATITIS	1	1.2%	1	2.5%	0	
MALIGNANCY	1	1.2%	0		1	2.3
HYPOKALEMIA	1	1.2%	1	2.5%	0	

The above table shows the various diseases for which patient got admitted. Among these, the patients who got admitted for sepsis, were more prone to develop acute kidney injury. In the 83 patients, 31 were admitted for sepsis with a percentage of 37.2%.

13 patients who got admitted for decompensated liver disease developed AKI with a percentage of 15.6%.

Among the 83 AKI‘s, 10 were admitted for primary renal problem with a percentage of 12%. Among the expired patients, 37.2 % were admitted for sepsis and 20.9% were admitted for DCLD. The remaining were CNS 7%, CVD 9.3% and fulminant hepatitis was 7%.
Others were ADD, malaria, pancreatitis, copper sulphate, solanine poisoning and hypokalemia.

TABLE 7. COMORBID FACTOR – SYSTEMIC HYPERTENSION IN AKI.

SHT	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
Yes	23	27.7%	11	27.5%	12	27.9%
No	60	72.3%	29	72.5%	31	72.1%
			Chi square $(X)^2$=0.002		p=0.967	

Among 83 AKI patients 23 patients had SHT, 60 patients didn‘t have hypertension with a percentage of 27.7 and 72.3% respectively. In the expired group of patients, 12 had SHT and 31 did not have that, with a percentage of 27.9 and 72.1% respectively.

These values did not have statistical significance with a P value of 0.967.

TABLE 8. COMORBID FACTOR – T2DM IN AKI.

DM	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
Yes	34	59.0%	17	42.5%	17	39.5%
No	49	41.0%	23	57.5%	26	60.5%
			Chi square $(X)^2$=0.075		p=0.784	

Table 3 shows 34 out of 83 patients had diabetes mellitus and 49 don‘t have diabetes with a percentage of 59.0 and 41.0% respectively. Among the expired patients,

17 had diabetes and 26 on the otherside. 39.5% of the expired individuals had diabetes.

60.5% don‘t have this comorbid factor.

This is not statistically significant with a P value of 0.784.

TABLE 9. SPOT URINE SODIUM IN AKI – AN ANALYSIS

URINE SODIUM	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
<40	28	33.7%	9	22.5%	19	44.2%
>40	55	66.3%	31	77.5%	24	55.8%
			Chi square $(X)^2$ = 4.360		p=0.037*	

In 83 patients with AKI, 28 patients had spot urine sodium less than 40 and 55 patients had more than 40 and their percentage was 33.7, 66.3% respectively.

24 patients, who died had spot urine sodium more than 40 and 19 had less than 40 with a percentage of 55.8 and 44.2% respectively. This had a statistical significance with a P value of 0.037, which implies that spot urine sodium >40 is a predictor of mortality.

TABLE 10. SIGNIFICANCE OF FeNa IN AKI

FeNa	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
<1	29	34.9%	16	40.0%	13	30.2%
>1	54	65.1%	24	60.0%	30	69.8%
			Chi square $(X)^2$=0.870		p=0.351	

In total AKI patients 54 had FeNa >1 and 26 had less than 1.
The percentage was 65.1% and 34.9%. 30 out of 43 expired individuals had FeNa >1 and 13 individuals had <1%.

The percentage was 69.8 and 30.2% respectively. Although the death rate was more in the patients with FeNa >1, it was not statistically significant. The p value was 0.351.

TABLE 11. URINE ABNORMALITIES IN AKI

URINE ROUTINE	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
NORMAL	37	44.6%	14	35.0%	23	53.5%
SEDIMENT	46	55.4%	26	65.0%	20	46.5%
			Chi square $(X)^2=2.867$		p=0.090	

Among the 83 patients 46 had active sediments in the urine and 37 had no abnormalities with a percentage of 55.4 and 44.6% respectively.

In the 43 expired patients, 20 had active sediments and 23 had no sediments with 46.5% and 53.5% respectively.

The association between this urinary abnormality and death rate is not statistically significant with a p value of 0.090.

TABLE 12. URINE OUTPUT – A PREDICTOR OF MORTALITY

URINE OUTPUT	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
NON	45	54.2%	29	72.5%	16	37.2%
OLIGURIC						
OLIGURIC	38	45.8%	11	27.5%	27	67.8%
			Chi square $(X)^2=10.398$		p=0.001*	

Out of 83 patients, 38 were oliguric and 45 were non oliguric with 45.8% and 54.2% respectively. Among the expired 27 were oliguric and 16 were non oliguric. The percentage was 67.8% and 37.2% respectively. Oliguria was one of the predictor of mortality with statistical significance.

The P value was 0.001.

TABLE 13. HYPOTENSION AND AKI

HYPOTENSION	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
NO	43	51.8%	27	67.5%	16	37.2%
YES	40	48.2%	13	27.5%	27	62.8%
			Chi square $(X)^2=7.615$		p=0.006*	

Among the patients with AKI 40 persons had hypotension and 43 persons don‘t have hypotension during the course of hospital stay with a percentage of 48.2% and 51.8%.

Out of 43 expired individuals, 27 had hypotension and 16 didn‘t have that. The percentage was 62.8%, 37.2%.

This was statistically significant with a p value around 0.006.
Hypotension is a predictor of mortality in AKI.

TABLE 14. VENTILATOR SUPPORT IN AKI

VENTILATORY SUPPORT	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
NO	46	55.4%	27	67.5%	19	44.2%
YES	37	44.5%	13	27.5%	24	55.8%
			Chi square $(X)^2=4.559$		p=0.033*	

In total no AKI patients, 37 needed ventilator support and 46 didn‘t need that support. The percentage was around 44.5 and 55.4% respectively.

In 43 expired patients, 24 were on ventilator support and 19 were not on ventilator with the percentage around 55.8% and 44.2%.

This increased percentage had statistical significance with p value of 0.033.

Thus ventilator support in AKI patients is a predictor of mortality.

TABLE 15. DISTRIBUTION OF ACUTE AND ACUTE ON CHRONIC RENAL DISEASE

DURATION	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
ACUTE	46	55.4%	21	52.5%	25	58.1%
ACUTE ON CHRONIC	37	44.6%	19	47.5%	18	41.9%
			Chi square $(X)^2$=0.267		p=0.605	

Patients presented as acute renal failure without pre-existing renal disease were 46 (out of 83) which was 55.4%. Those who had underlying renal disease presenting as acute on pre existing renal disease were 37 out of 83(44.6%).

Among the expired, 25 were labelled as acute and 18 were have acute on chronic renal disease with 58.1% and 41.9% respectively.

Although there is increased percentage of acute presentation, it had no statistical significance. The p value was 0.605.

TABLE 16. DISTRIBUTION OF TYPE OF AKI:

PATHOLOGY	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
PRE-RENAL	25	30.1%	14	35.0%	11	25.6%
INTRINSIC-RENAL	58	69.9%	26	65.0%	32	74.4%
			Chi square $(X)^2$=0.873		p=0.350	

Among the 83 patients, 58 had intrinsic AKI and 25 had prerenal AKI with a percentage of 69.9%, 30.1%.

In 43 expired patients 32 had intrinsic renal and 11 had pre renal disease. The percentage was 74.4% and 25.6%.

This is not statistically significant with a p value of 0.350.

TABLE 17. DISTRIBUTION OF SEVERITY IN AKI

RIFLE CATEGORY	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
RIFLE-R	3	3.6%	2	5.0%	1	2.3%
RIFLE-I	36	43.4%	17	42.5%	19	44.2%
RIFLE-F	44	53.0%	21	52.5%	23	53.5%
			Chi square $(X)^2$=0.427		p=0.808	

Among the AKI patients, 3 were in the risk category, 36 in the injury, 44 in the failure category with the percentage of 3.6%, 43.4%, 53.0% respectively.

In the expired patients, 23 were in the failure category, 19 were in the injury category, 1 in the risk category. The percentages were 53.5%, 44.2%, 2.3% respectively.

This increase in ‗failure' percentage was not statistically significant to predict as a marker of mortality. P value was 0.808.

TABLE 18. INTERVENTIONS IN AKI

DIALYSIS	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
NONE	58	69.9%	29	72.5%	29	67.4%
PD	9	10.8%	5	12.5%	4	23.3%
HD	16	19.3%	6	15.0%	10	9.3%
			Chi square $(X)^2=1.004$		p=0.605	

Out of the 83 patients, 58 did not undergo any procedures. 16 underwent hemodialysis and 9 underwent peritoneal dialysis with the percentages 19.3% and 10.8% respectively.

In the expired patients, 10 underwent hemodialysis, 4 on peritoneal dialysis, 29 were not on any support with 9.3%, 23.3%, 67.4% respectively.

These percentages were not statistically significant as the p value was 0.605

TABLE 19. THE MEAN FOR AGE, SPOT Na, FeNa, CREATININE

PARAMETER	TOTAL		OUTCOME				Mann Whitney U test
			Discharged		Expired		
	Mean	SD	Mean	SD	Mean	SD	P value
AGE	49.96	14.23	50.28	16.13	49.67	12.39	0.616
INITIAL CREATININE	2.69	1.69	2.78	1.99	2.60	1.37	0.774
PEAK CREATININE	4.48	2.38	4.51	2.46	4.46	2.32	0.845
SPOT SODIUM	61.80	29.83	67.48	29.77	56.51	29.24	0.082
FeNa	1.14	0.37	1.12	0.36	1.17	0.37	0.601

The mean age for the patients developing AKI was 49.96 with SD of 14.23. Among the expired mean age was 49.67 with SD of 12.39. Mean for the initial creatinine was 2.69 with 1.69 SD. For the expired 2.60 was the mean initial creatinine.

For the peak creatinine, the mean was 4.48. Regarding the FeNa,
the mean was 1.14 with SD 0.37.

TABLE 20. CAUSES OF AKI

AKI CAUSE	TOTAL		OUTCOME			
			Discharged		Expired	
	Number	Percent	Number	Percent	Number	Percent
DRUG	2	2.4%	2	5.0%	0	0%
GN	4	4.8%	2	5.0%	2	4.7%
HRS	6	7.2%	1	2.5%	5	11.6%
HUS	6	7.2%	2	5.0%	4	9.3%
INFECTION	38	45.8%	17	42.5%	21	48.8%
RHABDO	1	1.2%	1	2.5%	0	0%
SHOCK	22	26.5%	12	30.0%	10	23.3%
TOXIN	4	4.8%	3	7.5%	1	2.3%

Among the causes, infection top the list with 38 cases (45.8%). Next come the shock due to various causes around 22 cases (26.5%). Other etiologies include HRS and HUS (7.2% each), toxins and glomerulo nephritis (4.8% each).

Among the expired patients, infection top the list and next comes shock, with 48.8%, 23.3% respectively. HRS was 11.6% among the expired.

TABLE 21. MULTIVARIATE LOGISTIC REGRESSION TO PREDICT MORTALITY IN AKI

S.No	PARAMETER	ODDS RATIO (EXP[B])	SIGNIFICANCE (p)
1	Oliguria	9.756	<0.001
2	Hypotension	6.490	0.003
3	Mechanical Ventilation	2.288	0.135

Multivariate logistic regression analysis was performed to analyse the parameters which were significantly influencing mortality in AKI in the univariate model (with p value <0.05). Oliguria and hypotension were the factors which were more likely to predict mortality in AKI with Odds ratio of 9.7 and 6.5 respectively. Mechanical Ventilation also had an Odds ratio of 2.3 in predicting mortality, but it fell short of significance in the final regression model (p=0.13).

DISCUSSION

Acute kidney injury is a clinical condition that complicates other diseases and when it is associated with other diseases the mortality and morbidity will increase.

Also it can occur as a primary problem with its complications resulting in mortality and morbidity. Acute kidney injury is caused by various etiological factors and environmental factors. After identifying AKI, the foremost thing is to find out the cause for it.

There are many studies, that are ongoing in the acute kidney injury correlating with various comorbibities. Already plenty of studies have been done on this one, still we are in a state to need know more about it.

Studies were done regarding the epidemiology, aetiology, severity, and outcome of patients on dialysis. Also AKI had been studied to find the heterogenous factors in relation to adult and paediatric population, in urban and tropical setting, also in developing countries and developed countries.

To assess the severity of the disease, various criterias were developed to manage them effectively. Studies had been done on these criterias to test the efficacy of the criteria in predicting the disease course.

AKI is traditionally classified into three: the community, in hospital, and in ICU. The predominant factors causing AKI were different in different settings. Also the mortality is varying with each entity.

There are plenty of literature on acute kidney injury in various scenarios in our western counterpart. On the contrary, there were very limited studies in our Indian population, especially in the southern side.

We conducted the study in the intensive medical care ward, in Stanley medical college from may 2012 to October 2012. The total admissions were 700 during that period. Of whom 83 patients developed AKI. The patients who stayed less than 24 hours excluded from the study and also those who already labelled as stage 5 CKD on hemodialysis.

The incidence of AKI in our ICU was 11.9%. According to the western literature the range of incidence was 5% – 15 % which is comparable to our data.

Regarding the sex distribution 62.7% were males, 37.3% were females. There is a male predominance in the data which implies male were prone to development of AKI. Also among the expired patients 62.8% were males. But these were not statistically significant.

In our study age distribution is more centred around **50 – 59** years of age and in individuals **more than 60 years**. But among the expired individuals, persons aged >60 years tops the list along with the persons between 40- 49. These were not significant to take as a predictor of mortality.

Comorbid factors like diabetes, hypertension were less in the AKI patients. More patients developed AKI without these comorbidities. The patients without diabetes and hypertension were more on the expired group.

The P values for these were more than 0.05.

Spot urine sodium is a marker used in AKI patients. If it is more than 40 which implies tubular dysfunction and intrinsic renal involvement, in the absence of diuretic usage. In 83 patients, 66.3% had

spot na >40. Also 77.5% expired persons had spot urine sodium > 40. Although it is not fool proof for tubular dysfunction, it proves as predictor of mortality in AKI patients, which is statistically significant.

Manytimes urinary abnormalities in AKI helps in diagnosis of the disease, which is more commonly in glomerular diseases and in UTI. In the study group, 55.4% had active sediments in the urine and in the mortality group 46.8% had active sediments. But these were not statistically significant.

The renal failure patients were usually categorized into oliguric, nonoliguric. It neither differentiates acute and acute on chronic nor does find prerenal or intrinsic renal. Nearly 45.8% was oliguric in the AKI patients and in the expired group it was 67.8% which is statistically significant as a predictor of mortality.

Oliguria usually occurs in various diseases like cardiac failure, hypovolemic shock, other than renal failure. If it is associated with AKI it is a significant factor in predicting the mortality.

In acute kidney injury patients 48.2% were hypotensive, and in the expired group 62.8 % were hypotensive. Hypotensive individuals include those persons who developed hypotension atleast one time during their ICU stay. This was statistically significant with a p value of 0.006, which predicts the mortality. Thus hypotension in AKI is a significant factor in predicting the mortality.

In ICU setting, patients will be connected to the ventilator due to various reasons. Among the AKI patients in our study 44.5% were connected to the ventilator and in the expired 55.8% were connected to the ventilator. Ventilator support is a predictor of mortality in AKI patients in ICU with significant P value of 0.033.

Acute kidney injury can occur on previously normal patients or in patients with underlying renal disease. In our study 55.4% presented as acute and 44.6% were acute on chronic renal disease. It doesn‘t have any influence on mortality. Usually underlying diabetes or hypertension had some proteinuria which results in renal injury.

We categorized the patients into prerenal and intrinsic renal based on clinical scenario, fena, hydration status and creatinine measurements. In AKI patients 69.9% were intrinsic renal and 30.1%were labelled as prerenal. Among the expired patients, 74.4% were intrinsic renal. Although it is not statistically significant, there were more intrinsic renal failure in the expired group.

Acute kidney injury patients can be managed conservatively or they may undergo dialysis. In our study patients, 69.9% was managed conservatively and 19.3% were on HD, and 10.8% on PD. Only 9.3% of the individuals on HD expired but the ratio is not statistically significant.

In acute kidney injury the severity is assessed with the help of RIFLE criteria which has more sensitivity. Many studies have proved that it is an independent predictor of mortality. But in our study among the AKI patients 53% were in the failure category, 43.4% were in injury category, and 3.6% in risk category . In the expired group, 53.5% were in the failure category and 44.2% in the injury category, but this not statistically significant. This may be due to less sample size and also less numbers in the R category.

Among the continuous variables like age, creatinine, spot Na, the mean and standard deviation were calculated. The mann whitney U test was used to find out the significance of the variable in predicting the mortality. The mean for age, peak creatinine, spot sodium were 49.96, 4.48, 61.80 respectively. The mean age among the expired was 49.67, spot sodium was 56.51.

Regarding the FeNa the mean was 1.17 with the standard deviation of 0.37 but this is also not statistically significant.

In the intensive care setting, patient will be admitted for various diseases involving various organs. Certain diseases were more prone for developing AKI. In our ICU, infection causes 45.8% of AKI. shock causes 26.5% of the cases, remaining cases were caused by the hepato renal syndrome, haemolytic uremic syndrome, glomerulonephritis, toxins, and drugs in decreasing order of percentage.

Among the expired, infection was the predominant cause of AKI with a percentage of 48.8% and shock causes 23.3%. The others were HRS, HUS, glomerulonephritis, toxin in decreasing order. Infection is the major cause of AKI in our study, which has been confirmed by other many studies, next was the shock from various causes which results in AKI.Infection is also the major cause of mortality in patients with AKI.

Copper sulphate poisoning is the most common cause of toxin induced AKI in our ICU. But the mortality is less in copper sulphate due to forced alkaline diuresis as a treatment modality.

There were only two cases of AKI occurred due to drugs. But there were no deaths. Due to more number of decompensated liver disease patients getting admitted in our ICU, a significant number of cases of AKI were caused by HRS, apart from infection causing AKI in the DCLD patients.

The above told statistical analysis were done by the univariate analysis, pearson chi- square test to predict the mortality with the associated variables. Further to increase the statistical significance, the factors

which predict the mortality with significance according to univariate analysis were included in the multivariate regression analysis. It confirmed that **oliguria and hypotension** significantly predicted the mortality. The **mechanical ventilation** predicts with less significance.

Hou et al[30] did a study on AKI in early days and reported a incidence of 4.9 percentage which was less comparable to the present status and the mortality rate was 25%. Few years later**, Nash et al**[31] found that the inhospital AKI incidence was around 7.2%, and the mortality rate was 19.4%. The predominant causes were decreased perfusion, toxins and major surgeries. These were the earlier data.

Sean bagshaw et al reported from a multicenter study which was conducted in Australian ICUs that,incidence of AKI in ICU was 5.2% with a yearly increase of 2.8% the mortality rate of AKI patients was 42.7%. The total duration of stay was more in the survivors than those expired.

Schaefer JH et al[25] found out the outcome predictors of acute kidney injury in ICU setting. They reported that the mortality rate was 56.7% in AKI patients in ICU. Also they found mechanical ventilation, hypotension were the significant predictors of mortality. The results of this study closely resembled our study results.

Brivet FG et al[26] did a multicenter evaluation of AKI in ICU. They preferably analysed the severe AKI. Their sample size was 360. Their results showed a mortality rate of 58%, which is higher than that of our study. The predictor of mortality were age, oliguria, sepsis, severity of illness, delayed renal failure, and previous hospitalisation. The predictors of mortality in this study partially resembles our study. Among the AKI patients 16 were prerenal, 282 were intrinsic renal, and 17 were post renal. As in our study the intrinsic renal group was more.

Abosaif NY et al[27] did a study on the outcome of AKI patients in intensive care setting according to RIFLE. They had 60 patients in risk category, 56 in injury category, 43 in failure category. They reported that ,those patients with failure category had increased death rate. They confirmed the ability of RIFLE criteria in predicting mortality. Also they found the RIFLE is correlating with the severity illness scores like APACHE II and SAPS score. In our study there were less patients in the R category. Also we
couldn‘t prove that RIFLE criteria predicts the mortality. As the severity increases the death rate doesn‘t show a rise in statistically significant manner.

Chologitas et al[28] did a study among the decompensated liver disease patients in ICU to find out the correlation of mortality with the severity of AKI. The overall mortality was 61.2%. They analysed with multivariate regression method, which showed RIFLE is a independent factor associated with mortality. But it is less useful than other severity scores like SOFA, APACHE II.

The famous **PICARD**[32] **(the program to improve care in acute renal disease**) study was conducted in 5 centers as a prospective observational cohort study over 3 years . They found a incidence of 25% - 60%, and reported a heterogenicity of distribution of AKI among all aspects. The common causes include ATN, intrinsic renal disease due to sepsis, nephrotoxin administration, cardiac diseases, and liver diseases. This mainly gave a conclusion of changing trends in the epidemiology of AKI.

The BEST study[33] **(the beginning and ending supportive therapy for the kidney**) is the largest prospective cohort study conducted over this topic. The mortality rate was around 60%. The predominant causes were septic shock, postoperative states, cardiac diseases, and toxin administration. The predictors of mortality were old age, sepsis, oliguria, blood urea nitrogen, severity score. Our study partially resembles this study in certain variables.

Ostermann et al[29] evaluated the utility of RIFLE in ICU setting. They found that AKI had an incidence of 35.8%. Among that17.2% were in risk category, 11% in I category and 7.6% in failure category. The mortality was more in the failure category.

RIFLE criteria predicts the outcome of renal failure but the associated multi organ dysfunction, severity of illness for which patients are admitted had a more significant impact in determining the outcome.

Cruz et al. did a prospective study and calculate the AKI incidence in ICU setting. It was around 10.8% the incidence closely resembles our study and 3.3% were required dialysis. Among the AKI patients, 19% were in Risk, 35% in Injury, and 46% in Failure category. As in our study this study has also more number of in failure category. The most common causes of AKI were prerenal 38.9% and sepsis 25.6%.

In the Indian studies for example, study on hospital acquired AKI conducted by **anupama kaul et al** over 12 months in a prospective manner, showed that baseline creatinine value, maximum RIFLE category, decreased urine output, metabolic acidosis were the predictors of mortality. They concluded that the epidemiology of AKI has been more or less similar to the western data.

Recently D Juneja et al did a study in ICU of a tertiary care hospital in New Delhi. They reported that patients with increased severity of AKI according to RIFLE had increased mortality. The mortality for the patients in failure group was 38% which is lower than our mortality rate.

Sural S et al did a study on acute kidney injury in ICU. Their results showed, the mortality rate was around 90%. The primary reasons for admissions were sepsis and multi organ dysfunction. They found out MODS is the only predictor of mortality with statistical significance.

Although the mortality rate in our study is high, it is comparable to the western data. Among the AKI patients, more common reasons for admission in ICU were sepsis, decompensated liver disease and cardio vascular diseases.

Although many studies has been proved the RIFLE criteria as a predictor of mortality our study couldn‘t prove that. This may be due to less sample size. Analysis done by multi variate regression showed oliguria, hypotension were the significant predictors of mortality. Ventilator support as a predictor of mortality has somewhat less statistical significance.

LIMITATIONS OF OUR STUDY:

- The sample size is small.
- It has been done in a single center.
- The postoperative cases, trauma cases, surgical cases were not been included.
- We didn‘ t use other severity scores like APACHEII, SAPS, SOFA.
- Only the in hospital mortality has been calculated.
- We didn‘t take urine output in consideration to diagnose AKI.
- Single group of population has been studied, so we cannot find out heterogenous epidemiology of acute kidney injury.

SUMMARY AND CONCLUSION

Acute kidney injury, a common problem in ICU, has a strong impact in the mortality and morbidity. Although there are rampant studies available in the west, there are less than a handful of study in south India. We had few similarities and dissimilarities in comparison to the western literature.

Results comparable to study done elsewhere:

- Incidence of AKI is11.7%
- Mortality rate is 51.8%
- Most common causes of AKI are sepsis, shock, and hepatorenal syndrome.
- Predictors of mortality are persistent oliguria requiring renal replacement therapy,hypotension, ventilator support.
- Incidence of AKI is more than acute on chronic kidney disease. Results dissimilar to study done elsewhere:
- Severity of AKI as per RIFLE did not correlate with mortality.
- Patients in RIFLE(R) were less in number.
- Age had no say in the mortality.
- Coexistent diabetes and hypertension did not influence the mortality.

There is one parameter, which is not taken into consideration in other studies (to the best of my knowledge), which is a independent predictor of mortality, is spot urine sodium (> 40). Further studies on large scale are required to prove its significance.

In short, infections and hypotension are the most common cause of mortality. Diligent care should be taken to find the etiology and to maintain fluid homeostasis. Patients who are oliguric and/or on ventilator should be managed with special precautions, as they are significant predictors of mortality.

BIBILOGRAPHY

1. Brenner and Rector‘s the kidney 8th edition.
2. William F. Ganong review of medical physiology 22nd edition.
3. Harrison‘s principles of internal medicine 18th edition.
4. Robert W Schrier manual of nephrology 7th edition.
5. Bellomo R, Ronco C, Kellum JA et al. Acute renal failure - definition, outcome measures, animal models, fluid therapy and informationtechnology needs: the Second International Consensus Conference of theAcute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8:R204-R212.
6. Jurgenfloege, Richard J.Johnson, John Feehaly comprehensive clinical nephrology 4th edition.
7. De Vriese AS. Prevention and treatment of acute renal failure in sepsis. *J Am SocNephrol*. 2003;14:792-805.
8. Riedemann NC, Guo RF, Ward PA. The enigma of sepsis. *J ClinInvest*. 2003;112:460-467.
9. Schrier RW, Wang W. Acute renal failure and sepsis. *N Engl J Med*. 2004;351:159-169. 10.Shroyer AL, Coombs LP, Peterson ED, et al. The Society of Thoracic Surgeons: 30-day operative mortality and morbidity risk models. *Ann Thorac Surg*. 2003;75:1856-1864; discussion 64-65.
11. Thakar CV, Arrigain S, Worley S, et al. A clinical score to predict acute renal failure after cardiac surgery. *J Am Soc Nephrol*.2005;16:162-1
12. Ronco C, House AA, Haapio M. Cardiorenal syndrome: Refining the definition of a complex symbiosis gone wrong. *Intensive Care Med*. 2008;34:957-962.
13. Oxford text book of Nephrology.
14. Duvoux C, Zanditenas D, Hezode C, et al. Effects of noradrenalin and albumin in patients with type I hepatorenal syndrome: A pilot study. *Hepatology*. 2002;36:374-380.
15. Alessandria C, Ottobrelli A, Debernardi-Venon W, et al. Noradrenalinvsterlipressin in patients with hepatorenal syndrome: A prospective,randomized, unblinded, pilot study. *J Hepatol*. 2007;47:499-505.

16. Lameire N, Van Biesen W, Vanholder R. The changing epidemiology of acute renal failure. Nat ClinPractNephrol 2006;2:364-377.

17. Mehta RL, Pascual MT, Soroko S, et al. Spectrum of acute renal failurein the intensive care unit: The PICARD experience. *Kidney Int*. 2004;66:1613-1621.

18. Ronco C. Continuous dialysis is superior to intermittent dialysis in acute kidney injury of the critically ill patient. Nat ClinPractNephrol 2007;3:118-119.

19. Carvounis CP, Nisar S, Guro-Razman S. Significance of the fractional excretion of urea in the differential diagnosis of acute renal failure. Kidney Int 2002;62:2223-2229.

20. Molitoris BA, Levin A, Warnock DG, et al. Improving outcomes of acute kidney injury:report of an initiative. Nat ClinPractNephrol 2007;3:439-442.

21. Parikh C, Cantley L, Devarajan P, et al. Biomarkers of acute kidney injury - early diagnosis, pathogenesis and recovery. J Investig Med 2007;55(7):333-340.

22. Nguyen MT, Devarajan P. Biomarkers for the early detection of acute kidney injury. *PediatrNephrol*. 2008;23:2151-2157.

23. Perazella MA, Coca SG, Kanbay M, et al. Diagnostic value of urine microscopy for differential diagnosis of acute kidney injury in hospitalizedpatients. *Clin J Am SocNephrol*.2008;3:1615-1619.

24. Preston RA, Stemmer CL, Materson BJ, et al: Renal biopsy in patients 65 years of age or older: An analysis of the results of 334 biopsies. *J Am GeriatrSoc* 1990; 38:669-674

25. Intensive Care Med. 1991;17(1):19-24.Outcome prediction of acuterenal failure in medical intensive care**.**Schaefer JH, Jochimsen F, Keller F, Wegscheider K, DistlerA.Source**.**Department of Internal Medicine, Free University, Berlin, FRG.

26. Crit Care Med. 1996 Feb;24(2):192-8.Acute renal failure in intensive care units--causes, outcome, and prognostic factors of hospital mortality; a prospective, multicenter study. French Study Group on Acute Renal Failure.Brivet FG, Kleinknecht DJ, Loirat P, LandaisPJ.SourceDepartment of Intensive Care, Hôpital Antoine BéclèreClamart, France.

27. Am J Kidney Dis. 2005 Dec;46(6):1038-48. The outcome of acute renal failure in the intensive care unit according to RIFLE: model application, sensitivity, and predictability. Abosaif NY, Tolba YA, Heap M, Russell J, El NahasAM.SourceSheffield Kidney Institute and Intensive Care Unit, Northern General Hospital, University of Sheffield, UK.

28. J GastroenterolHepatol. 2009 oct; 24(10): 163947. RIFLE classification as predictive factor of mortality in patients with cirrhosis admitted to intensive care unit.Cholongitas E, Calvaruso V, Senzolo M, Patch D, Shaw S, O'Beirne J, Burroughs AK.SourceThe Royal Free Sheila Sherlock Liver Centre and Department of Surgery, Royal Free Hospital, Hampstead, London NW3 2QG, UK.

29. Crit Care Med. 2007 Aug;35(8):1837-43; quiz 1852.Acute kidney injury in the intensive care unit according to RIFLE.Ostermann M, Chang RW.Source;Department of Intensive Care, Guy's and St Thomas' Hospital,London,UK.marlies@ostermann.freeserve.co.uk

30. Hou SH, Bushinsky DA, Wish JB, Cohen JJ, Harrington JT: Hospital-acquired renal insufficiency: A prospective study. *Am J Med***74** :243–248,1983.

31. Nash K, Hafeez A, Hou S: Hospital-acquired renal insufficiency. *Am J Kidney Dis***39** :930– 936,2002

32. Mehta RL, Pascual MT, Soroko S, Savage BR, Himmelfarb J, Ikizler TA, Paganini EP, Chertow GM: Spectrum of acute renal failure in the intensive care unit: The PICARD experience. *Kidney Int66:1613-1621 ,2004.*

33. Uchino S, Bellomo R, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Doig GS, Oudemans van Straaten H, Ronco C, Kellum JA: External validation of severity scoring systems for acute renal failure using a multinational database. *Crit CareMed***33** :1961–1967,2005.

PROFORMA

- **NAME :**
- **SL. NO:**
- **AGE /SEX:**
- **IP NO:**
- **DATE OF ADMISSION:**
- **DATEOF IMCU ADMISSION**
- **DATE OF DISCHARGE:**

- ***CLINICAL COURSE***
- **URINE ANALYSIS**

URINE ROUTINE

SPOT URINE Na+

URINE PCR
FeNa

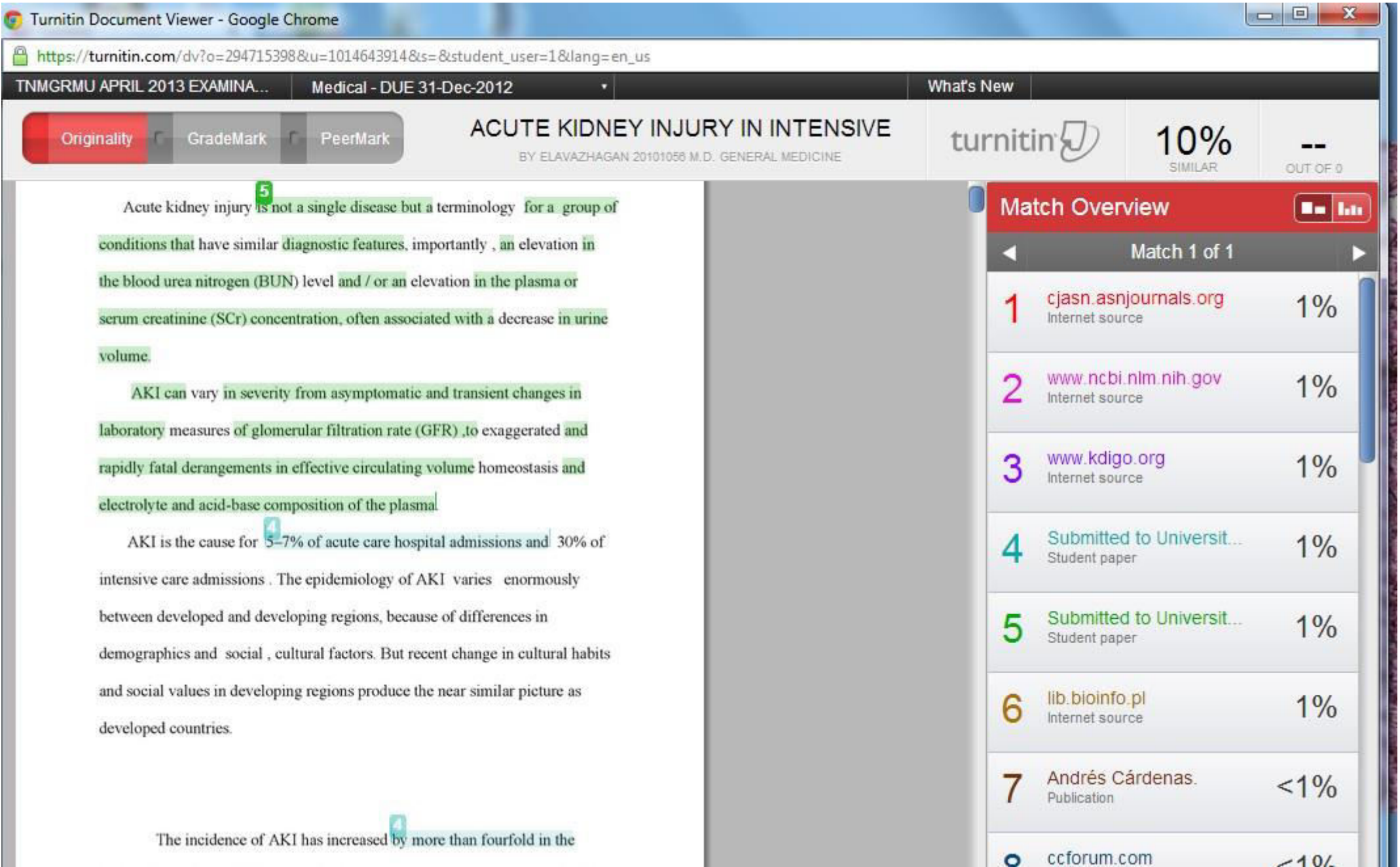
- CBC
- RBS
- RFT

	ADMISSION	**PEAK**	**DISCHARGE**
UREA			
CREATININE			

- **ELECTROLYTES**:
- **URINE OUTPUT**
- **ABG**
- **USG ABDOMEN**
- **OTHER RELEVANT INVESTIGATIONS**
- **DIAGNOSIS:**
- **DIALYSIS: PD/HD**
- **OUTCOME: DISCHARGED / EXPIRED**

KEY TO MASTER CHART

SHT	Systemic Hypertension
DM	Diabetes Mellitus
INIT-CR	Initial Creatinine
PEAK- CR	Peak Creatinine
DIS-CR	Discharge Creatinine
FENA	Fractional Excretion of Sodium
VENT	Ventilatory Support
CHRO	Chronicity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ACUTE KIDNEY INJURY IN INTENSIVE
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Acute kidney injury is not a single disease but a terminology for a group of conditions that have similar diagnostic features, importantly , an elevation in the blood urea nitrogen (BUN) level and / or an elevation in the plasma or serum creatinine (SCr) concentration, often associated with a decrease in urine volume.
AKI can vary in severity from asymptomatic and transient changes in laboratory measures of glomerular filtration rate (GFR) ,to exaggerated and rapidly fatal derangements in effective circulating volume homeostasis and electrolyte and acid-base composition of the plasma.
AKI is the cause for 5–7% of acute care hospital admissions and 30% of intensive care admissions . The epidemiology of AKI varies enormously between developed and developing regions, because of differences in demographics and social , cultural factors. But recent change in cultural habits and social values in developing regions produce the near similar picture as developed countries.
The incidence of AKI has increased by more than fourfold in the
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SL.No.	NAME	AGE	AGEGROUP	SEX	DURATION	ADMIN_FOR	SHT	DM	INIT_CR	PEAK_CR	DIS_CR	SPOT_NA	FENA	UROUTINE	URINE	HYPOTENSI	VENT	PATH	CHRO	RIFLE	AKI_CAUSE	DIALYSIS	OUTCOME
1	Hussian	58	50-59	M	12	CVD	Y	Y	1.60	7.00	3.40	40.00	1.20	A+	Non	No	No	IR	A/C	F	Drug	No	Dis
2	Subbbiah	73	>60	M	5	Sepsis	Y	N	2.20	5.00	0.00	70.00	1.10	Nor	OLI	No	Yes	IR	A/C	F	Infection	PD	Dis
3	Sivalingam	55	50-59	M	18	CVD	Y	N	1.10	8.20	0.00	80.00	1.03	A+	Non	Yes	Yes	IR	acute	F	Shock	PD	Dis
4	Rajarajan	36	30-39	M	20	DCLD	N	N	0.90	5.60	0.00	41.00	1.50	A2+/RBC+	OLI	No	No	IR	acute	F	Infection	No	Dis
5	Ravi	40	40-49	M	5	DCLD	N	N	1.30	1.80	1.20	28.00	0.90	Nor	Non	No	No	PR	acute	R	Infection	No	Dis
6	Ramamurthy	65	>60	M	3	CVD	N	N	1.50	2.20	0.00	17.00	0.70	Nor	OLI	Yes	Yes	PR	acute	I	Shock	No	Exp
7	Venkatesan	56	50-59	M	3	Sepsis	Y	N	2.80	6.10	2.20	80.00	1.30	A2+/PUS	Non	No	Yes	IR	A/C	F	Infection	HD	Dis
8	Subramanian	54	50-59	M	3	CVD	N	N	1.40	2.80	0.00	40.00	0.70	Nor	OLI	Yes	Yes	PR	acute	I	Shock	No	Exp
9	Praveen	27	<30	M	10	Sepsis	N	N	2.30	2.30	0.90	56.00	0.60	Nor	Non	No	No	PR	acute	I	Infection	No	Dis
10	Mani	49	40-49	M	7	Sepsis	N	Y	1.60	3.60	1.30	100.00	0.90	A+	Non	No	No	PR	A/C	I	Infection	No	Dis
11	suseela	68	>60	F	4	Sepsis	Y	Y	1.20	3.10	0.00	60.00	1.20	PUS+	OLI	Yes	Yes	IR	A/C	I	Infection	No	Dis
12	baby francina	53	50-59	F	9	Sepsis	Y	Y	6.40	6.40	6.10	155.00	1.10	A+/PUS+	Non	No	Yes	IR	A/C	F	Infection	PD	Dis
13	kathija	42	40-49	F	25	CNS	Y	Y	1.90	2.50	1.30	100.00	0.80	A+	Non	Yes	No	PR	A/C	I	Shock	No	Exp
14	sharmila	18	<30	F	12	CNS	Y	N	1.40	3.20	1.80	91.00	1.20	Nor	Non	No	No	IR	A/C	I	Rhabdo	No	Dis
15	saraswathy	57	50-59	F	6	Renal	N	N	4.20	4.20	1.80	68.00	0.90	RBC+	OLI	No	No	IR	acute	F	GN	HD	Dis
16	ayarnisha	54	50-59	F	4	Sepsis	Y	Y	0.60	4.50	0.00	68.00	1.40	A+/PUS+	Non	No	Yes	IR	A/C	F	Infection	No	Dis
17	Lakshmi	79	>60	F	4	Sepsis	N	Y	3.70	4.10	0.00	95.00	1.40	A+/PUS+	Non	No	Yes	IR	A/C	F	Infection	No	Dis
18	muniammal	62	>60	F	7	CNS	Y	N	1.70	3.50	1.90	18.00	1.30	A+	Non	No	No	IR	A/C	I	Drug	No	Dis
19	Rani	50	50-59	F	3	Sepsis	N	N	6.20	8.00	0.00	80.00	1.10	PUS+	OLI	No	Yes	IR	acute	F	Infection	PD	Dis
20	Kalaiyarasan	40	40-49	M	3	CVD	N	N	1.70	4.80	0.00	15.00	1.10	Nor	OLI	Yes	Yes	IR	acute	F	Shock	No	Dis
21	Rajesh	22	<30	M	8	Pancreatitis	N	N	8.70	12.00	0.00	80.00	1.30	A+/RBC+	OLI	No	No	IR	A/C	I	HUS	HD	Dis
22	Deivanayagi	62	>60	F	8	Sepsis	N	Y	2.50	2.60	1.10	60.00	0.70	A+	Non	Yes	No	PR	A/C	I	Shock	No	Dis
23	Rukmani	65	>60	F	6	Renal	N	Y	6.20	10.20	3.20	40.00	1.10	RBC+	OLI	No	No	IR	acute	F	HUS	HD	Dis
24	Elumalai	70	>60	M	9	DCLD	N	N	1.80	4.90	2.00	90.00	1.60	Nor	OLI	No	No	IR	acute	F	HRS	No	Dis
25	Vadivel	50	50-59	M	7	Sepsis	N	Y	0.80	2.80	1.40	133.00	0.90	A+	Non	Yes	No	PR	acute	I	Shock	No	Dis
26	Devaki	70	>60	F	14	CNS	N	Y	2.20	4.00	0.00	80.00	1.70	PUS+	Non	No	Yes	IR	A/C	F	Infection	No	Dis
27	Ramasamy	53	50-59	M	3	DCLD	N	Y	1.80	1.80	1.30	40.00	0.90	A+	Non	Yes	No	PR	acute	I	Shock	No	Dis
28	Akbar Ali	44	40-49	M	5	Hypokalemia	N	N	3.70	5.20	1.50	57.00	1.40	Nor	Non	No	Yes	IR	acute	F	Toxin	PD	Dis
29	Raja	40	40-49	M	12	CuSo4	N	N	0.90	1.80	1.10	110.00	1.80	A+/RBC+	Non	No	No	IR	acute	I	Toxin	No	Dis
30	Mythili	50	50-59	F	3	Sepsis	N	Y	2.70	2.70	2.10	78.00	1.60	A+	Non	No	Yes	IR	A/C	I	Infection	No	Dis
31	muniammal	40	40-49	F	7	Sepsis	N	Y	2.30	4.20	1.80	80.00	1.50	Nor	OLI	No	No	IR	A/C	F	Infection	No	Dis
32	Theresa	66	>60	F	9	CNS	Y	N	0.80	1.60	0.00	40.00	0.80	Nor	Non	Yes	Yes	PR	acute	R	Shock	No	Exp
33	Subramani	52	50-59	M	5	Sepsis	N	Y	3.90	4.20	0.00	80.00	1.80	A+/PUS+	Non	No	Yes	IR	acute	F	Infection	No	Dis
34	Murugan	57	50-59	M	14	CNS	N	N	0.70	2.20	0.90	28.00	0.70	Nor	Non	Yes	No	PR	acute	R	Shock	No	Dis
35	Jayaraj	25	<30	M	6	Malaria	N	Y	5.00	8.80	2.40	80.00	1.70	A+/RBC+	OLI	No	No	IR	acute	F	Infection	HD	Dis
36	Parameswari	40	40-49	F	3	Renal	N	N	2.10	2.40	1.00	60.00	1.20	A+/PUS+	Non	No	No	IR	A/C	I	Infection	No	Dis
37	Muthukrishna	55	50-59	M	6	Renal	N	N	8.30	8.30	4.40	72.00	0.70	A+/RBC+	Non	No	No	IR	acute	F	GN	HD	Dis
38	Jenath	50	50-59	F	3	Sepsis	Y	Y	0.90	2.50	0.00	100.00	2.00	PUS+	OLI	Yes	Yes	IR	A/C	I	Infection	No	Exp
39	Mathu	56	50-59	M	5	DCLD	N	N	2.20	4.90	0.00	28.00	1.10	Nor	Non	Yes	Yes	IR	acute	F	Infection	PD	Exp

40	Sumathi	34	30-39	F	3	Renal	N	N	3.40	7.00	2.80	42.00	1.20	RBC+	OLI	No	No	IR	acute	F	HUS	HD	Exp
41	Kurshid	56	50-59	F	6	Renal	Y	N	2.10	7.00	4.80	54.00	0.80	A+/RBC+	OLI	No	No	IR	A/C	F	GN	HD	Exp
42	Esther	50	50-59	F	5	Sepsis	N	Y	7.10	8.70	2.10	40.00	1.20	A+/PUS+	OLI	No	No	IR	A/C	F	Infection	HD	Exp
43	Kasthuri	60	>60	F	6	Renal	N	Y	3.80	6.20	2.60	40.00	1.20	A+/RBC+	OLI	No	No	IR	acute	F	HUS	HD	Exp
44	Govindhamm	45	40-49	F	6	Sepsis	Y	Y	3.20	5.80	1.30	74.00	1.30	A+/PUS+	OLI	Yes	No	IR	acute	F	Infection	HD	Exp
45	Shanmugam	38	30-39	M	6	Sepsis	N	Y	2.10	2.90	0.00	27.00	1.10	Nor	Non	Yes	Yes	IR	A/C	I	Infection	No	Exp
46	Kabbar	62	>60	M	3	Sepsis	N	N	2.60	3.50	0.00	22.00	1.10	Nor	OLI	Yes	Yes	IR	A/C	F	Infection	No	Exp
47	Ebenezer	80	>60	M	5	CNS	Y	N	1.50	4.20	1.80	20.00	0.50	Nor	Non	Yes	No	PR	A/C	F	Shock	No	Dis
48	Francis	45	40-49	M	3	malignancy	N	Y	1.60	2.50	0.00	44.00	0.60	Nor	Non	Yes	No	PR	acute	I	Shock	No	Exp
49	Valli	35	30-39	F	3	solanine	N	N	1.60	2.00	0.00	60.00	1.30	Nor	Non	Yes	Yes	IR	acute	I	Toxin	No	Exp
50	Kanchana	40	40-49	F	5	Sepsis	N	Y	0.60	4.00	1.80	133.00	1.90	A+/PUS+	Non	Yes	No	IR	acute	F	Infection	No	Exp
51	Senthil	26	<30	M	2	F.hepatitis	N	N	1.20	2.40	0.00	120.00	1.30	Nor	Non	Yes	Yes	IR	acute	I	Shock	No	Exp
52	Mani	52	50-59	M	7	CuSo4	N	N	1.60	1.90	1.10	86.00	0.80	HB+	Non	No	No	PR	acute	I	Toxin	No	Dis
53	Salwarbe	75	>60	F	7	Sepsis	N	Y	2.10	5.10	0.00	104.00	2.10	A+/PUS+	Non	No	Yes	IR	A/C	F	Infection	No	Exp
54	Sellammal	65	>60	F	2	Sepsis	N	Y	1.90	2.40	0.00	80.00	0.70	A+/PUS+	Non	Yes	Yes	PR	A/C	F	Infection	No	Exp
55	Kathuri	65	>60	F	10	Sepsis	N	Y	4.40	13.90	3.50	107.00	1.90	A+	OLI	Yes	No	IR	A/C	F	Infection	HD	Exp
56	Periyanna	19	<30	M	5	ADD	N	N	2.40	2.40	1.60	22.00	0.70	Nor	Non	Yes	No	PR	acute	I	Shock	No	Dis
57	Srinivasan	50	50-59	M	4	ADD	N	N	3.20	3.20	0.80	62.00	0.80	Nor	Non	Yes	No	PR	acute	I	Shock	No	Dis
58	Devadas	48	40-49	M	8	Sepsis	N	N	2.90	3.70	1.80	72.00	1.50	Nor	Non	No	No	IR	acute	I	Infection	No	Exp
59	Sekar	48	40-49	M	4	DCLD	N	Y	6.50	6.80	0.00	90.00	1.50	Nor	OLI	Yes	Yes	IR	A/C	F	Infection	No	Exp
60	Mathu	38	30-39	M	4	DCLD	N	N	1.50	6.50	0.00	28.00	1.40	Nor	OLI	No	Yes	IR	acute	F	HRS	No	Exp
61	Rajendiran	53	50-59	M	3	DCLD	N	N	2.20	5.20	0.00	40.00	1.30	Nor	OLI	No	No	IR	acute	F	HRS	No	Exp
62	Vasanthi	50	50-59	F	6	Sepsis	N	Y	2.10	2.40	1.90	70.00	0.50	K+	Non	Yes	No	PR	A/C	I	Shock	No	Dis
63	Durai	65	>60	M	2	Sepsis	N	N	4.80	5.80	0.00	80.00	1.80	PUS+	OLI	Yes	Yes	IR	A/C	F	Infection	PD	Exp
64	Padmanaban	66	>60	M	3	DCLD	N	N	2.20	2.80	0.00	42.00	1.30	Nor	OLI	No	Yes	IR	acute	I	Infection	No	Exp
65	Prithivirajan	46	40-49	M	2	DCLD	Y	Y	3.50	3.80	0.00	60.00	1.30	Nor	OLI	Yes	Yes	IR	A/C	F	Infection	No	Exp
66	Perumal	54	50-59	M	2	DCLD	N	N	4.10	6.20	0.00	40.00	1.10	Nor	OLI	No	No	IR	acute	F	HRS	No	Exp
67	anandhan	55	50-59	M	3	DCLD	N	N	3.20	5.60	0.00	40.00	1.10	Nor	OLI	No	No	IR	acute	F	HRS	No	Exp
68	Jayasree	37	30-39	F	3	F.hepatitis	N	N	2.10	2.40	0.00	64.00	0.60	PUS+	Non	Yes	Yes	PR	acute	I	Shock	No	Exp
69	Shakir	43	40-49	M	5	DCLD	N	N	2.20	3.40	1.80	28.00	1.01	PUS+	OLI	Yes	Yes	IR	acute	I	Infection	No	Exp
70	Abdul kasab	62	>60	M	2	Sepsis	N	N	1.30	2.10	0.00	26.00	0.70	Nor	Non	Yes	Yes	PR	acute	I	Infection	No	Exp
71	Mari	42	40-49	F	2	Sepsis	Y	Y	2.60	3.20	0.00	46.00	1.10	A+/PUS+	OLI	Yes	Yes	IR	A/C	I	Infection	PD	Exp
72	Senthil	20	<30	M	5	F.hepatitis	N	N	2.30	2.40	1.60	56.00	0.70	Nor	Non	Yes	No	PR	acute	I	Shock	No	Dis
73	Raja	30	30-39	M	3	Renal	N	N	4.50	6.00	2.80	30.00	1.10	RBC+	OLI	No	No	IR	acute	F	HUS	HD	Exp
74	Subramani	73	>60	M	3	Sepsis	Y	Y	2.80	3.10	0.00	80.00	1.30	A+/PUS+	Non	Yes	Yes	IR	A/C	I	Infection	No	Exp
75	Murugan	45	40-49	M	7	Sepsis	N	N	2.60	5.80	1.80	66.00	1.20	Nor	OLI	No	No	IR	acute	F	Infection	HD	Exp
76	dharmendiran	35	30-39	M	4	CNS	Y	N	1.50	2.80	0.00	58.00	0.90	Nor	Non	Yes	No	PR	acute	I	Shock	No	Exp
77	Mohan	47	40-49	M	6	Renal	N	N	3.20	5.80	1.90	30.00	1.10	RBC+	OLI	No	No	IR	acute	F	HUS	HD	Exp
78	Ganesan	28	<30	M	3	CVD	N	N	1.70	2.80	0.00	28.00	0.90	Nor	OLI	Yes	Yes	PR	acute	I	Shock	No	Exp
79	Ramamurthy	70	>60	M	5	ADD	Y	Y	3.70	4.20	2.20	70.00	0.80	Nor	Non	Yes	No	PR	A/C	F	Shock	No	Dis
80	Anwar basha	60	>60	M	3	F.hepatitis	N	N	3.20	6.80	0.00	30.00	1.20	Nor	OLI	No	No	IR	A/C	F	HRS	PD	Exp
81	Selvendiran	52	50-59	M	3	CVD	Y	Y	1.80	2.80	0.00	30.00	0.90	Nor	OLI	Yes	Yes	PR	A/C	I	Shock	No	Exp
82	Ravi	45	40-49	M	4	Sepsis	Y	Y	2.10	3.40	0.00	70.00	1.30	A+	Non	Yes	Yes	IR	A/C	I	Infection	No	Exp
83	Bangaramma	35	30-39	F	5	Renal	Y	N	2.90	5.20	3.40	80.00	0.90	A+	OLI	No	No	IR	A/C	F	GN	HD	Exp

INSTITUTIONAL ETHICAL COMMITTEE,
STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Study on acute kidney injury in intensive care setting

Principal Investigator : Dr.B.Elavazhagan

Designation : PG in M.D (GM)

Department : Department of General Medicine
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 11.06.2012 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

12/10/12

MEMBER SECRETARY,
IEC, SMC, CHENNAI

சுய ஒப்புதல் படிவம்
ஆய்வு செய்யப்படும் தலைப்பு

"தீவிர சிகிச்சை பிரிவில் தீவிர சிறுநீரக திறனிழப்பு பற்றிய ஓர் ஆய்வு"

ஆராய்ச்சி நிலையம் : அரசு ஸ்டான்லி மருத்துவமனை
சென்னை - 600 001.

பங்கு பெறும் நோயாளியின் பெயர் : வயது :

பங்கு பெறும் நோயாளியின் எண் : பாலினம் : ஆண் ☐ பெண் ☐

நோயாளியின் விலாசம் :

நோயாளி இதனை (✓) குறிக்கவும்.

மேலே குறிப்பிடப்பட்டுள்ள மருத்துவ ஆய்வின் விவரங்கள் எனக்கு விளக்கப்பட்டது. என்னுடைய சந்தேகங்களை கேட்கவும். அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டது. ☐

நான் என்னை இவ்வாய்வில் தன்னிச்சையாகதான் பங்கேற்க அனுமதிக்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும் எந்த சட்ட சிக்கலுக்கும் உட்படாமல் என்னை இவ்வாய்வில் இருந்து விலக்கி கொள்ளலாம் என்றும் அறிந்து கொண்டேன். ☐

இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்த மேலும் ஆய்வு மேற்கொள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். என்னை ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன். ☐

இந்த ஆய்வின் மூலம் கிடைக்கும் தகவல்களையும், பரிசோதனை முடிவுகளையும் மற்றும் சிகிச்சை தொடர்பான தகவல்களையும் மருத்துவர் மேற்கொள்ளும் ஆய்வில் பயன்படுத்திக் கொள்ளவும் அதை பிரசுரிக்கவும் என் முழு மனதுடன் சம்மதிக்கிறேன். ☐

இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக்கொள்கிறேன் எனக்கு கொடுக்கப்பட்ட அறிவுரைகளின்படி நடந்து கொள்வதுடன் இந்த ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்றும் உறுதி அளிக்கிறேன். என் உடல்நலம் பாதிக்கப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய் குறி தென்பட்டாலோ உடனே அதனை மருத்துவ அணிக்கு தெரிவிப்பேன் என உறுதி அளிக்கிறேன். ☐

நோயாளியின் கையொப்பம் ..... இடம் ..... தேதி

கட்டைவிரல் ரேகை (இந்த படிவம் படித்து காட்டப்பட்டு புரிந்து கைரேகை அளிக்கின்றேன்)

பங்கு பெறுபவரின் பெயர் மற்றும் விலாசம் .....

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ஆய்வாளரின் கையொப்பம் ..... இடம் ..... தேதி

ஆய்வாளரின் பெயர் .....