"PROGNOSTIC INDICATORS IN ACUTE RENAL FAILURE"

By

DR. CHRIS PHILIP MATHEW

Dissertation Submitted to the

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In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE

IN

GENERAL MEDICINE

Under the guidance of

DR. B.N. RAGHAVENDRA PRASAD, M.D.,

PROFESSOR AND HEAD OF DEPARTMENT

Department of General Medicine

Sri Devaraj Urs Medical College

Tamaka , Kolar.

MAY 2012

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Date:

Place: Kolar

Signature of the Guide

DR. B.N. RAGHAVENDRA PRASAD , M.D.,

Professor and HOD

DEPARTMENT OF GENERAL MEDICINE

SRI DEVARAJ URS MEDICAL COLLEGE

TAMAKA, KOLAR

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Dr. B.N. RAGHAVENDRA PRASAD, M.D.
Professor & HOD
Department of General Medicine
Sri Devaraj Urs Medical college
Tamaka, Kolar.

Dr. M.B.SANIKOP
Principal
SDUMC,
Tamaka, Kolar.

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Dr. Chris Philip Mathew

Sri Devaraj Urs Academy of Higher Education and Research, Karnataka

SRI DEVARAJ URS MEDICAL COLLEGE, TAMAKA, KOLAR

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Signature of Member Secretary

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Signature

Dr. CHRIS PHILIP MATHEW

ABSTRACT

Title: Prognostic indicators in acute renal failure.

Introduction: Acute renal failure complicates 45% of cases in the general setup and up to 70% cases in the intensive care unit setup. Knowing the possibility of death is essential to determine line of treatment and explaining prognosis to patient and relatives. Multiple organ failure is a grave prognostic indicator in acute renal failure.

Objective: To study the relation of indices to outcome in patients with acute renal failure.

Materials and methods: All patients above 18 years of age with acute renal failure who were admitted to R.L. Jalappa hospital and research center between April 2010 and June 2011 were included in the study. Those patients with preexisting chronic renal failure were excluded from the study. Statistical package for social sciences software version 14 was used for statistical analysis.

Results: Need for respiratory support, comatose state, thrombocytopenia and increasing number of complications are significant prognostic indicators according to this study. The mortality rate of patients in acute renal failure in this study was 26%.

Conclusion: Acute renal failure continues to be a leading cause of mortality in the hospital setup.

Prognostic scoring will help not only to explain prognosis but also in triaging patients in case of natural or man made catastrophes causing massive influx of patients to hospitals.

TABLE OF CONTENTS

Topic **Page number**

LIST OF FIGURES

Figure number **Topic** **Page number**

LIST OF TABLES

LIST OF CHARTS

INTRODUCTION

INTRODUCTION

Acute renal failure is a syndrome characterized by a rapid (hours to weeks) decline in glomerular filtration rate.[1] It is a condition in which a patient with no known previous renal impairment develops rapidly failing renal function with an acute increase in serum levels of substances excreted by the kidney.[2] An increase in creatinine more than 3 times of normal range or a decrease in glomerular filtration rate greater than 75% or urine output less than 400ml for 24 ours or anuria for 12 hours is evidence of acute renal failure.[3]

Acute renal failure (also called Acute Kidney Injury) complicates approximately 5% of hospital admissions and 30% of admissions to intensive care units.[4]

While acute renal failure complicates around 45% cases in general series and close to 70% cases in intensive care unit series, functional outcome is usually good among the surviving patients. As is true for any severe clinical condition, a prognostic estimation of acute renal failure is of great utility for both the patients and their families and the medical specialists for analysis of therapeutic maneuvers and options.[5]

A $\geq$ 101% increment of creatinine with respect to its baseline before nephrology consultation is associated with significant increase of in-hospital mortality.[6] Multiple organ failure is a poor prognostic factor in patients with acute renal failure in the setting of the intensive care unit.[7]

Aminoglycosides are the single biggest cause for drug induced acute renal failure.[8]

OBJECTIVE

OBJECTIVE OF THE STUDY

To study the relation of indices to outcome in patients with acute renal failure.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

Acute renal failure (also known as acute kidney injury) is a syndrome characterized by a rapid decline in glomerular filtration rate and retention of nitrogenous waste products like blood urea nitrogen and creatinine.[9] However in certain situations, the blood urea nitrogen and serum creatinine values may rise without an acute decline in glomerular filtration rate in chronic renal insufficiency and enhanced urea or creatinine production, inhibition of proximal tubule creatinine secretion, or circulating substances that cross-react with creatinine in laboratory assays.[10-19] Acute renal failure is a syndrome characterized by a rapid (hours to weeks) decline in glomerular filtration rate.[1] It is a condition in which a patient with no known previous renal impairment develops rapidly failing renal function with an acute increase in serum levels of substances excreted by the kidney.[2] An increase in creatinine more than 3 times of normal range or a decrease in glomerular filtration rate greater than 75% or urine output less than 400ml for 24 hours or anuria for 12 hours is evidence of acute renal failure.[3]

Inspite of these limitations blood urea nitrogen and creatinine are likely to remain the main method of diagnosis of acute renal failure in the foreseeable future.[9]

ETIOLOGY AND PATHOPHYSIOLOGY

The causes of acute renal failure have been categorized into prerenal azotemia, intrinsic renal parenchymal disease and postrenal obstruction.[20]

Prerenal Azotemia

Prerenal azotemia is the most common cause of acute kidney injury.[21,22]

Hypovolemia leads to mean arterial pressure fall which leads to activation of arterial and cardiac baroreceptors which leads to activation of sympathetic nervous system, the renin – angiotensin - aldosterone system and release of antidiuretic hormone.[23-26] Glomerular perfusion, ultrafiltration pressure and filtration rate are preserved through compensatory mechanisms during mild hypoperfusion, however these compensatory renal responses are overwhelmed during states of moderate to severe hypoperfusion.[27]

Figure-1

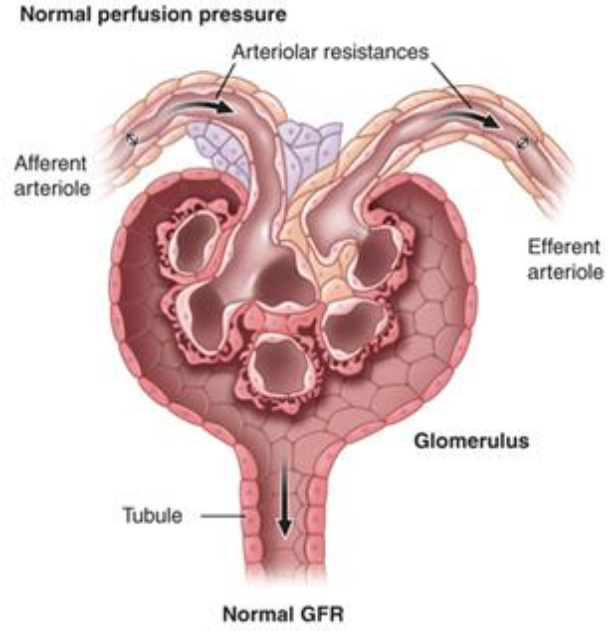


Figure-2

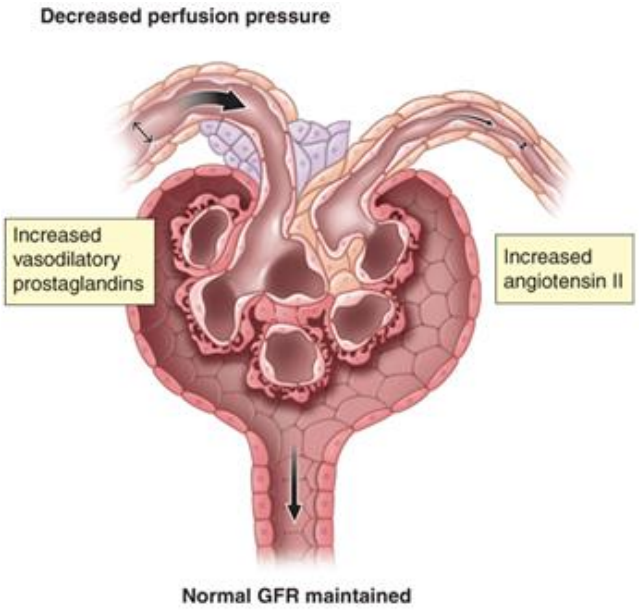


Figure-3

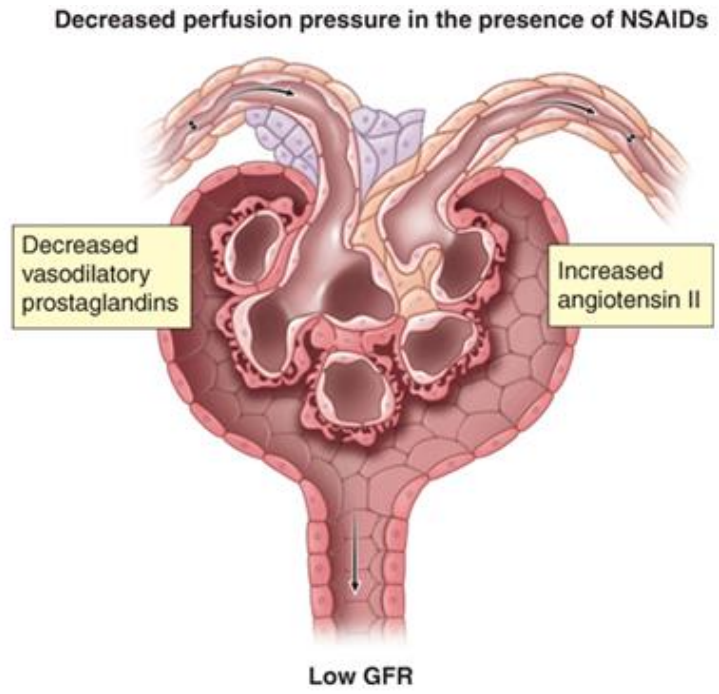
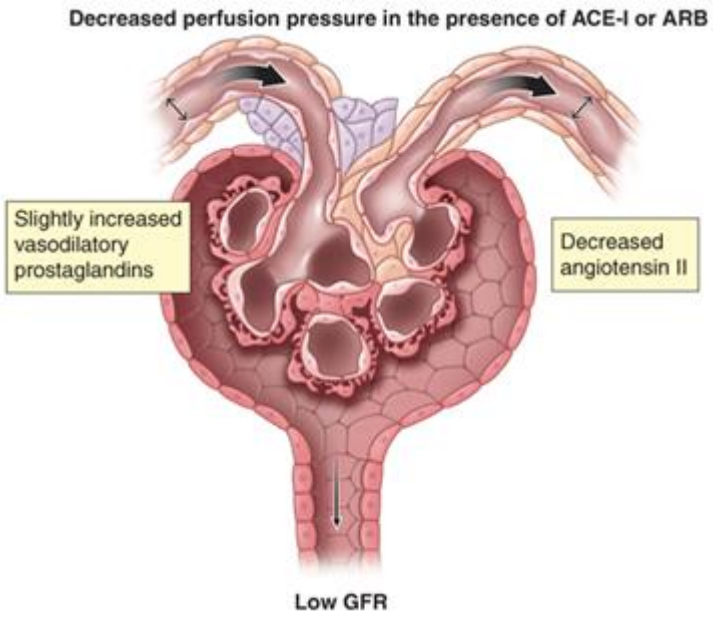


Figure-4

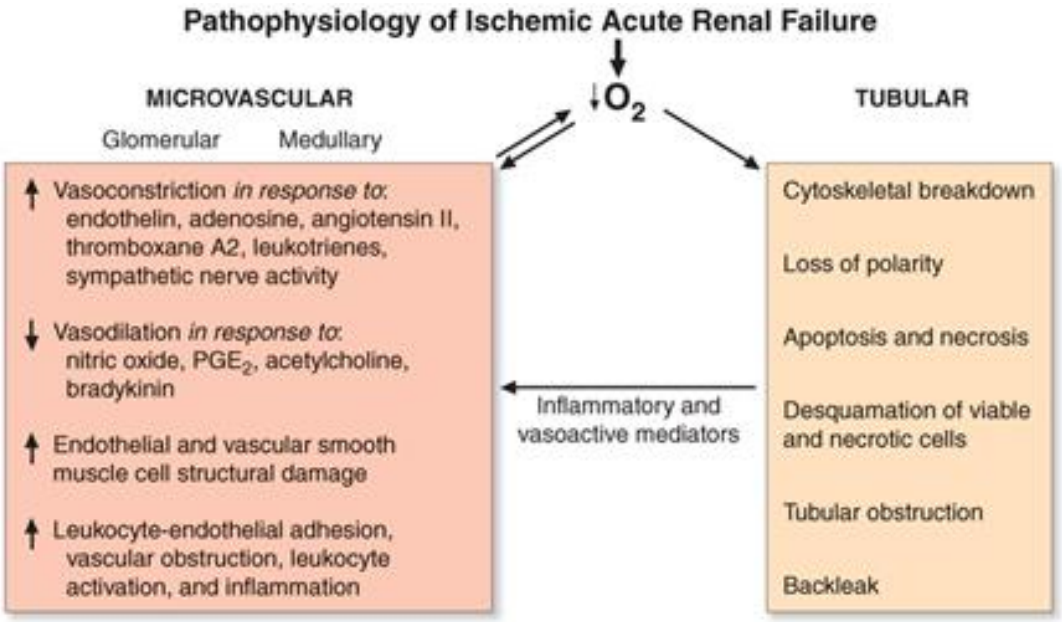


Intrinsic Renal Failure

Intrinsic renal failure is classified into diseases of the large renal vessels, microvasculature and glomeruli, acute tubular necrosis and diseases of the tubulointerstitium of which acute tubular necrosis accounts for 90% of acute intrinsic renal azotemia.[4,28,29] Acute tubular necrosis may be ischaemic or nephrotoxic. Ischaemic acute tubular necrosis is observed most frequently after major surgery, trauma, severe hypovolemia, overwhelming sepsis or burns.[30-32]

The increasing number of antimicrobial, anticancer and contrast agents causing nephrotoxic acute tubular necrosis requires clinicians to be increasingly vigilant.[33]

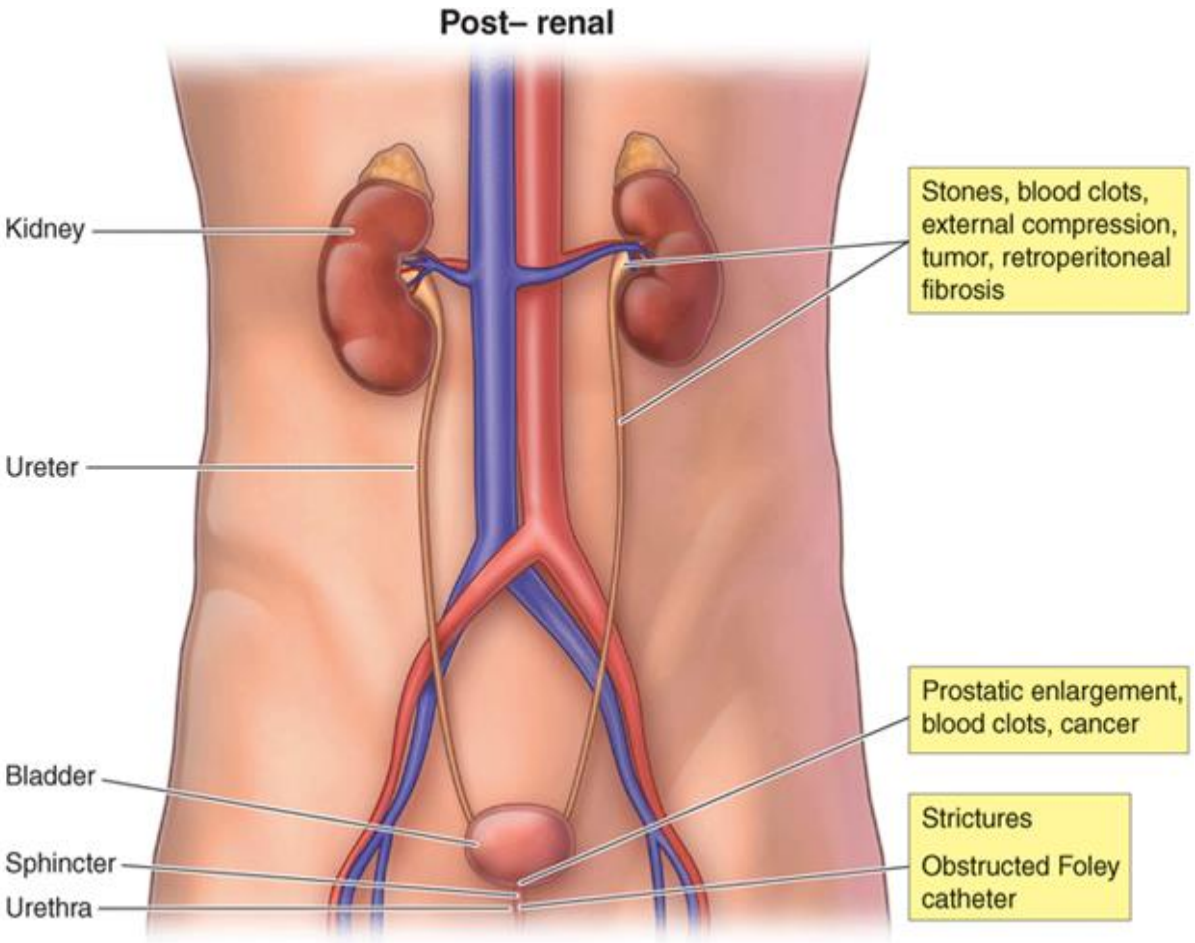
Figure-5



Post renal azotemia

Post renal azotemia due to urinary tract obstruction is responsible for less than 5% of cases of acute renal failure. Since one kidney has sufficient clearance capacity to excrete the nitrogenous waste products on a daily basis, the acute renal failure resulting from obstruction requires either obstruction at bladder neck, bilateral ureteric obstruction or unilateral ureteric obstruction in a patient with only one functioning kidney or underlying chronic renal insufficiency.[34]

Figure-6 – Sites of obstruction in post renal azotemia



PATHOLOGY

A profound decrease in the glomerular filtration rate is the effect of renal injury. There are at least three major mechanisms that have been proposed to explain the fall in glomerular filtration rate.

1. Drop in the glomerular filtration pressure due to afferent arteriolar vasoconstriction and proximal tubular obstruction.[35-39] Endothelial cell injury is thought to be the cause of afferent arteriolar vasoconstriction.[40]

2. Tubular back-leakage leading to fall in effective glomerular filtration rate. In the setting of denuded basement membranes and loss of tight junctions between those cells that are critical to maintaining separation of tubular filtrate and surrounding interstitium, the glomerular filtrate that enters the tubular space is allowed to leak back into the tubular interstitium and consequently reabsorbed into the systemic circulation.[41]

3. Tubular obstruction is a result of cast formation from sloughed tubular epithelial cells.

Besides a fall in glomerular filtration rate, there is also a decreased ability of the kidney to concentrate urine following acute kidney injury. This is due in part to the loss of aquaporin water channel expression in different parts of the nephron including the collecting duct and the proximal tubules.[42] Blocking inflammation with alpha

melanocyte stimulating hormone infusion can partially normalize aquaporin expression and allow the kidney to retain concentrating ability. The addition of erythropoietin is protective by maintaining aquaporin expression and concentrating ability.[43] Sodium and acid base transporters are also dysregulated by acute kidney injury.[44]

Inflammation

Inflammation plays a central role in acute kidney injury. From initiation to extension to repair, the inflammatory cells and soluble mediators are likely major determinants of the outcome of acute renal failure. A number of different inflammatory cells and soluble mediators have been shown to be necessary for causing full renal damage and loss of glomerular filtration.[45]

Microvasculature

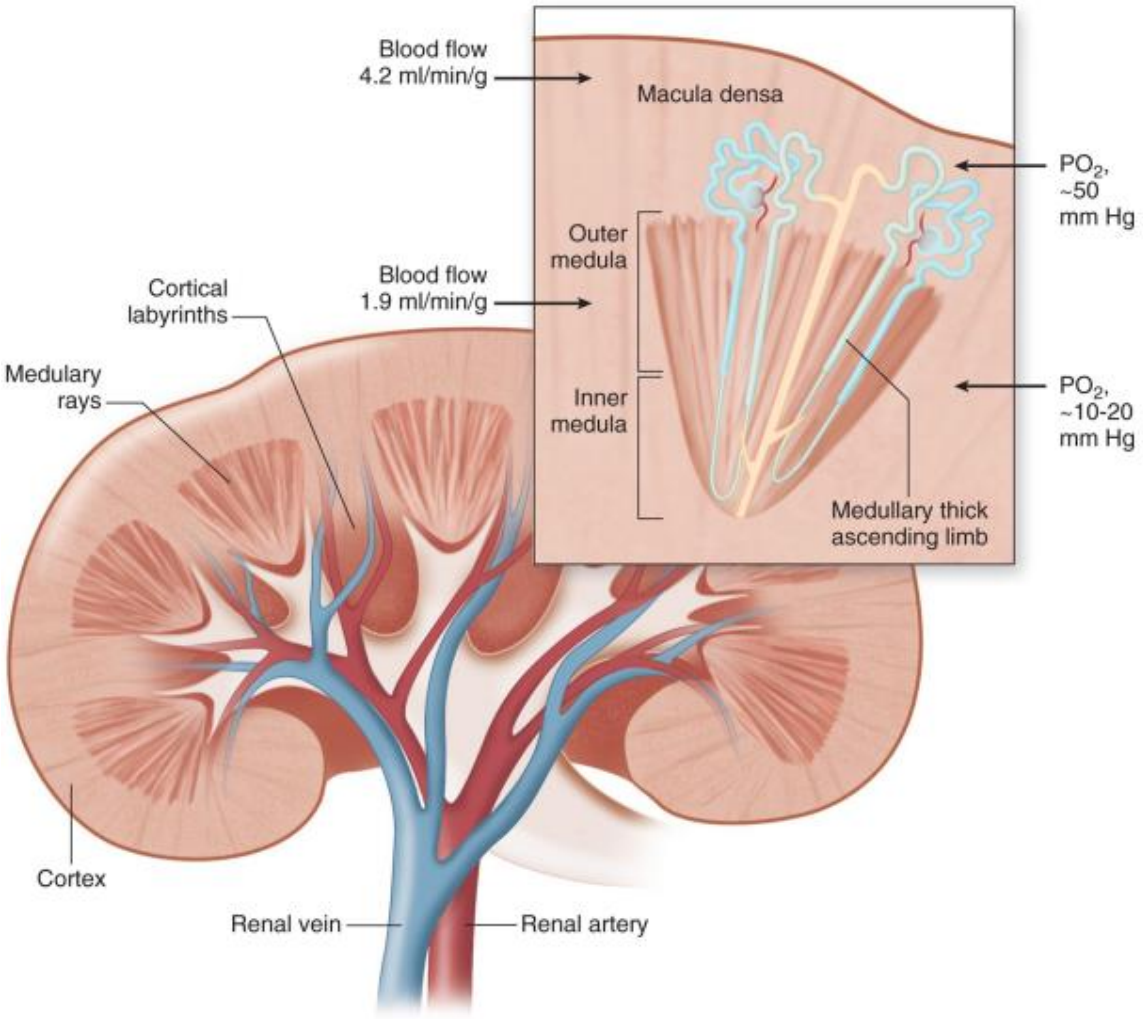
The kidney receives 20% to 25% of cardiac output and most of that blood flow goes towards the renal cortex.[46-48] Postglomerular vessels branching from the efferent arterioles eventually become the vessels of the vasa recta. The low flow state in the vasa recta is an important aspect of the countercurrent multiplier allowing appropriate trafficking of water and solutes.[47]

However the low flow state leaves the medulla relatively hypoxic when compared with the other regions of the kidney. Unlike the renal cortex with a partial pressure of

oxygen of about 50 mm of Hg, the outer medulla has a partial pressure of oxygen in the 10-20 mm of Hg range.[49]

Consequently very slight decreases in the blood flow and oxygen delivery can lead to anoxic damage. Hypoxia in the renal medulla can also predispose to other forms of renal injury, such as damage from aminoglycoside antibiotics.[50]

Figure-7 - Anatomic and physiologic features of renal cortex and medulla.



Leukocytes

Infiltrating neutrophils are infrequently seen on biopsies of human acute tubular necrosis but are known to infiltrate the kidney following an acute experimental ischemic insult.[51] Early inflammation is characterized by margination of neutrophils to vascular endothelium. Tethering interactions between selectins and their ligands initially slows neutrophils allowing firmer adhesion and transmigration by integrins and their ligands.[52]

Apoptosis

Apoptosis, or programmed cell death, plays an important role in the pathophysiology of acute renal failure. Apoptosis differs from cellular necrosis. Cellular necrosis is characterized by swelling of cells, loss of plasma membrane integrity, and eventually cell rupture with spillage of cellular contents into the extracellular space. In apoptosis, the cell nucleus and cytoplasm condense and then split off into smaller apoptotic bodies. Cytoplasmic organelles, including the mitochondria, are often intact and are phagocytized by macrophages or other cells, which leads to less spillage of cellular contents to cause inflammation.[53]

The effects of apoptosis on the host may change during the course of acute renal failure, ranging from harmful to beneficial, depending on the phase of disease. Initially, apoptosis may be deleterious to the kidney and overall renal function,

whereas during the recovery phase, apoptosis may be an important mechanism to regulate cell number and morphology.[54] The signs of apoptosis in the kidney, initially heralded by DNA fragmentation in the cells of the thick ascending limb, can be seen within 15 minutes of a hypoxic insult in the rat kidney.[55] The same findings were seen following a radiocontrast nephropathy injury model in rats. These early findings of apoptosis often precede any discernable deterioration in renal function. A second peak in the amount of apoptosis in renal tissue occurs days to weeks after the initial insult.[54] This peak often follows removal of necrotic tubular cells from the area, and may be a way to help regulate the number of newly generated cells.[55]

Endothelial Cell

The endothelial cell plays an important role in the development of acute renal failure. When an initial insult damages the endothelium of the renal vessels, the result is an endothelial bed that is ineffective in regulating local blood flow and cell migration into tissues, and preventing coagulation.[40,56]

Many of the endothelial changes in acute renal failure are more functional rather than structural in origin. It was found that tubuloglomerular feedback is preserved in prolonged ischemic acute renal failure, and that excessive Nitric Oxide as well as endothelium-derived hyperpolarizing factor antagonize autoregulation and cause endothelial dysfunction and a drop in glomerular filtration rate.[57]

Renal Tubular Epithelial Cells

The renal tubular epithelial cells, which are visible on routine light microscopy as well as urine analysis, are the most obvious cell type injured in acute renal failure. Injury and loss of epithelial cells, through necrosis or apoptosis can lead to loss of kidney function and apparent drop in glomerular filtration rate through processes of back-leakage of glomerular filtrate and tubular obstruction. The renal tubular cell has a remarkable ability to recover from an ischemic injury.[58]

Stem Cells

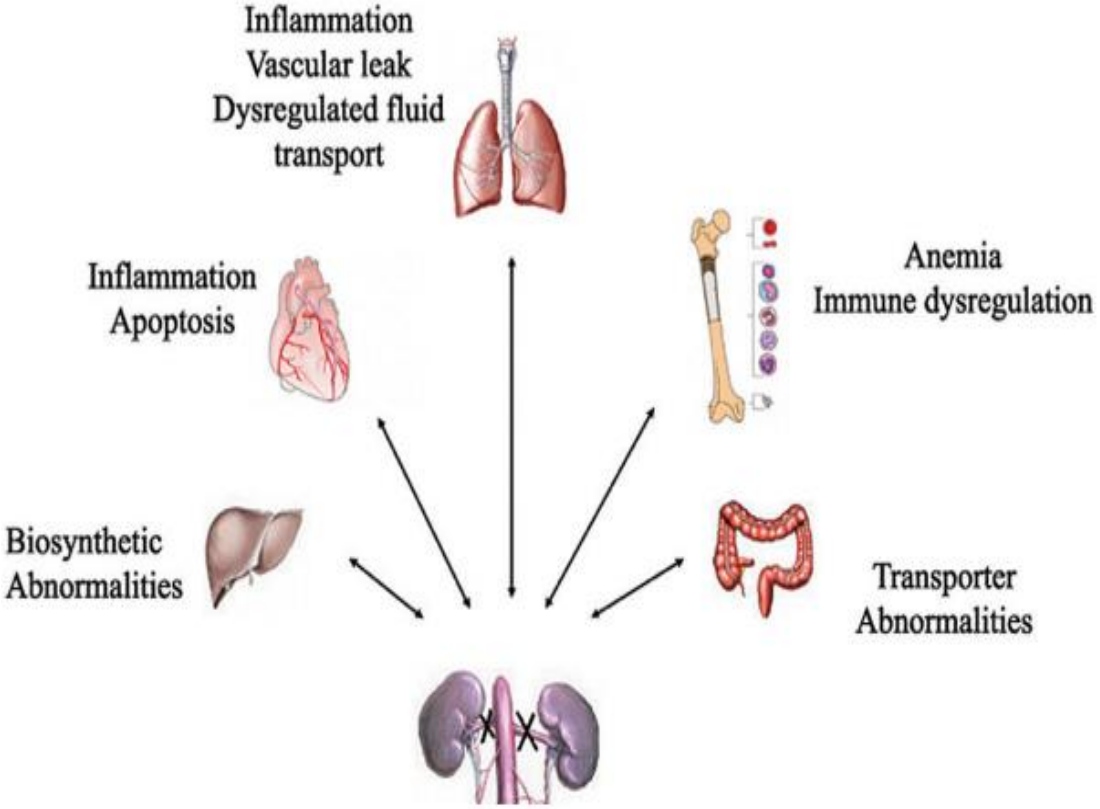
Infusions of mesenchymal stem cells at the time of, or up to 24 hours following an ischemic insult to the kidney, provided significant renal protection. Contrary to the initial thoughts, the renoprotective effects of mesenchymal stem cells are due more likely due to paracrine effects than to their differentiation into target kidney cells.[59,60] Mesenchymal stem cells infusions can also lead to improvement of acute renal failure by providing endothelial progenitor cells to repair injured microvasculature.[61,62]

Distant Organ Pathophysiology

Acute renal failure is a systemic disease, and with the availability of dialysis, most deaths during acute renal failure are due to hypotension, cardiorespiratory failure,

sepsis, and gastrointestinal bleeding. Organ cross-talk during acute renal failure may help explain the excess morbidity and mortality associated with even mild degrees of acute kidney impairment.[63]

Figure-8 – Distant organ effects following ischemic acute kidney injury



CLINICAL FEATURES

Prerenal Azotemia

1. Evidence of true volume depletion (thirst, postural or absolute hypotension and tachycardia, low jugular venous pressure, dry mucous membranes, weight loss, fluid output greater than input).

2. Decreased effective circulatory volume (e.g., heart failure, liver failure).

3. History of treatment with Non Steroidal anti-inflammatory drugs or Angiotensin Converting Enzyme Inhibitors.[73]

Intrinsic Renal Azotemia

Diseases involving large renal vessels

1. Renal artery thrombosis - History of atrial fibrillation or recent myocardial infarct, nausea, vomiting, flank or abdominal pain.

2. Atheroembolism - Usually > 50 years, recent manipulation of aorta, retinal plaques, subcutaneous nodules, palpable purpura, livedo reticularis, vasculopathy, hypertension.

3. Renal vein thrombosis - Evidence of nephrotic syndrome or pulmonary embolism, flank pain.[73]

Diseases involving small renal vessels

1. Glomerulonephritis or vasculitis - Compatible clinical history (e.g., recent infection) sinusitis, lung hemorrhage, rash or skin ulcers, arthralgia, hypertension, edema.

2. Hemolytic Uremic Syndrome or Thrombotic Thrombocytopenic Purpura - Compatible clinical history (e.g., recent gastrointestinal infection, cyclosporine, anovulants), pallor, ecchymoses, neurologic abnormalities.

3. Malignant Hypertension - Severe hypertension with headaches, cardiac failure, retinopathy, neurological dysfunction, papilledema.[73]

Acute Tubular Necrosis

1. Ischemia - Recent hemorrhage, hypotension, surgery often in combination with Angiotensin Converting Enzyme Inhibitor or Non Steroidal Anti Inflammatory Drugs or chronic renal insufficiency.

2. Exogenous toxin - Recent radiocontrast study, nephrotoxic antibiotic or chemotherapy often with coexistent volume depletion, sepsis or chronic renal insufficiency.

3. Endogenous toxin – Coma, seizures, drug abuse, trauma (rhabdomyolysis); recent blood transfusion (hemolysis); recent chemotherapy (tumor lysis), bone pain (myeloma), ethylene glycol ingestion.[73]

Acute diseases of tubulointerstitium

1. Allergic interstitial nephritis - Recent ingestion of drug and fever, rash, loin pain or arthralgia.

2. Acute bilateral pyelonephritis - Fever, flank pain and tenderness, toxic state.[73]

Post renal azotemia

Abdominal and flank pain, palpable bladder.[73]

The clinical course of acute tubular necrosis can be divided into 3 phases – the initiation phase, the maintenance phase and the recovery phase.

The initiation phase is the period when patients are exposed to the ischemia or toxins and parenchymal renal injury is evolving but not yet established. Acute tubular necrosis is potentially preventable during this period, which may last hours to days.

The maintenance phase is one during which parenchymal injury is established and glomerular filtration rate stabilizes at a value of 5 to 10 mL/min.[64,65] Urine output is usually lowest during this period. The maintenance phase typically lasts 1 to 2 weeks.
The recovery phase is the period during which patients recover renal function through repair and regeneration of renal tissue. Its onset is typically heralded by a gradual increase in urine output and a fall in serum creatinine, although the latter may lag behind the onset of diuresis by several days. This post-acute tubular necrosis diuresis may reflect appropriate excretion of salt and water accumulated during the

maintenance phase, osmotic diuresis induced by filtered urea and other retained solutes, and the actions of diuretics administered to hasten salt and water excretion.[65-67] Occasionally, diuresis may be inappropriate and excessive if recovery of tubule reabsorptive processes lags behind glomerular filtration, although this phenomenon is more common after relief of urinary tract obstruction. [68-71]

INVESTIGATIONS

Prerenal Azotemia

Blood urea nitrogen/creatinine ratio above 20

Hyaline casts, Fractional Excretion of Sodium < 1%, Urinary sodium < 10 mEq/L

Specific gravity > 1.018.[72]

Intrinsic Renal Azotemia

Diseases involving large renal vessels

1. Renal artery thrombosis – Mild proteinuria, occasional red cells

2. Atheroembolism – Often normal, eosinophiluria, rarely casts. Hypocomplementemia.

3. Renal vein thrombosis – Proteinuria, hematuria[73]

Diseases involving small renal vessels

1. Glomerulonephritis or vasculitis – Anti nuclear antibody, anti neutrophil cytoplasmic antibody, anti glomerular basement membrane antibody, decreased complement levels. Red blood cell or granular casts, red blood cells, white blood cells, proteinuria.

2. Hemolytic Uremic Syndrome or Thrombotic Thrombocytopenic Purpura - May be normal, red blood cells, mild proteinuria, rarely red blood cell or granular casts. Schistocytes on peripheral blood smear, elevated Lactate dehydrogenase, anemia, thrombocytopenia.

3. Malignant Hypertension - May be normal, red blood cells, mild proteinuria, rarely red blood cell casts.[73]

Acute Tubular Necrosis

1. Ischemia - Muddy brown granular or tubule epithelial cell casts, Fractional excretion of sodium > 1%, Urinary sodium > 20 mEq/L, Specific gravity = 1.010.

2. Exogenous toxin - Muddy brown granular or tubule epithelial cell casts, Fractional excretion of sodium > 1%, Urinary sodium > 20 mEq/L, Specific gravity = 0.010.

3. Endogenous toxin – Urine supernatant tests positive for heme in absence of red cells, elevated blood myoglobin, blood creatine kinase in rhabdomyolysis. Pink urine supernatant with heme positive in absence of red cells, anemia, elevated blood haptoglobin in hemolysis. Urate crystals in urine, blood hypocalcemia, hyperphosphatemia, hyperuricemia in tumor lysis. Dipstick negative proteinuria in myeloma. Oxalate crystals in ethylene glycol ingestion.[73]

Acute diseases of tubulointerstitium

1. Allergic interstitial nephritis - White blood cell casts, white blood cells (frequently eosinophiluria), red blood cells, rarely red blood cell casts, proteinuria (occasionally nephrotic) in urine.

2. Acute bilateral pyelonephritis - Leukocytes, occasionally white cell casts, red blood cells, bacteria in urine.[73]

Post renal azotemia

Frequently normal urine, hematuria if stones, hemorrhage, prostatic hypertrophy.[73]

MANAGEMENT

Prerenal azotemia

Severe acute blood loss should be treated with packed red blood cells.

Crystalloid or colloid should be used for less severe acute hemorrhage or plasma loss.

Cardiorenal syndrome (renal hypoperfusion from poor cardiac output) may require use of

a) inotropic agents,
b) preload- and afterload-reducing agents,
c) antiarrhythmic drugs, and
d) mechanical aids such as an intraaortic balloon pump.

Cirrhosis and Hepatorenal Syndrome

a) Administration of intravenous fluids as a volume challenge may be required diagnostically as well as therapeutically.
b) Peritonitis should be ruled out by culture of ascitic fluid.
c) Albumin may prevent acute renal failure in those treated with antibiotics for spontaneous bacterial peritonitis.
d) The definitive treatment of the hepatorenal syndrome is orthotopic liver transplantation.[73]

Intrinsic acute kidney injury

Acute glomerulonephritis or vasculitis may respond to immunosuppressive agents or plasmapheresis.

Allergic interstitial nephritis due to medications requires discontinuation of the offending agent.

Scleroderma renal crisis should be treated with Angiotensin converting enzyme inhibitors.

Rhabdomyolysis may require upto 10 litres of fluid per day. Alkaline fluids may be beneficial in preventing tubular injury and cast formation, but carry the risk of worsening hypocalcemia.

Diuretics may be used if fluid repletion does not achieve urinary flow rates of 200–300 ml/h.[72]

Postrenal acute kidney injury

Transurethral or suprapubic bladder catheterization for urethral strictures or functional bladder.

Ureteric obstruction by percutaneous nephrostomy tube placement or ureteral stent placement.

Supportive measures

1. Volume Management

Hypervolemia in oliguric or anuric acute kidney injury may be life threatening due to acute pulmonary edema, especially since many patients have coexisting pulmonary disease, and acute kidney injury likely increases pulmonary vascular permeability. Fluid and sodium should be restricted, and diuretics may be used to increase the urinary flow rate. There is no evidence that increasing urine output itself improves the natural history of acute kidney injury, but diuretics may help to avoid the need for dialysis in some cases. In severe cases of volume overload, furosemide may be given as a bolus (200 mg) followed by an intravenous drip (10–40 mg/h), with or without a thiazide diuretic. Diuretic therapy should be stopped if there is no response.[73]

2. Electrolyte and Acid-Base Abnormalities

Metabolic acidosis is not treated unless severe (pH <7.20 and serum bicarbonate <15 mmol/L).

Acidosis can be treated with oral or intravenous sodium bicarbonate, but overcorrection should be avoided because of the possibility of metabolic alkalosis, hypocalcemia, hypokalemia, and volume overload.

Hyperphosphatemia can be treated by limiting intestinal absorption of phosphate using phosphate binders (calcium carbonate, calcium acetate, sevelamer, or aluminum hydroxide).[72]

3. Malnutrition

Inadequate nutrition may lead to starvation ketoacidosis and protein catabolism. Excessive nutrition may increase the generation of nitrogenous waste and lead to worsening azotemia.[72]

4. Anemia

Uremic bleeding may respond to desmopressin or estrogens, but may require dialysis in the case of longstanding or severe uremia. Gastrointestinal prophylaxis with proton pump inhibitors or histamine receptor blockers is required. Venous thromboembolism prophylaxis is important and should be tailored to the clinical setting; low-molecular-weight heparin and factor Xa inhibitors have unpredictable pharmacokinetics in severe acute renal failure and should be avoided.[72]

5. Dialysis Indications and Modalities

Dialysis is indicated when medical management fails to control volume overload, hyperkalemia, acidosis, in some toxic ingestions, and when there are severe complications of uremia (asterixis, pericardial rub or effusion, encephalopathy, uremic bleeding). The initiation of dialysis should not await the development of a life-threatening complication of renal failure. Many nephrologists initiate dialysis for

acute renal failure empirically when the blood urea nitrogen exceeds 100 mg/dL in patients without clinical signs of recovery of kidney function.

Hemodialysis can be employed intermittently or continuously, and can be done through convective clearance, diffusive clearance, or a combination of the two. Vascular access is through the femoral, internal jugular, or subclavian veins. Hemodialysis is an intermittent procedure that removes solutes through diffusive and convective clearance. Hemodialysis is performed 3–4hours per day, three to four times per week, and is the most common form of renal replacement therapy for Acute Kidney Injury. One of the major complications of hemodialysis is hypotension, particularly in the critically ill. To counter the risk of hypotension, slow low efficiency dialysis can be used.[72]

PROGNOSIS

An ideal prognostic scoring system should be simple with limited clinical variables and parameters so that early and easy prognosis is made possible. Predicting the death of a patient in acute kidney injury with statistical certainty opens up ethical issues but also helps to provide optimal management strategies.

Early prognostic information is necessary to be able to provide a degree of assurance to the patient's attendants or to inform them that the statistical chance of survival of a particular patient very low. However prognostic scoring can only predict the prognosis of a group of patients and cannot guarantee survival or predict death of any particular patient as there will be those who survive against all odds. Hence no patient

should be excluded from dialysis, assisted respiration, or any other means of supportive treatment.

Prognostic scoring will be particularly helpful in natural or man made catastrophes where there is a sudden influx of patients but facilities are limited, triage must be done to give resources to those in whom better prognosis is expected.[74]

METHODOLOGY

MATERIALS AND METHODS

Source of Data

Patients who were admitted to R.L. Jalappa Hospital and Research Center, Tamaka, Kolar, attached to Sri Devaraj Urs Medical College from April 2010 to June 2011 with acute renal failure or developing the same during their stay in the hospital as evidenced by an increase in creatinine more than 3 times of normal range or a decrease in glomerular filtration rate greater than 75% or urine output less than 400ml for 24 hours or anuria for 12 hours.

Method of collection of data

Subjects were selected according to the following criteria with detailed history and physical examination. The prognostic indicators to be correlated with outcome – recovery or death – are

1. Age
2. Gender
3. Hypotension
4. Coma
6. Jaundice
7. Oliguria
8. Nephrotoxic medication
9. Respiratory support
10. Thrombocytopenia

Inclusion Criteria

1. Patients aged above 18 years of age.
2. Patients diagnosed to have acute renal failure.

Exclusion Criteria

Patients with chronic renal failure.

Study population and sample size

50 cases of acute renal failure were acquired during the study period.

Statistical Method

The data collected has been analyzed by Statistical package for social sciences software version 14 (Chicago, Illinois) using chi square descriptive analysis and Pearson chi square test. Tests of significance of p value less than 0.05 was employed.

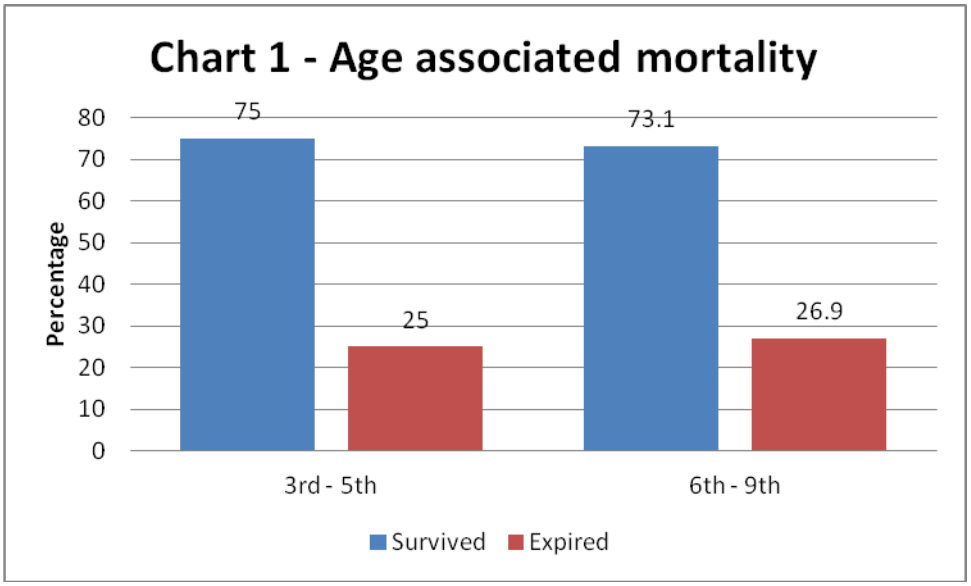
RESULTS

RESULTS

Table 1 - Age associated mortality

Age (decades)	Survived	Expired	Total	Mortality rate (percentage)
3rd - 5th	18	6	24	25%
6th - 9th	19	7	26	26.9%

p value – 0.877, difference of freedom – 1, Pearson chi square test value – 0.024



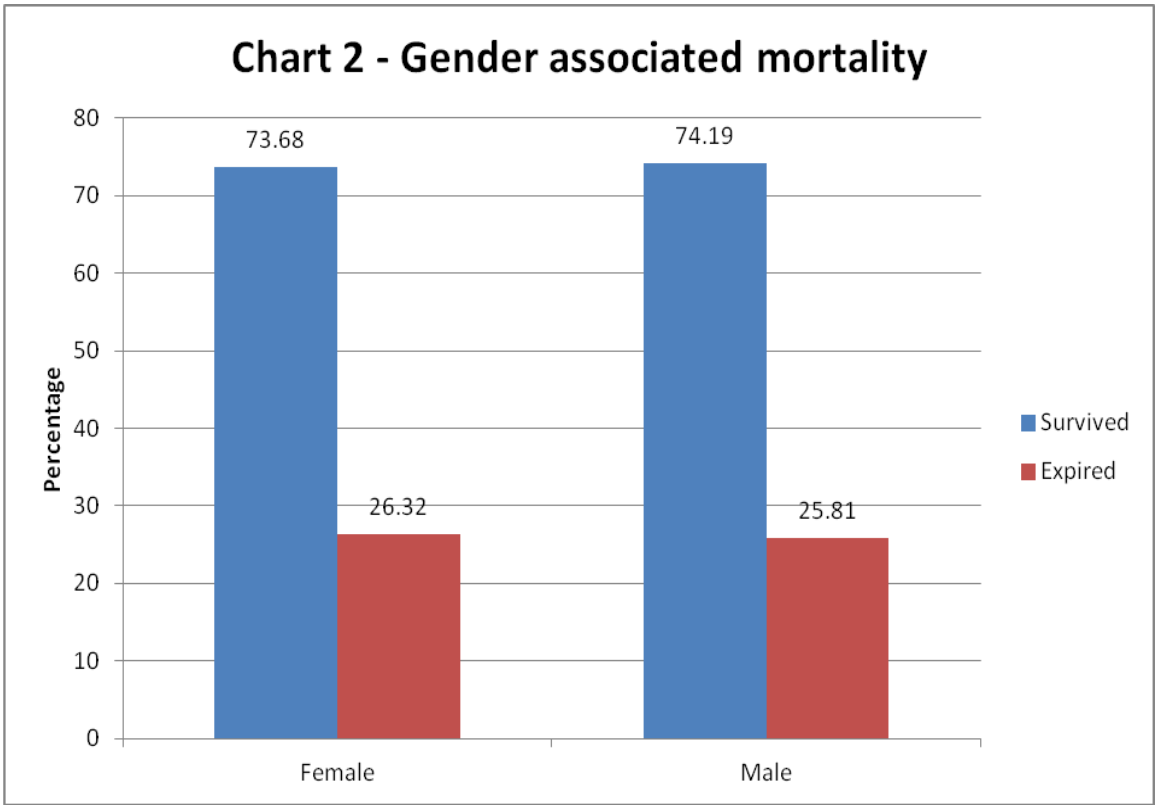
Out of patients in the 18-49 years age group, 6 out of 24 people expired and 7 out of 26 people expired in the 50-80 years age group.

There was no significant difference in mortality between younger and older age groups.

Table 2 - Gender associated mortality

	Survived	Expired	Total	Mortality rate (percentage)
Female	14	5	19	26.32
Male	23	8	31	25.81

p value – 0.968, difference of freedom – 1, Pearson chi square test value – 0.002

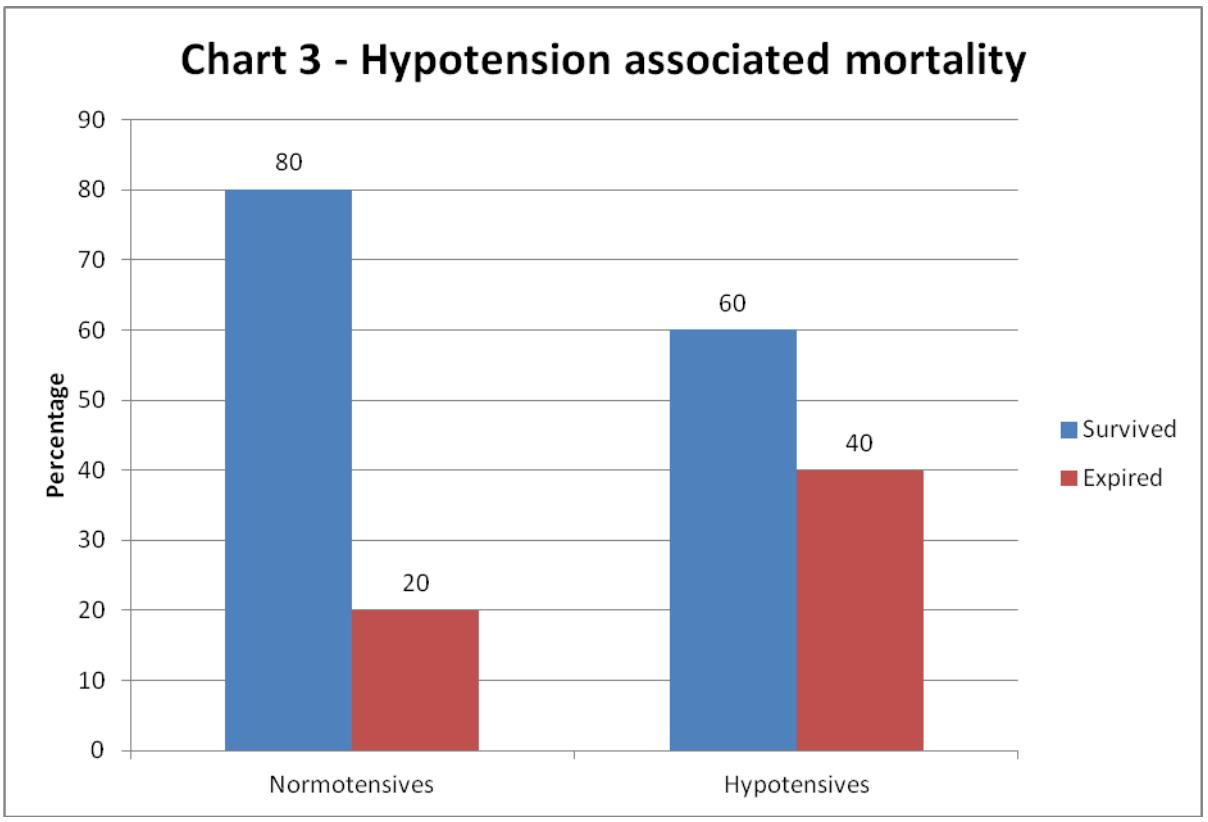


There were more males (31) than females (19) who suffered from acute renal failure. However the difference in mortality was not significant as compared between the two gender groups.

Table 3 - Hypotension associated mortality

	Survived	Expired	Total	Mortality rate (percentage)
Normotensive	28	7	35	20
Hypotensive	9	6	15	40

p value – 0.140, difference of freedom – 1, Pearson chi square test value – 0.002

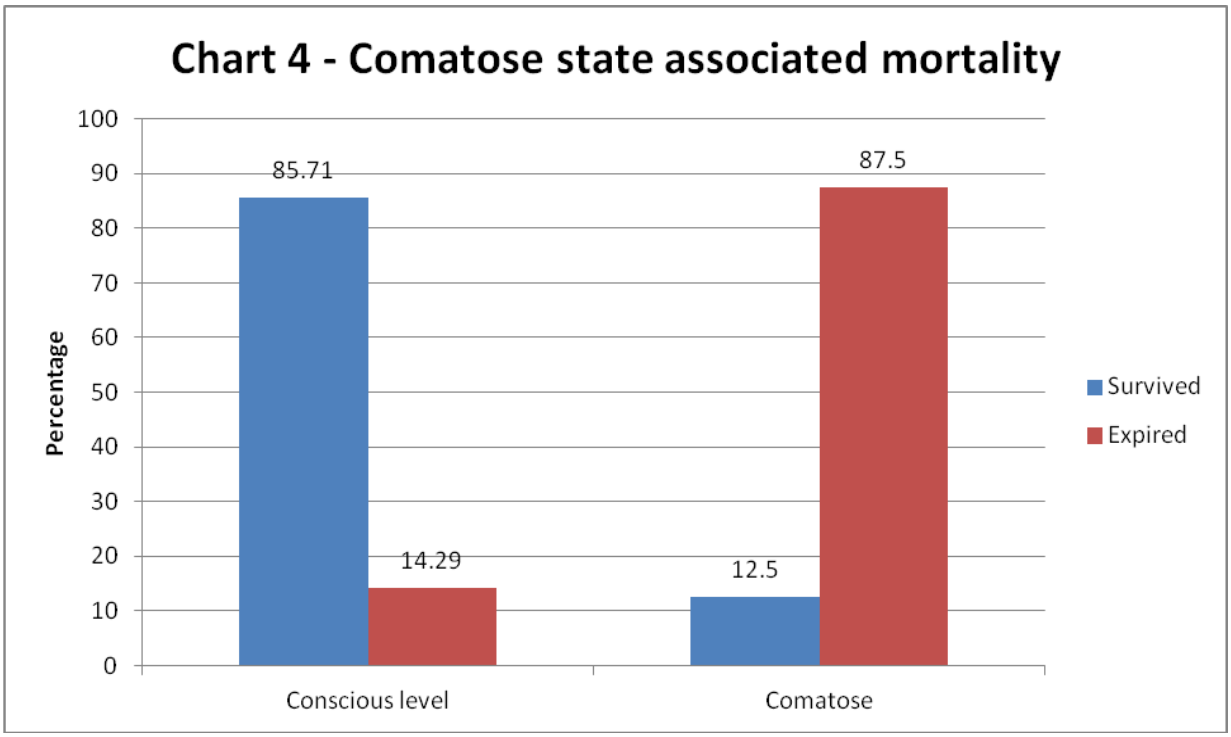


The p value showed that there was no statistically significant difference between normotensives and hypotensives as 7 out of 35 normotensives and 6 out of 15 hypotensive patients expired.

Table 4 - Comatose state associated mortality

	Survived	Expired	Total	Mortality rate (percentage)
Conscious	36	6	42	14.29
Comatose	1	7	8	87.5

p value – 0.001, difference of freedom – 1, Pearson chi square test value – 18.722.

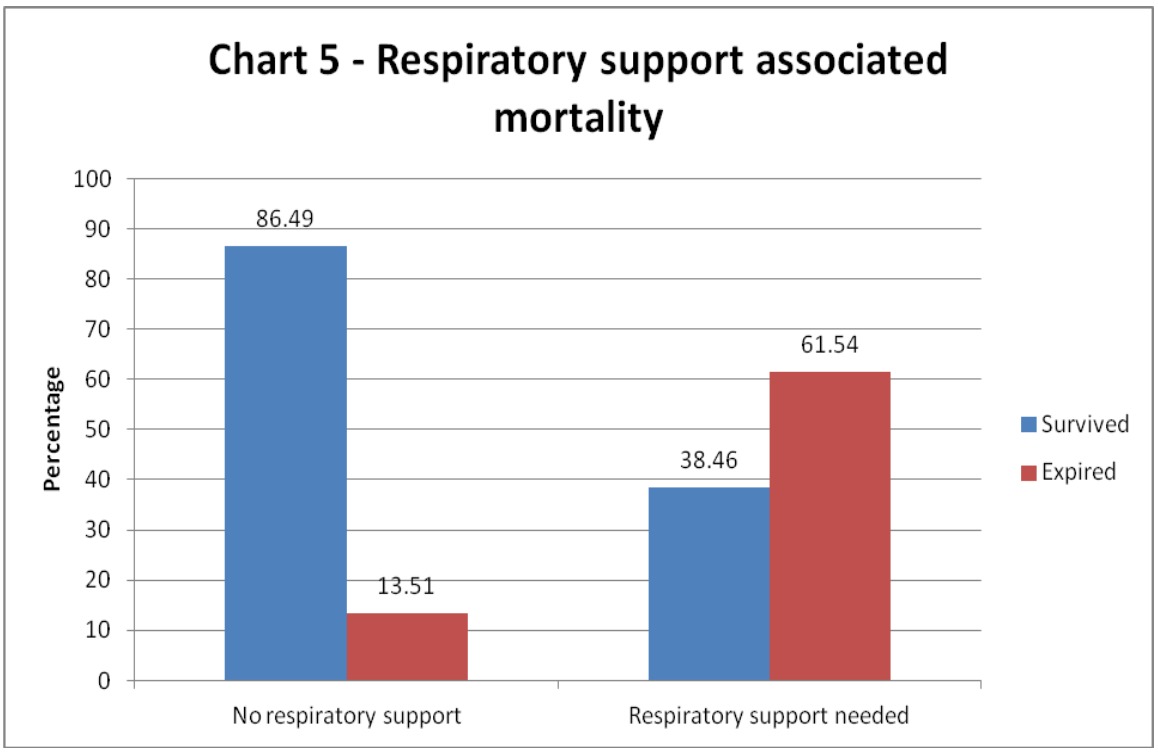


The consciousness level of the patient was a significant predictor of mortality in this study with 7 out of 8 comatose patients expiring.

Table 5 - Respiratory support associated mortality

	Survived	Expired	Total	Mortality rate (percentage)
Normal Respiration	32	5	37	13.51
Respiratory support	5	8	13	61.54

p value – 0.001, difference of freedom – 1, Pearson chi square test value – 11.532.

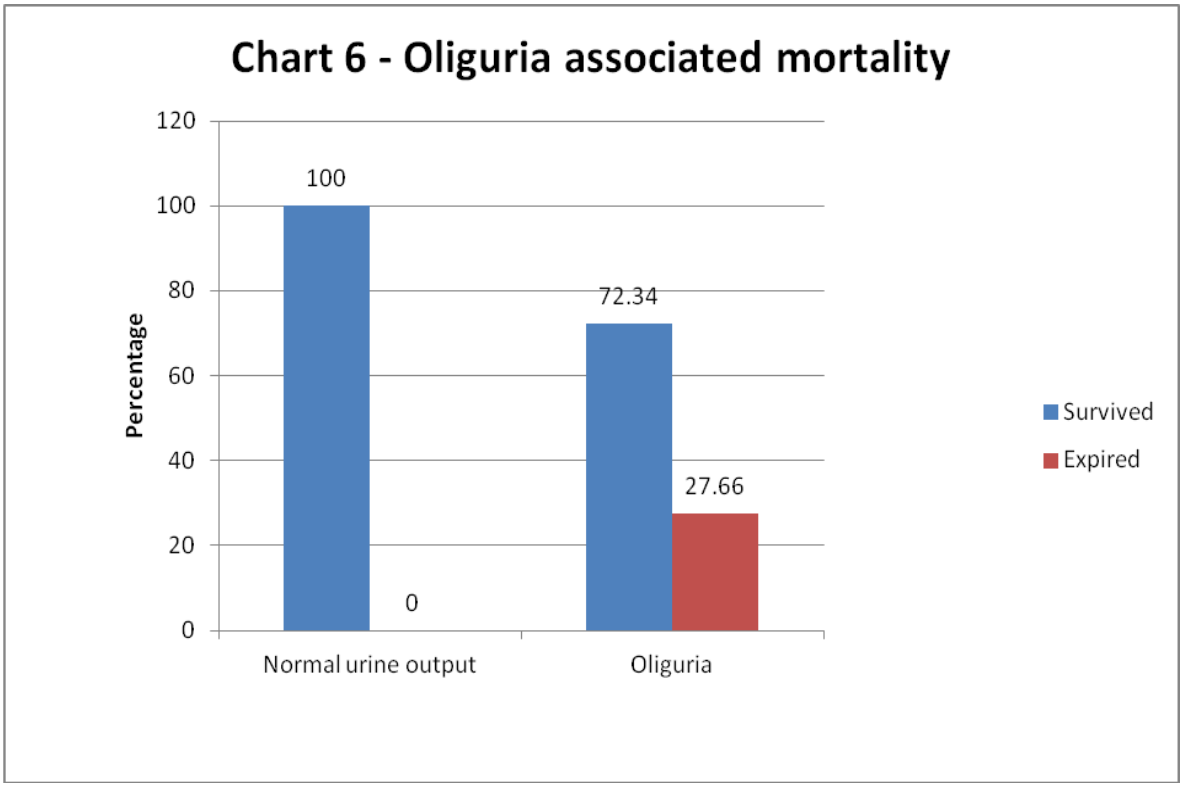


More than half (61.54%) of the patients requiring some kind of respiratory support expired showing that the need for respiratory support was another statistically significant independent predictor of mortality.

Table 6 - Oliguria associated mortality

	Survived	Expired	Total	Mortality rate (percentage)
Normal output	3	0	3	0
Oliguria	34	13	47	27.66

p value – 0.290, difference of freedom – 1, Pearson chi square test value – 1.121

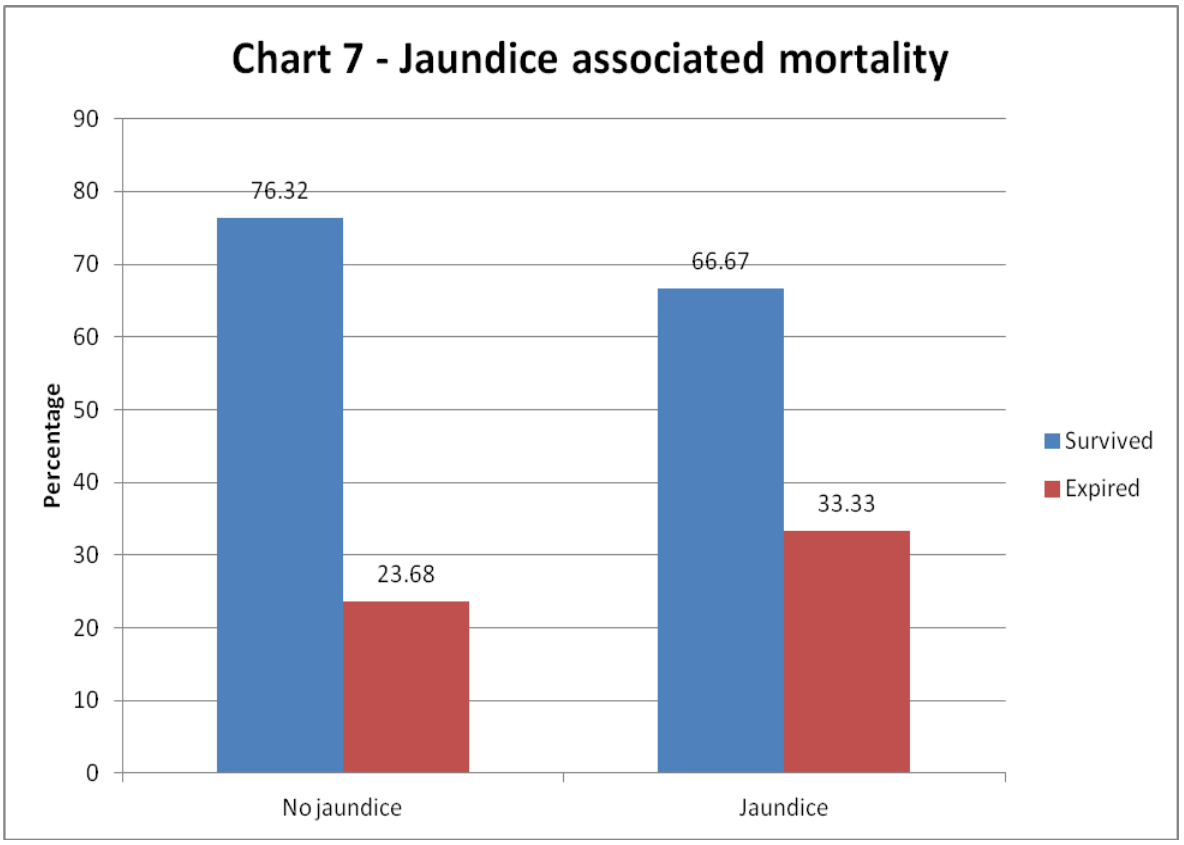


While none of the patients with normal urine output expired, 13 out of 47 oliguric renal failure patients expired. However statistical significance could not be attributed since almost all (47/50) the cases were in oliguria.

Table 7 - Jaundice associated mortality

	Survived	Expired	Total	Mortality rate (percentage)
No jaundice	29	9	38	23.68
Jaundice	8	4	12	33.33

p value - 0.506, difference of freedom – 1, Pearson chi square test value – 0.441

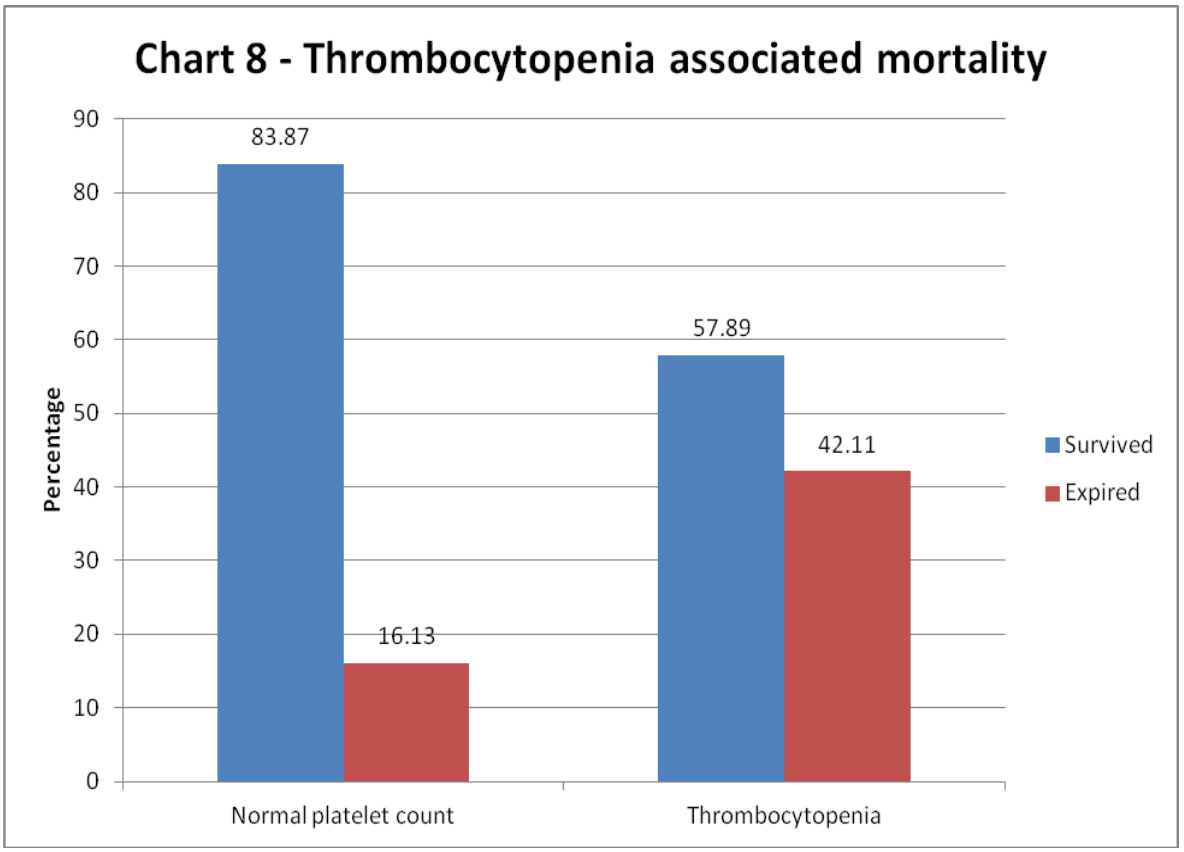


9 out of 38 patients with normal and 4 out of 12 patients elevated bilirubin levels respectively expired.

Table 8 - Thrombocytopenia associated mortality

	Survived	Expired	Total	Mortality rate (percentage)
Normal platelet count	26	5	31	16.13
Thrombocytopenia	11	8	19	42.11

p value – 0.042, difference of freedom – 1, Pearson chi square test value – 4.131.



5 out of 31 patients with normal platelet count and 8 out of 19 patients with thrombocytopenia expired making thrombocytopenia an important predictor for mortality in acute renal failure.

Table 9 - Number of complications associated mortality

Number of complications	Survived	Expired	Total	Mortality rate (percentage)
1	15	0	15	0
2	13	3	16	18.75
3	9	2	11	18.18
4	0	6	6	100
5	0	2	2	100

p value – 0.001, difference of freedom – 5, Pearson chi square test value – 28.826.

The mortality rate of patients increased as the number of complications increased.

Patients with only one complication had no mortality.

Patients with 2 or 3 complications had just under 20% of mortality.

However patients with 4 or 5 complications had 100% mortality.

Treatment Modality

66% of the patients diagnosed to be acute renal failure underwent dialysis.

Total mortality rate

13 out of 50 patients expired. Mortality rate in this study was 26%.

DISCUSSION

DISCUSSION

Age

Patients were divided into 2 groups – those from 18-49 years and those from 50-80 years.

There was no significant difference in mortality between younger and older age groups in this study. This finding does not correlate with that of Stott et al[75] in London, UK and Chertow et al[76] in Massachusetts wherein increased age corresponded with higher mortality. This study finding however does correlate with the findings of Oliveira et al[77] in London and Obialo et al[78] in Georgia, USA where in both instances the elderly did not have a poor prognosis compared to the younger age groups. This is significant as it means that aggressive treatment need not be withheld in the elderly.

Gender

Obialo et al[78] had also significantly higher men affected with acute renal failure as compared to women but they found that mortality was higher in females than males. While this study agrees with Obialo et al that more men than women are affected, it does not find any statistically significant difference in mortality between men and women.

Hypotension

Hypotension was defined as any patient with blood pressure lower than or equal to 90mmHg systolic or those requiring inotropic support. While Vincent et al[79] showed that hypotension can itself cause acute renal failure, this study finds that mortality rate between hypotensives and normotensives is not statistically significant.

Comatose

Patients were divided into 2 groups – those with Glasgow coma scale equal to or less than 8 and those with score 9 or above. Samimagham et al[80] found that low Glasgow coma score was an important predictor of mortality in acute renal failure and my study also came to the same conclusion that consciousness level is an independent predictor of mortality.

Respiratory support

Respiratory support was recognized as any patient requiring support to maintain oxygen saturation whether it be by venturi mask or ventilator support. There was a significant correlation between the need for respiratory support and mortality which was in agreement with Kuiper et al[81] where they found that mechanical ventilation may aggravate or even initiate acute renal failure.

Oliguria

Oliguria was defined as urine output less than 400ml/day. While oliguria was found to be an early predictor of mortality in critically ill patients by Macedo et al[82], a statistical significance could not be made out in this study as almost all (94%) cases of acute renal failure were oliguric and there were not sufficient non oliguric patients to compare the findings with.

Jaundice

Jaundice was defined as total bilirubin greater than 1.5mg/dl. While Amerio et al[83] found that rise in total bilirubin was directly proportional to rise in mortality, this study did not find any such difference in mortality.

Thrombocytopenia

Thrombocytopenia was defined as total platelet count less than 1.5 lakhs/cumm. While little over 16% of the patients with normal platelet count expired due to acute renal failure, as many as 42% of patients with acute renal failure in thrombocytopenia expired. These findings correlate with Chertow et al[84] where thrombocytopenia was associated with increased mortality.

Number of complications

Complications included hypotension (cardiovascular system), comatose (central nervous system), decreased urine output (nephrology), need for respiratory support (respiratory system), thrombocytopenia (haematology) and jaundice (hepatology). Each complication represents a different organ system in the body. No patient had all 6 complications. Brivet et al[85] found that mortality increased with increase in number of organ systems involved. This study agrees with the findings of Brivet et al as there was a significant correlation between increase in number of complications and increase in mortality. While patients with only 1 organ system involvement had no mortality, those with 2 or 3 organ systems involved had a mortality rate of just under 20% and those with 4 or 5 organ systems involvement had 100% mortality.

Treatment modality

66% of the patients diagnosed to be acute renal failure required hemodialysis. This finding correlates with the Robertson et al[86] study in which 63.9% of patients in acute renal failure required dialysis.

Mortality rate

The mortality rate in this study was 26% as compared to 34% by Levy et al[87]. The lower rate of mortality was probably due to increased awareness by hospital staff, early detection of renal failure, inter-departmental coordination and early intervention in management of acute renal failure.

SUMMARY

SUMMARY

Age, gender, hypotension, oliguria and jaundice were not statistically significant independent predictors of mortality in patients with acute renal failure.

Need for respiratory support, comatose state, thrombocytopenia and increasing number of systems involved were reliable predictors of mortality.

While more men than women were affected with acute renal failure, there was no difference in mortality between the two groups. The number of people affected in third to fifth decades and sixth to ninth decades were comparable and there was no difference in mortality between the two groups. While hypotension was not an independent predictor of mortality. Oliguria and jaundice were also not statistically significant predictors of mortality.

61.54% of the patients requiring respiratory support expired when compared with 13.51% mortality in those not requiring respiratory support making respiratory support an independent risk factor for mortality. 87.5% of comatose patients as opposed to 14.29% of conscious patients in acute renal failure expired making level of consciousness an important predictor of mortality in this study. Thrombocytopenia was also an important predictor of mortality as 42% patients with thrombocytopenia expired as compared to 16% with normal platelet count. Increase in number of complications was virtually proportional to mortality rate making it a significant factor to predict mortality in those with acute renal failure. Mortality rate of patients in acute renal failure was 26% in this study.

CONCLUSION

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Need for respiratory support, comatose state, thrombocytopenia and increasing number of systems involved were reliable predictors of mortality.

This study is useful as it reveals a prognosticating system in which ‘number of complications’ may be utilized to predict the possibility of mortality in a patient with acute renal failure. It consists of only 6 variables and its simplicity makes it practical to employ in the wards and may be used to explain prognosis to the patient and his/her relatives.

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BIBLIOGRAPHY

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ANNEXURES

Annexure A : Proforma

"PROGNOSTIC INDICATORS IN ACUTE RENAL FAILURE"

GUIDE : PROF. DR. B. N. RAGHAVENDRA PRASAD

Case No.: I.P. No. :

Name : Age :

Address: Sex :

Date of admission:

HISTORY

Chief complaints

History of presenting illness

Fever / Vomiting / Diarrhoea / Difficulty breathing / Blood loss / Nephrotoxic drug intake / Altered mental status / Seizures / Snake bite / Burns / Loin to groin pain / Recent surgery.

Past History

Diabetes mellitus / Systemic hypertension

Drug history

Aminoglycosides/ Amphotericin B/ Angiotensin Converting Enzyme inhibitors/ Non Steroidal Anti-Inflammatory Drugs/ Radiocontrast agents/ Alcohol/ Lithium/ Cyclosporine/ Cisplatin/ Ethylene glycol

EXAMINATION

General physical examination

Glasgow Coma Scale - /15

Pallor / Icterus / Cyanosis / Clubbing / Lymphadenopathy / Pedal Edema

Vitals

Pulse _____/min Blood Pressure _____mm Hg

Respiratory Rate _____cycles/min Temperature _____^{0}Celsius

Systemic examination

1. Cardiovascular system examination - Pericardial rub

2. Respiratory system examination - Crepitations / Rhonchi / Pleural effusion

3. Abdominal examination - Ascites

4. Central nervous system examination – Encephalopathy

INVESTIGATIONS

1. Blood urea

2. Serum creatinine

3. Hemoglobin levels

4. Total leukocyte count

5. Platelet count

6. Total Bilirubin

7. Other (Oliguria)

FINAL DIAGNOSIS –

TREATMENT GIVEN - Hemodialysis / Respirator support / Intravenous fluids, diuretics

OUTCOME -

SIGNATURE OF GUIDE

DATE -