Original Research Article

Causes of mortality in patients with acute kidney injury at Mahatma Gandhi Medical (MGM) College and Hospital, Jamshedpur - A tertiary care centre in Jharkhand

Mangesh Dorai[1], Soumyadeb Roy[2*]

[1]Senior Resident, [2]Senior Resident
Department of General Medicine, MGM Medical College and Hospital, Jamshedpur, Jharkhand, India
[*]Corresponding author email: **neelroy66@gmail.com**

International Archives of Integrated Medicine, Vol. 5, Issue 5, May, 2018.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 24-04-2018 **Accepted on:** 07-05-2018
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Mangesh Dorai, Soumyadeb Roy. Causes of mortality in patients with acute kidney injury at Mahatma Gandhi Medical (MGM) College and Hospital, Jamshedpur - A tertiary care centre in Jharkhand. IAIM, 2018; 5(5): 167-173.

Abstract

Background: Acute kidney injury (AKI), previously called acute renal failure (ARF), is an abrupt loss of kidney function that develops within 7 days. Its causes are numerous. Generally it occurs because of damage to the kidney tissue caused by decreased renal blood flow (kidney ischemia) from any cause such as low blood pressure, exposure to substances harmful to the kidney, an inflammatory process in the kidney, or an obstruction of the urinary tract that impedes the flow of urine. AKI is diagnosed on the basis of characteristic laboratory findings, such as elevated blood urea nitrogen and creatinine, or inability of the kidneys to produce sufficient quantity if urine.

Materials and methods: All patients aged above 18 years with features of AKI as per AKIN (Acute Kidney Injury Network) criteria which is defined as an increase in serum creatinine of 0.3 mg/dl or more within 48 hours of observation or 1.5 times baseline or greater, which is known or presumed to have occurred within 7 days, or a reduction in urine volume below 0.5 ml/kg/h for 6 hours were included in this study. A total of 146 patients were included in this study.

Results: Causative factors of AKI were decreased renal perfusion, nephrotoxic drugs, septicemia, intravascular hemolysis, hepato-renal syndrome, urinary catheterization and volume depletion. In this study, thirty four deaths out of 146 cases were documented and most common cause was septicemia followed by peripheral circulatory failure and uremia. Most common organisms involved were pseudomonas and acinetobacter.

Conclusion: Drug induced AKI can be prevented if used with discretion in patients with associated risk factors. The meticulous and appropriate monitoring of hydration status, fluid and electrolyte imbalance, use of nephrotoxic drugs particularly aminoglycosides, efficient control of infection and sepsis maintenance of adequate diuresis and hydration in surgical settings and patients undergoing radio contrast study are the main steps towards the prevention of hospital acquired acute renal failure.

Key words

Acute kidney injury, Nephrotoxic drugs, Serum creatinine, Blood urea, Renal hypoperfusion.

Introduction

AKI may lead to a number of complications, including metabolic acidosis, high potassium levels, uremia, changes in body fluid balance, and effects on other organ systems, including death. People who have experienced AKI may have an increased risk of chronic kidney disease in the future. Management includes treatment of the underlying cause and supportive care, such as renal replacement therapy. The clinical picture is often dominated by the underlying cause. The symptoms of acute kidney injury result from the various disturbances of kidney function that are associated with the disease. Accumulation of urea and other nitrogen-containing substances in the bloodstream lead to a number of symptoms, such as fatigue, loss of appetite, headache, nausea and vomiting [1]. Marked increase in the potassium level can lead to abnormal heart rhythms which can be severe and life-threatening [2]. Fluid balance is frequently affected, though blood pressure can be high, low or normal [3]. Pain in the flanks may be encountered in some conditions such as clot in renal vasculature or inflammation of the kidney; this is the result of stretching of the fibrous tissue capsule surrounding the kidney [4]. If the kidney injury is the result of dehydration, there may be thirst as well as evidence of fluid depletion on physical examination [4]. Physical examination may also provide other clues as to the underlying cause of the kidney problem, such as a rash in interstitial nephritis (or vasculitis) and a palpable bladder in obstructive nephropathy [4]. AKI can be caused by systemic disease (such as a manifestation of an autoimmune disease, e.g. lupus nephritis), crush injury, contrast agents, some antibiotics, and more. The most common cause is dehydration and sepsis combined with nephrotoxic drugs, especially following surgery or contrast agents. Acute kidney injury is diagnosed on the basis of clinical history and laboratory data. A diagnosis is made when there is a rapid reduction in kidney function, as measured by serum creatinine, or based on a rapid reduction in urine output, termed oliguria (less than 400 ml of urine per 24 hours).

Aim of the study

To know the causes of mortality in patients with acute kidney injury at Mahatma Gandhi Medical (MGM) College and Hospital, Jamshedpur - A tertiary care centre in Jharkhand.

Materials and methods

All patients aged above 18 years with features of Acute Kidney Injury (AKI) as per AKIN (Acute Kidney Injury Network) criteria [5] which is defined as an increase in serum creatinine of 0.3 mg/dl or more within 48 hours of observation or 1.5 times baseline or greater, which is known or presumed to have occurred within 7 days, or a reduction in urine volume below 0.5 ml/kg/h for 6 hours. This study was done at Mahatma Gandhi Medical College and Hospital, Jamshedpur, Jharkhand, India during the period March 2016 to February 2018. Patients with pre-existing renal disease and those who received renal transplantation were excluded from the study. A total of 146 patients met the above requirements and were evaluated prospectively. All 146 patients with clinical (uremic symptoms or oliguria or anuria of recent onset) and laboratory evidence of azotemia as per AKIN criteria were eligible. The informed consent was taken from the patients to carry out this study. Demographic

information including age, sex, weight, and height, duration of ICU and hospital stay were obtained. Clinical data collected included primary diagnosis, past medical history, presence of co morbidities, surgical status, physical examination findings, lab investigations, treatment history, hospital course and need for renal replacement therapy (RRT). Baseline and peak levels of serum creatinine, urine output were documented. Data regarding laboratory investigations were collected to confirm the etiology of AKI, which included complete urine analysis, metabolic panel, lipid profile, blood culture, hematology profile, coagulation profile. Radiological tests, serological tests were also done.

Results

In this study, age of the youngest patient was 18 years and oldest patient was 72 years. 76 cases were males (52%) and 70 were females (48%). Causative factors of AKI were decreased renal perfusion, nephrotoxic drugs, septicemia, intravascular hemolysis, hepato-renal syndrome, urinary catheterization and volume depletion. Among the above mentioned caused most common cause in this study was decrease renal perfusion- 54 cases (36%) and least common cause was urinary catheterization – 3 cases (4.38%). The most common drug group involved was NSAIDs (**Table – 1**).

Table - 1: Clinical features in patients of acute kidney injury in our hospital.

Parameter	No of patients	%
Oliguria	89	61
Non- Oliguria	41	28
Neuropsychiatric features	7	4.8
Hyperkalemia (>5.5 meq/L)	4	2.73
Pulmonary edema	2	1.39
Pericarditis	2	1.39
Bleeding diathesis	1	0.68

In this study, almost all the patients with AKI had mild to moderate elevated levels of creatinine and blood urea and few patients had severe elevation of creatinine and urea levels (**Table – 2, 3**).

Table - 2: Creatinine profile of patients with AKI in our hospital.

Range of Serum Creatinine	No. of patients at admission	No. of patients discharged	No. of patients Died
<1.5	0	91	2
1.5-2.9	46	7	4
3-4.9	33	6	8
5-7.9	40	4	7
>8	27	4	13
Total	146	112	34

Table - 3: Blood Urea profile in patients of AKI in our hospital.

Range of Blood Urea	No of patients at admission	No. of patients discharged	No. of patients Died
<100	59	82	4
100-199	48	13	10
200-299	26	10	11
>300	13	7	9
Total	146	112	34

Table - 4: Causes of mortality in patients of acute kidney injury in our hospital (n = 34).

Cause of death	No of Patients	%
Septicemia	16	47.00
Peripheral circulatory failure	5	14.70
Uremia	5	14.70
Hyperkalemia	3	8.85
Gastrointestinal bleed	3	8.85
Pulmonary edema	2	5.90
Total	**34**	**100.0**

In this study, thirty four deaths were documented and most common cause was septicemia followed by peripheral circulatory failure and uremia. Most common organisms involved were pseudomonas and acinetobacter (**Table – 4**).

Discussion

Acute Kidney Injury (AKI) is associated with a high risk of mortality and morbidity, especially in critically ill patients who needs intensive care. AKI is common in the clinic, occurring in 8% of all in-hospital patients and in approximately 50% of ICU patients [6]. The definition of AKI according to the AKIN criteria is an absolute increase of more than 0.3 mg/dl or atleast a 50% increase in serum creatinine levels from baseline. Our study used this definition to diagnose AKI.

According to newly proposed classification not three (initiation, maintenance and recovery) but four phases (initiation, extension, maintenance and recovery) of ARF have been recognized. The initiation phase with nonspecific hemodynamic changes may evolve into the extension phase which is characterized by alterations in renal perfusion leading to hypoxia. In the next phase an inflammatory response predominates resulting in epithelial and endothelial injury which occurs mainly in the cortico-medullary part of a kidney.

Currently there are two theories of pathogenic mechanism of acute tubular necrosis.

- Tubular
- Vascular

Tubular Effects

- Tubular obstruction
- Back leak (increased permeability)

Tubular

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 ARF. Injury and loss of epithelial cells, through necrosis or apoptosis can lead to loss of kidney function and apparent drop in GFR 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. The tubular epithelial cell progresses through a series of morphological changes that finally lead to restoration of normal structure and function. These steps include an initial loss of cell polarity and brush border, which contributes to alter solute trafficking. Some cells die and are sloughed into the tubular lumen, and the remaining viable cells dedifferentiate and proliferate leading to final restoration of normal epithelium. The initial insult to the tubular epithelial cell depletes cellular ATP, which, in turn, leads to disruption of the apical actin cytoskeleton in a fashion that mirrors the changes in vascular endothelial cells in the kidney (see the section on endothelial cells earlier). This structural change in the cell leads to the formation of membrane-bound vesicles or blebs that can either be internalized or shed into the tubular lumen as part of the cellular debris leading to cast formation and tubular obstruction [7].

Some elements of the basolateral cytoskeleton in epithelial cells are disrupted during AKI. The Na,K-ATPase that is found in the basolateral membrane as well as integrins that help tether cells to the basement membrane are both affected during IRI. The loss of the Na, K-ATPase decreases proximal tubular sodium reabsorption and increases the fractional excretion of sodium (FeNa) contributing to tubuloglomerular feedback and drop in GFR. The elevated FeNa is a hallmark of intrinsic AKI (see previous section of this chapter). Loss of integrin polarity, particularly the b1 integrins, away from the basolateral membrane to the apical domain can lead to detachment of viable cells from the basement membrane and sloughing of cells into the tubular lumen.

Vascular effects

The effect of renal injury, whether from ischemia or from other causes, is a profound decrease in the GFR. This large decrease in filtration capacity of the kidney often occurs in the absence overwhelmingly evident damage to the kidney as seen on light microscopy. There are at least three major classic proposed mechanisms for the fall in GFR, as determined by micro puncture studies on animals and indirect methods in humans. The first mechanism is a drop in the filtration pressure in the glomerulus. This drop in

pressure is caused by afferent arteriolar vasoconstriction and proximal tubular obstruction. This first mechanism leads to a direct fall in the GFR. Afferent arteriolar vasoconstriction is thought to be a result of endothelial cell injury. This leads to an imbalance in vasoactive substances, with a predominance of vasoconstrictive activity. The second mechanism, tubular back-leakage, leads to a fall in the effective GFR. Glomerular filtrate that enters the tubular/urinary space is allowed to leak back into the renal interstitium and consequently be reabsorbed into the systemic circulation. Back- leakage of glomerular filtrate occurs in the setting of damage and loss of epithelial cells (denuded basement membranes) and loss of tight junctions between those cells that are critical to maintaining separation of tubular filtrate and the surrounding interstitium. Tight junctions are disrupted in the setting of adenosine tri phosphate (ATP) depletion, allowing back- leakage of sodium and other solutes into the renal interstitium. The third mechanism, tubular obstruction, is a result of cast formation from sloughed tubular epithelial cells as well as THP. THP tends to polymerize and form a gel that can further trap cells and tubular cell debris following AKI. The concentration of various molecules in the renal tubules in evolving ATN further promotes THP gel formation.

Besides a fall in GFR, there is also a decreased ability of the kidney to concentrate urine following AKI. 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, as has been shown in animal models [8]. Inflammation plays a central role in AKI. From initiation to extension through repair, inflammatory cells and soluble mediators are likely major determinants of the outcome from AKI.

In this study, age of the youngest patient was 18 years and oldest patient was 72 years. 76 cases were males (52%) and 70 were females (48%). Causative factors of AKI were decreased renal perfusion, nephrotoxic drugs, septicemia, intravascular hemolysis, hepato-renal syndrome, urinary catheterization and volume depletion. Among the above mentioned caused most common cause in this study was decrease renal perfusion- 54 cases (36%) and least common cause was urinary catheterization – 3 cases (4.38%). The most common drug group involved was NSAIDs.

In this study, almost all the patients with AKI had mild to moderate elevated levels of creatinine and few patients had severe elevation of creatinine levels.

In our study, the patients were included from general medicine wards and their specialties. This difference in the group of patients included in various studies may be the cause for difference in the incidence of hospital acquired ARF in different studies. The incidence in our study is quite close to the Chandigarh study despite the inclusion of patients from various other departments in Chandigarh study probably because ARF rarely develops in those additional departments like dermatology, ophthalmology, ENT and psychiatry [9].

Despite the wide variation in the spectrum of etiological factors observed in different studies, only few etiological factors, such as nephrotoxic drugs, decreased renal perfusion, surgery and septicemia were operating in majority of the cases of hospital acquired renal failure [9, 10, 11]. Decreased renal perfusion was the etiological factor, being responsible in 30 (30%) patients in the present study which is similar to the reports of Hou, et al. where also the same etiological factors were responsible for hospital acquired acute renal failure; in maximum number of patients (42%) [12]. In the Chandigarh study nephrotoxic drugs were the most common etiological factor responsible for hospital acquired acute renal failure being responsible in 29% of the patients [9]. Decreased renal perfusion and intravascular hemolysis are the commonest cause of hospital acquired acute renal failure in our study. The observations

highlight the need of maintaining adequate renal perfusion in the hospitalized patients. Thus all the critically ill patients must be watch daily for their hydration status and fluid balance. The use of nephrotoxic must be carefully monitored in serious patients and intensive care units. Administration of nephrotoxic drugs specially the aminoglycosides was the most frequent (29%) cause of hospital acquired acute renal failure in Chandigarh study while nephrotoxic ARF was seen in 8 (8%) patients in our study. This highlights the need to monitor renal function carefully in every patient who receives aminoglycoside drugs such as gentamycin and amikacin. All patients who are getting aminoglycosides should have their base line serum creatinine done before the start of therapy and aminoglycosides should preferably be avoided if the patient is already having renal disease or other risk factors for hospital acquired acute renal failure. Non-steroidal anti-inflammatory drugs (NSAIDs) can produce AKI, particularly in patients with certain risk factors such as congestive heart failure, cirrhosis, age greater than 60 year and diabetic nephropathy [13, 14]. Non-steroidal anti-inflammatory drugs were responsible in 12(12%) patients in our study. Radiographic contrast media was responsible in 3(3%) cases in the present study while it was operating in 4 per cent patients in the study of Jha, et al [9]. The incidence of contrast associated ARF varies from 20-22 per cent.

Conclusion

To conclude, Drug induced AKI can be prevented if used with discretion in patients with associated risk factors. The meticulous and appropriate monitoring of hydration status, fluid and electrolyte imbalance, use of nephrotoxic drugs particularly aminoglycosides, efficient control of infection and sepsis maintenance of adequate diuresis and hydration in surgical settings and patients undergoing radio contrast study are the main steps towards the prevention of hospital acquired acute renal failure. In this study, 112 cases recovered well after replacement therapy and other etiology specific treatment. 34 patients died due septicemia, peripheral circulatory failure, uremia and others.

References

1. Skorecki K, Green J, Brenner BM (2005). Chronic renal failure. In Kasper DL, Braunwald E, Fauci AS, et al. Harrison's Principles of Internal Medicine, 16th edition, New York, NY: McGraw-Hill, p. 1653–63.
2. Weisberg LS. Management of severe hyperkalemia. Crit. Care Med., 2008; 36(12): 3246–51.
3. Tierney, Lawrence M., Stephen J. McPhee, Maxine A. Papadakis. Current Medical Diagnosis and Treatment, 44th edition, McGraw-Hill, 2005, p. 871.
4. Brady HR, Brenner BM (2005). Chronic renal failure. In Kasper DL, Braunwald E, Fauci AS, et al. Harrison's Principles of Internal Medicine, 16th edition, New York, NY: McGraw-Hill, p. 1644–53.
5. Molitoris BA, Levin A, Warnock DG, et al. Improving outcomes from acute kidney injury. J Am Soc Nephrol., 2007; 18: 1992-1994.
6. Hoste EA, Schurgers M. Epidemiology of acute kidney injury: how big is the problem? Crit Care Med., 2008; 36: S146–151.
7. Donhoe J.F., Venkatchalam M.A., Bernard D.B., Levinsky N.G. Tubular leakage and obstruction after renal ischemia, structural functional correlation. Kidney Int., 1989; 13: 208-210.
8. Teschan P.E. and Lawson N.L. Studies in acute renal failure. Prevention by osmotic dieresis and observation on the effect of plasma and extracellular volume expansion 1966, 3:1-4.
9. Jha V., Malhotra H.S., Sakhuja V., Chugh K.S. Spectrum of hospital acquired acute renal failure in the developing countries, Chandigarh study.

Quarterly Journal of Medicine, New Series, July 1992; 303: 497-505.

10. Brady Hr, Singer G.G. Acute Renal Failure. Lancet, 1995; 346: 1533- 1540.
11. Lameire N, Van Biesen W., Vanholdre R. Acute Renal Failure. Lancet, 2005; 365: 417-430.
12. Hou S.H., Bushinsky D.A., Wish J.B. Cohen J.J, Harrington J.T. Hospital acquired renal insufficiency. A prospective study. Am. J. Med., 1983; 74: 243-248.
13. Rasmussen H.H., Ibels, L.S. Acute renal failure multivariate analysis of causes and risk factors. Am. J. Med., 1982; 73: 211- 213.
14. Blackshear J.L., Davidman M., Stillman M.T. Identification of risk for renal insufficiency from non-steroidal anti-inflammatory drugs. Arch. Intern. Med., 1983; 143: 1130-1134.