Outcomes in Sepsis-Induced Acute Kidney Injury: A Prospective Observational Study

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ABSTRACT

Introduction: Acute Kidney injury (AKI) is often multifactorial, with sepsis being only one of the factors in its pathogenesis particularly in critically ill patients. It often leads to worse clinical outcomes, increased duration of hospitalization, need for intensive care and mortality. Our objective in the current study was to analyze the various factors associated with sepsis-related AKI and clinical outcome.

Material and Methods: The study included all patients with sepsis admitted to medical Intensive care unit (ICU). These patients were subjected to laboratory investigations and radiological imaging. The APACHE II score was assessed and patients were grouped by RIFLE categories for risk, injury, and failure. Course in the hospital was observed for a period of 28 days or till discharge/death of the patients.

Results: Of the 320 patients with sepsis, 31.2% developed AKI due to sepsis. The overall mortality rate of AKI patients with sepsis was 58%. The mortality rate increased significantly as renal function deteriorated ($p=0.020$). It was also observed that the mortality increased significantly with increase in the severity of sepsis ($p<0.005$). Multivariate logistic regression analysis revealed sepsis severity, RIFLE class, high APACHE II score were the independent predictors of mortality.

Conclusion: The present study revealed high overall mortality rate. Males sex, sepsis severity, RIFLE class, high APACHE II score, and Vasopressor Use were the independent predictors of mortality in sepsis-induced AKI, while age had no independent prognostic value.

Keywords: Sepsis, Acute Kidney Injury, Outcome

INTRODUCTION

Acute Kidney injury (AKI) is often multifactorial, with sepsis being only one of the factors in its pathogenesis particularly in critically ill patients. The spectrum of injury ranges from mild to advanced, sometimes requiring renal replacement therapy. Sepsis-induced AKI is characterized by a rapid and often profound decline in the kidneys' ability to filter blood and eliminate nitrogen waste products, usually evolving over hours to days after the onset of sepsis.[1] Limited understanding of pathophysiologic mechanisms has precluded the development of effective therapies for sepsis-induced AKI. It often leads to worse clinical outcomes, increased duration of hospitalization, need for intensive care and mortality. Even in patients with less severe infections, the incidence of AKI is as high as 16% to 25%.[2] The incidence of AKI increases with severity of sepsis. Our objective in the current study was to analyze the various factors associated with sepsis-related AKI and clinical outcome.

MATERIAL AND METHODS

This was a prospective observational study included all patients with sepsis who had been admitted to medical Intensive care unit (ICU) of a 1000 bedded tertiary care hospital, located in North India.

After obtaining approval from the institutional ethics board, 168 patients were screened for the study and a total of 100 consecutive patients who fulfilled the inclusion criteria, were included in this study. Exclusion criteria were age younger than 18 years, hospital or ICU stay < 24 hours, surgical causes of acute kidney injury, and seizures.

The detailed history with special emphasis on duration of illness, urine output, fever and other associated symptoms, co-morbid conditions and underlying kidney disease was taken. Patients were then subjected to a detailed general and systemic examination. Hematological and biochemical investigations including complete blood count, serum creatinine, urinalysis, blood culture and arterial blood gas (ABG) was done in all patients. Radiological investigations like x-ray and ultrasonography were done in selected patients. Sepsis was defined when patients met the criteria for SIRS and an infectious source was documented or strongly suspected based on clinical presentation. Blood culture is frequently used as the "gold standard" diagnostic method for sepsis.[3]

The definition of AKI includes a change in Serum Creatinine Concentration within 2–7 days and oliguria for 6 or more hours. The stage is defined by the peak rise in Serum Creatinine Concentration compared with previous values and nadir in urine output and is related to risk for complications and prognosis.[4]

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How to cite this article: Ruchita Sharma, Amit Shukla, Ajay Kumar Mishra, Davendra Kumar, Mehboob Subhani Siddiqui, Abhishek Dixit. Outcomes in sepsis-induced acute kidney injury: a prospective observational study. International Journal of Contemporary Medical Research 2018;5(5):E22-E25.

DOI: http://dx.doi.org/10.21276/ijcmr.2018.5.5.15

		RIFLE Risk(n=14)	RIFLE Injury (n=49)	RIFLE Failure (n=37)	p-value
Age > 60 years%		57.1	57.1	27.0	0.014
Male%		85.7	40.8	62.2	0.006
Focus of infection	Urological	42.9	26.5	56.8	0.107
	Pulmonary	21.4	46.9	13.5	
	GI	14.3	6.1	10.8	
APACHE II >=25%		14.3	51.0	32.4	0.027
Sepsis%		42.9	16.3	35.1	0.179
Severe Sepsis%		28.6	53.1	40.5	
Septic Shock%		28.6	30.6	24.3	
Vasopressor Use%		35.7	36.7	24.3	0.450
Mortality%		35.7	71.4	48.6	0.020

Table-1: Baseline characteristics and renal function

		Odd ratio	95% CI	P-value
Age		0.89	0.43-1.98	0.782
Sex		3.3	1.41-7.70	0.006
APACHE II		1.81	1.43-2.29	<0.005
Sepsis		0.024	0.005-0.11	<0.005
Severe sepsis		2.74	1.19-6.32	0.018
Septic shock		6.70	2.11-21.28	0.001
RIFLE	Risk	0.34	0.10-1.12	0.077
	Injury	3.04	1.32-6.97	0.009
	Failure	0.54	0.23-1.24	0.148
Vasopressor Use		3.00	1.18-7.60	0.021

Table-2: Multiple logistic regression analysis evaluating predictors of mortality

Severe sepsis was defined as the presence of 2 or more systemic inflammatory response syndrome criteria, proven or suspected infection and associated organ dysfunction.[5] Septic shock was defined as sepsis-induced hypotension with systolic arterial blood pressure (BP), 90 mm Hg despite adequate fluid (crystalloid or colloid) resuscitation.

Patients were grouped by RIFLE categories for risk, injury, and failure.[6] In this study, baseline serum creatinine was determined based on patient's available record prior to admission or the lowest level of Creatinine while under hospitalization. Urine output was measured within 24 h from admission. Modification of diet in renal diseases (MDRD formula) was used to calculate the glomerular filtration rate (GFR). We used glomerular filtration rate (GFR) criteria or urine output criteria, whichever gives a more severe classification.

The APACHE II score was assessed in all the patients. Course in the hospital was observed for a period of 28 days or till discharge/death of the patients, whichever was earlier. Length of hospitalization and in-hospital outcome were also documented. When necessary, the hospital records provided information regarding patient survival or date of death.

STATISTICAL ANALYSIS

Descriptive statistics were expressed as means ± standard deviation. The primary analysis compared hospital survivors with non-survivors. Chi-square/Fisher Exact test has been used to find the significance of study parameters on the categorical scale between two or more groups. The logistic regression test was performed to identify independent factors impacting mortality in sepsis-induced acute kidney injury. All statistical tests were 2-tailed; a value of $P < 0.05$ was considered statistically significant.

RESULTS

A total of 850 patients were admitted in medical ICU during the study. Among them, 195 (60.9%) patients had sepsis as the primary diagnosis and the rest 125 (39.1%) patients developed sepsis after hospitalization. Of the 320 patients with sepsis, 31.2% developed AKI due to sepsis.

The median age (years) of the study population was 57±18.17. 55 (55%) were males and (45 (45%) were females. Male to female ratio was 1.2:1.

Among 100 cases of AKI, 22% cases had hypertension, 18% diabetes mellitus, and 8% cases had coronary artery disease. Twenty-seven (27%) patients had sepsis, 45 (45%) had severe sepsis, and (28) 28% had septic shock. Urinary tract was focus of infection in 40 (40%) patients followed by pulmonary 31 (31%), gastrointestinal tract 9 (9%), and others 20 (20%). The culture was positive in only 18% of cases.

According to RIFLE criteria, 14% were in risk stage, 49% at injury stage and 37% were at failure stage. Mean APACHE II score in risk 19.92, in injury 22.10 and in failure group was 22.05 respectively.

The overall mortality rate of AKI patients with sepsis was 58%. Twenty-five (45.5%) out of 55 males and 33(73.3) out of (45) females expired during the study period.

(Table 1) shows baseline characteristics and renal function of patients.

The mortality rate increased significantly as renal function deteriorated, 8.6% risk, 60.3% injury, and 31% in failure stage (p=0.020). It was also observed that the mortality increased significantly with increase in the severity of sepsis, 3.4% in sepsis, 55.2% in severe sepsis, and 41.4% in septic shock (p<0.005).

Multivariate logistic regression analysis revealed sepsis (sepsis odd ratio (OR) 0.024, 95% confidence interval (CI) 0.005-0.11, p<0.005; severe sepsis OR 2.74, 95%CI 1.19-6.32, p=0.018; septic shock OR 6.70, 95% CI 2.11-21.28, p<0.001), RIFLE class (Injury OR 3.04, 95% CI 1.32-6.97,

p=0.009), APACHE II ≥ 25 (OR 1.81, 95% CI 1.43-2.29, p <0.005), males (OR 3.3, 95% CI 1.41-7.70, p=0.006), and vasopressor use (OR 3.00, 95% CI 1.18-7.60, p=0.021) as independent predictor of mortality. (Table 2)

DISCUSSION

Several studies have reported that AKI is a common clinical problem in intensive care unit patients and is independently associated higher odds of death.[7,8,9,10]

In concordance with prior studies, the median age of the sepsis patients in the present study was 57±18 years.[11,12,13] We found that among patients admitted in our ICU, 37.64% patients had sepsis at the time of admission or developed during the course of hospitalization. An estimated 31.5% of sepsis patients had concomitant AKI. Single center studies have found 11% to 37% of septic patients have concomitant AKI.[1,14] However, multicenter studies have found sepsis to be a contributing factor in 46% to 48% of episodes of AKI.[15,16] Concurrence with previous studies, we observed that the predominant sources of sepsis were the urogenital tract, followed by pulmonary, and gastrointestinal infection.[13,15]

The APACHE II score demonstrated good discriminatory power in the sepsis population in the study. However, mean APACHE II score (21.11) in this study was slightly lower than that reported from prior studies.[15]

The 58% overall high in-hospital mortality rate observed in our study supports that have been reported in the literature. Bagshaw et al, in a multicentre prospective observational study which enrolled 1753 patients have reported mortality rates of up to 50% to 60%, depending on the severity of sepsis-induced AKI.[15] In another large multicentre epidemiologic study, Neveu et al. described an in-hospital mortality of 75% for patients with septic AKI.[16]

We also observed that the mortality increased significantly with increase in the severity of acute kidney injury, and sepsis (p=0.20,p<0.005 respectively). A systematic review shows that RIFLE criteria displayed a graded association with adverse outcomes. It also suggests that even mild degrees of kidney dysfunction may have a negative effect on the outcome. Compared with patients with RIFLE risk, patients with RIFLE injury had 2.2-fold greater odds of ICU mortality. These odds for RIFLE failure were 4.9-fold.[17]

In our study, multiple logistic regression revealed sepsis severity, RIFLE class, high APACHE II, vasopressor use, and patient's sex were found to be independent risk factors influencing mortality in acute kidney injury. Similar observations were reported from a previous study. Uchino et al, in a multicentre study, used a multivariable model to analyze the impact of different factors on mortality. It revealed significant associations between mortality and older age (odds ratio [OR] 1.02 [per year]), Simplified Acute Physiologic Score II (OR 1.02 [per point]), mechanical ventilation (OR 2.11), use of vasopressors and/or inotropes (OR 1.95), and sepsis (OR 1.36).[10]

CONCLUSION

The present study revealed high overall mortality rate. Males sex, sepsis severity, RIFLE class, high APACHE II score, and Vasopressor Use were the independent predictors of mortality in sepsis-induced AKI, while age had no independent prognostic value.

REFERENCES

1. Hoste EA, Lameire NH, Vanholder RC, et al. Acute renal failure in patients with sepsis in a surgical ICU: predictive factors, incidence, comorbidity, and outcome. J Am Soc Nephrol 2003;14:1022–30.
2. Murugan R, Karajala-Subramanyam V, Lee M, et al. Acute kidney injury in nonsevere pneumonia is associated with an increased immune response and lower survival. Kidney Int 2010;77:527–35.
3. Rangel-Frausto MS, Pittet D, Costigan M, Hwang T, Davis CS, Wenzel RP. The natural history of the systemic inflammatory response syndrome (SIRS). A prospective study. J Am Med Assoc 1995;273:117e23.
4. Kellum JA, Lameire N, Aspelin P. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. Kidney International Supplement 1s. 2012;2:1-138.
5. Bone RC, Balk RA, Cerra FB, et al. American-College of Chest Physicians Society of Critical Care Medicine Consensus Conference—definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. Crit Care Med 1992;20:864–74.
6. Bellomo R, Ronco C, Kellum JA, et al. Acute Dialysis Quality Initiative Workgroup. Acute dialysis quality initiative workgroup: acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the second international consensus conference of the acute dialysis quality initiative (ADQI) group. Crit Care 2004;8:R204–12.
7. M, Godinez-Luna T, Svenson LW, Rosenal T. Prognosis for long term survival and renal recovery in critically ill patients with severe acute renal failure: a population-based study. Crit Care 2005;9:R700-R709.
8. Korkeila M, Ruokonen E, Takala J. Costs of care, long-term prognosis and quality of life in patients requiring renal replacement therapy during intensive care. Intensive Care Med 2000;26:1824-1831.
9. Metnitz PG, Krenn CG, Steltzer H, Lang T, Ploder J, Lenz K, Le Gall JR, Druml W. Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients. Crit Care Med 2002;30:2051-2058.
10. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Ronco C. Beginning and Ending Supportive Therapy for the Kidney(BEST Kidney) Investigators: Acute renal failure in critically ill patients: a multinational, multicenter study. JAMA 2005;294:813-818.
11. Ostermann M, Chang RW. Acute kidney injury in the intensive care unit according to RIFLE. Crit Care Med 2007; 35:1837–1843.
12. Hoste EA, Clermont G, Kersten A et al. RIFLE criteria for acute kidney injury is associated with hospital mortality in critical ill patients: A cohort analysis. Crit

Care 2006; 10:R73.
13. Lopes JA, Jorge S, Resina C, Santos C, Pereira A, Neves J, et al. Acute renal failure in patients with sepsis. Crit Care 2007; 11: 411.
14. Yegenaga I, Hoste E, Van Biesen W, Vanholder R, Benoit D, Kantarci G, Dhondt A, Colardyn F, Lameire N. Clinical characteristics of patients developing ARF due to sepsis/systemic inflammatory response syndrome: results of a prospective study. Am J Kidney Dis 2004;43: 817-824.
15. Bagshaw SM, Uchino S, Bellomo R, Morimatsu H, Morgera S, Schetz M, Tan I, Bouman C, Macedo E, Gibney N, Tolwani A, Oudemans-van Straaten HM, Ronco C, Kellum JA, :Beginning and Ending Supportive Therapy for the Kidney (BEST Kidney) Investigators: Septic acute kidney injury in critically ill patients: clinical characteristics and outcomes. Clin J Am Soc Nephrol 2007; 2: 431-439.
16. Neveu H, Kleinknecht D, Brivet F, Loirat P, Landais P. Prognostic factors in acute renal failure due to sepsis. Results of a prospective multicentre study. The French Study Group on Acute Renal Failure. Nephrol Dial Transplant 1996;11: 293-299.
17. Ricci Z, Cruz D, Ronco C. The RIFLE criteria and mortality in acute kidney injury: a systematic review. Kidney Int 2008;73:538–46.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 19-04-2018; **Accepted:** 21-05-2018; **Published:** 02-06-2018