



Acute kidney injury in elderly ICU patients- A prospective study from Indian Sub-continent.

Prodip.k.Doley¹, Manjuri Sharma², Hamad Jeelani³, P.J.Mahanta⁴, Gayatri Pegu⁵,
Manzoor Parry⁶, Tazeen Jeelani⁷.

¹ Assistant Professor, Department of Nephrology, Gauhati Medical College and Hospital, Guwahati Assam, India.

² Professor and Head Department of Nephrology, Gauhati Medical College and Hospital, Guwahati Assam, India.

³ D.M scholar, Department of Nephrology, Gauhati Medical College and Hospital, Guwahati Assam, India.

⁴ Associate professor, Department of Nephrology, Gauhati Medical College and Hospital, Guwahati Assam, India.

⁵ Registrar, Department of Nephrology, Gauhati Medical College and Hospital, Guwahati Assam, India

⁶ D.M Student, Department of Nephrology, Gauhati Medical College and Hospital, Guwahati Assam, India.

⁷ Lecturer, Department of Pathology Govt. Medical College Srinagar J&K India.

ABSTRACT:

Background: Acute kidney injury is defined as a significant increase in serum creatinine (SCr) or a decrease in urine output. It is a common and important occurrence in intensive care unit patients with a prevalence ranging from 2 to 25%. It has been seen that patients >65 years of age had a 10-fold increased incidence of AKI, a higher risk of dialysis dependence and significantly lower rates of renal recovery. Many scores for assessing AKI are devised among which SOFA score (Sequential Organ Function Assessment) and APACHE-II (Acute physiology and chronic health evaluation) are commonly used in the majority of ICUs as predictive of mortality.

The aim of the study: The primary aim was to identify risk factors for AKI and in-medical ICU (intensive care unit) mortality.

Material methods: A Two-year observational study done prospectively from January 2016 to January 2018 at a tertiary care center. All patients were admitted to the medical ICU at Gauhati Medical College Hospital and were followed prospectively from the time of admission in ICU through ICU discharge. A total of 200 patients were included in the study.

Results: Two hundred (200) elderly patients (≥ 60 years) were included in the analysis. AKI developed in 58 patients (29%). AKI group had higher baseline creatinine, higher temperature, initial systolic blood pressure (SBP), heart rate, longer ICU stay and higher mortality rate (52.9% vs.47 %, $p < 0.001$) compared to the non-AKI group. Out of 200 patients, most of the patients were classified as KDIGO stage 2 (58.8%), followed by stage 3 (26.5%) in the survivor's group while as the reverse was true for non-survivors. Non-survivors had higher APACHE II and SOFA >11 score [18.25 ± 2.513 x 42 (82.4), $p < 0.001$] compared to survivor group [10.82 ± 8.472 x 20(13.4) x, $p < 0.001$]. The commonest etiological factor of AKI in elderly ICU patients was found to be sepsis in 38% (76) patients. Logistic regression analysis identified as factors associated with AKI SOFA >11 (odds ratio [OR] = 54.235, $p < 0.001$), sepsis (OR=1.698), and diabetes (OR=27.692). Oliguria baseline creatinine, SOFA >11,

APACHE II, need for renal replacement therapy (RRT) duration of stay in ICU, sepsis, and AKI severity (stage 3) were identified as predictors of death in logistic regression analysis.

Conclusion: Risk factors for AKI in elderly patients are SOFA>11 scores, higher APACHE II, the presence of sepsis, higher baseline creatinine and oliguria (<400 mL/day).

Key words: AKI, SOFA, APACHE-II, KDIGO stage. HAAKI.

Introduction

Acute kidney injury (AKI) is defined as a significant increase in serum creatinine (SCr) or a decrease in urine output (1). It is a common and important occurrence in the intensive care unit (ICU) patients (2) with a prevalence ranging from 2 to 25% (3). Age-dependent structural and functional alterations over time predispose the kidney to further injury, presumably from the interplay of intrinsic renal degeneration and multiple comorbidities (4), need for procedures and drugs that function as nephron-toxins(5). Baraldi A et al in their study showed that patients >65 years of age had a 10-fold increased incidence of AKI, a higher risk of dialysis dependence and significantly lower rates of renal recovery when compared to patients aged <65 years and have estimated that 40% of AKI in the elderly is due to acute tubular necrosis (ATN) and 30% due to pre-renal causes (6).

Prognostication is an important part of the management of any critically ill patient. It helps in predicting the reliable outcome of a patients' current standing. Among the many scores for assessing AKI, SOFA (Sequential Organ Function Assessment) and APACHE-II (Acute physiology and chronic health evaluation) are commonly used in the majority of ICUs as predictive of mortality (7). AKI in elderly patients has a poor prognosis despite advances in treatment in recent years. The mortality rate among the elderly patients with AKI in ICU patients is found to be 53% (8).

Most of the studies on AKI in elderly patients were performed in developed countries and data from developing countries is scarce. Moreover, patients were not only in ICU but also in the general wards of the hospital. Given the paucity of studies in this area, more studies and its effect on clinical outcomes are needed.

Material and methods: This was a two-year observational study done prospectively from January 2016 to January 2018 at a tertiary care center. All patients were admitted to the medical ICU at Gauhati Medical College Hospital, Guwahati Assam and were followed prospectively from the time of admission in ICU through ICU discharge. This study had 200 patients. Informed consent was obtained from the patients included in the study. Nephrology fellows visited the ICU daily from January 2016 to January 2018 and collected data on all elderly patients admitted in this ICU. Patients who fulfill the definition of Hospital Acquired Acute Kidney Injury (HAAKI) were included.

HAAKI was defined as the development of AKI any time after 48 hours of hospitalization, on a patient who was admitted with normal renal function (18) Diabetes was defined according to ADA criteria and AKI in diabetes was diagnosed in absence of proteinuria, diabetic retinopathy, neuropathy and normal creatinine level at the hospitalization.

Elderly persons were defined as any person ≥ 60 years of age, as per Maintenance and Welfare of Parents and Senior Citizens Act, 2007 government of India.

Inclusion criteria:

- Elderly >60 years old
- AKI was defined according to the Kidney Disease Improving Global Outcomes (KDIGO) criteria based on the increase of serum creatinine or decrease of urine output.

Exclusion criteria:

- All Chronic kidney disease (CKD) patients.
- Renal transplant patients.
- ICU stay <48 hrs.

The primary outcome was to identify risk factors for AKI and in-ICU mortality.

Baseline data, including demographics, medical history, and severity, were collected prospectively on each patient by review of the medical record (Table-1). Laboratory parameters were recorded for the first ICU day followed by vital signs and hemodynamic data for each day during ICU stay. Renal function was assessed daily based on creatinine levels and urine output. Serial APACHE II and SOFA score at admission were computed on the first ICU day, and AKI was classified according to the KDIGO stage after 7 days from AKI diagnosis. All elderly patients were divided into AKI and non-AKI group and survivors and non-survivors. The diagnosis was based on clinical history, results of physical examination, relevant blood tests, urinalysis, and

the findings on renal ultrasonography. Baseline creatinine was defined as the lowest serum creatinine value in the last 6 months before AKI or, for those without this measurement, the lowest value achieved during hospitalization in the absence of dialysis. The study was approved by the institutional ethical committee.

Results:

Two hundred elderly patients were included in the final analysis. AKI developed in 58 patients (29%) and most of the AKI episodes were diagnosed by the increase in serum creatinine than by urine output criteria. A comparison of baseline characteristics between elderly who did and did not develop AKI is shown in Table -1.

Table 1: Demographic and clinical characteristics of patients according to the presence of AKI

Characteristics	No. of patients (n=200)	AKI (n=58)	Non- AKI (n=142)	p- value
Age	74.88 ± 10.49	75.69±11.840	74.55±9.908	0.767
Baseline Creatinine (mg/dl)	1.17 ± 0.31	1.44±0.274	1.061±0.2455	0.001
Male (%)	107 (53.5)	28 (48.3)	79 (55.6)	0.344
Heart rate (bpm)	80.19 ± 12.28	92.50±10.16	75.16 ± 9.134	0.001
Initial SBP (mmHg)	141.25 ± 17.31	123.69 ±14.868	148.42 ±12.456	0.001
Hypertension (%)	75 (37.5)	20 (34.5)	55 (38.7)	0.573
Diabetes (%)	98 (49)	34 (58.6)	64 (45.1)	0.018
Others (%)	57 (28.5)	15 (25.9)	42 (29.6)	0.597
Temperature celsius	37.80 ± 0.992	38.47 ±1.047	37.53 ± 0.831	0.001
Respiratory rate /min	18.11 ± 0.945	18.07 ±1.212	18.13 ±0.815	0.657
Nor-adrenaline (%)	74 (37)	37 (63.8)	37 (26.1)	0.001
Mechanical ventilation (%)	66 (33)	20 (34.5)	46 (32.4)	0.776
Sepsis (%)	21(10.5)	10(17.2)	11(7.7)	0.047
Shock (%)	28(14.0)	13 (22.4)	15(10.6)	0.028
Drugs (%)	35 (17.5)	14 (24.1)	21 (14.8)	0.114
Drugs(including CIN)	45 (22.5)	12 (20.7)	33 (23.2)	0.695
Volume loss	21(10.5)	2(3.4)	19 (13.4)	0.038
Oliguria <400ml/day	69 (34.5)	34 (58.6)	35 (24.6)	0.001
Need of RRT	75 (37.5)	54 (93.1)	21 (14.8)	0.001
APACHE II	12.73 ± 8.091	15.28 ± 13.553	11.68 ±3.742	0.008
SOFA>11	62 (31)	39 (67.2)	23 (16.2)	0.001
AKI any degree	58 (29)	50 (86.2)	8 (5.6)	0.001
Deaths %	51	27(52.9%)	24 (47%)	0.001
ICU stay number of days	8.71±3.74	9.98±3.980	8.18±3.53	0.002

Table 2: Patient demographics and clinical characteristics according to outcome

Characteristics	Survivors (N=149)	Non- Survivors (N=51)	P-value
Age	75.20 ±10.737	73.94±9.760	0.503
Baseline Creatinine (mg/dl)	1.135±0.2898	1.27 ±0.333	0.009
Male (%)	80 (53.7)	13 (25.5)	0.001
Heart rate (bpm)	77.67 ± 10.968	87 ± 13.051	0.001
Initial SBP (mmHg)	143.58 ±16.365	134.41 ± 18.341	0.001
Hypertension (%)	49 (32.9)	26 (51.0)	0.021
Diabetes (%)	60 (40.3)	38 (74.5)	0.001
Others (%)	53 (35.6)	4 (7.8)	0.001
Temperature	37.74 ± 0.981	37.96 ± 1.019	0.165
Respiratory rate	18.12 ± 0.869	18.08 ±1.146	0.862
Nor adrenaline (%)	48 (32.2)	26 (51)	0.017
Mechanical ventilation (%)	10(6.7)	10(19.6)	0.008
Sepsis (%)	16(10.7)	14 (27.5)	0.004
Shock (%)	13 (8.7)	13 (25.5)	0.002
Drugs (%)	27 (18.1)	8 (15.7)	0.693
Drugs(including CIN)	32 (21.5)	13 (25.5)	0.554
Volume loss (%)	14 (9.4)	0	0.023
Oliguria <400mL/day	20 (13.4)	42 (82.4)	0.001
Need of RRT (%)	37 (24.8)	38 (74.5)	0.001
APACHE II	10.82 ± 8.472	18.25 ± 2.513	0.001
SOFA >11	20(13.4)	42 (82.4)	0.001
AKI any degree (n %)	33 (22.1)	26 (49)	0.001
ICU stay (days)	7.45±2.92	12.37±3.49	0.001
KDIGO (n %)			
Stage 1	5(14.7)	3(12.5)	0.81
Stage 2	20(58.8)	2(8.3)	0.001
Stage 3	9(26.5)	19(79.2)	0.001

Furthermore, AKI group had higher baseline creatinine, higher temperature, initial systolic blood pressure (SBP), heart rate, longer ICU stay and higher mortality rate (52.9% vs.47 %, $p<0.001$) compared to the non-AKI group. The groups were similar in age, gender, diabetes, hypertension, cardiovascular disease, need for noradrenaline use, and the need for mechanical ventilation at ICU admission (Table-1).

Out of 200 patients, most of the patients were classified as KDIGO stage 2 (58.8%), followed

by stage 3 (26.5%) in the survivor's group while as the reverse was true for non-survivors. Non-survivors had higher APACHE II and SOFA>11 score [$18.25 \pm 2.513 \times 42 (82.4)$, $p< 0.001$] compared to survivor group [$10.82 \pm 8.472 \times 20(13.4)$], $p<0.001$]. (Table-2).

Logistic regression analysis identified as factors associated with AKI SOFA>11 (odds ratio [OR] =54.235, $p<0.001$), sepsis (OR=1.698), and diabetes (OR=27.692) (Table 3).

The commonest etiological factor of AKI in elderly ICU patients was found to be sepsis in 38% (76) patients followed by drugs in 22.5% (45) and shock and drugs in 17.5% (35) of the patients. Volume loss as an etiological factor for AKI was exclusively found in females (Table-4).

In our study, we found diabetes as the commonest risk factor that was associated with AKI in elderly patients that were admitted in ICU, which included 34% (68) of the patients, out of which 67.6% were males and 32.4% were female

patients. Diabetes was followed by (CAD/CLD/COPD) in 28.5% (57) and hypertension in 22.5% (45) of the patients (Table-5). Adjusting for variables such as age, sepsis, APACHE II and SOFA>11 there was no significant change in the association between KDIGO AKI stage 3 and mortality. In this study, oliguria baseline creatinine, SOFA>11, APACHE II, sepsis, and AKI severity (stage 3) were identified as predictors of death in logistic regression analysis.

Table 3: Logistic outcome for AKI (n=200)

Characteristics	Odds ratio (95% CI *)	p- value
Age	0.924 (0.832-1.026)	0.141
Baseline creatinine	0.000 (0.000-0.083)	0.005
Respiratory rate	1.625 (0.724-3.644)	0.239
Initial systolic BP	1.057 (0.997-1.121)	0.064
Temperature	0.397 (0.137-1.144)	0.087
Sepsis	1.698 (.371-7.763)	0.495
Diabetes	27.692 (3.237-236.901)	0.002
AKI any degree	0.000 (0.000-0.007)	0.000
Stay in ICU (days)	0.479 (0.329-0.698)	0.000
SOFA>11	54.235 (4.919-597.972)	0.001
APACHE II	0.918 (0.860-0.979)	0.009
Use of mechanical ventilation	0.989 (0.146-6.692)	0.991
Use of Nor-Adrenalin	11.333 (1.708-75.183)	0.012
Oliguria< 400 ml/day	0.056 (0.010-0.315)	0.001
Need of RRT	38.636 (3.048-489.765)	0.005

*CI= confidence interval

Table 4: Etiology of AKI in elderly ICU patients (N=200)

Etiology of AKI	Gender		Total
	Males	females	
Drugs(including CIN*)	23 (51.1%)	22 (48.9%)	45
Sepsis	64 (84.2%)	12 (15.8%)	76
Sepsis + shock	7 (23.3%)	23 (76.7%)	30
Shock + drugs	13 (37.1%)	22 (62.9%)	35
Volume loss	0 (0%)	14 (100%)	14
Total	107(53.5%)	93 (46.5%)	200

*CIN= contrast-induced nephropathy.

Table 5: Risk factors for AKI in elderly ICU patients (n=200)

Risk factors of AKI	Gender		Total
	Male	Female	
Diabetes	46 (67.6%)	22 (32.4%)	68
Diabetes + Hypertension	21 (70.0%)	9 (30.0%)	30
Hypertension	32 (71.1%)	13 (28.9%)	45
Others (CAD,CLD,COPD,CVA*)	8 (14.0%)	49 (86.0%)	57
Total	107 (53.5%)	93 (46.5%)	200

CAD= coronary artery disease, CLD= chronic liver disease, COPD= chronic obstructive pulmonary disease, CVA= cerebro vascular accident

Statistical analysis: Statistical analysis was done by using Chi-Square test and logistic regression analysis. Variables were considered significant if the p-value is <0.05.

DISCUSSION:

Our study in elderly patients admitted to the medical ICU in Gauhati Medical College and Hospital, Guwahati Assam, indicates that AKI is very frequent and suggest that it has an important impact on in-hospital mortality of geriatric patients. The incidence of AKI is increasing over time and is most common in elderly individuals. Studies in literature have shown that the AKI incidence among elderly patients ranges from 22% to 40%, with most patients having stage 1 disease (9). We in our study found that 29% of geriatric patients had AKI and most of them had AKI stage 1, which is similar to that found in the literature. In our study, the risk factors for AKI in elderly patients were SOFA>11, higher APACHE II, the presence of sepsis, diabetes, higher baseline creatinine and oliguria<400ml/day. Our findings were consistent with the previous studies performed in ICU in younger populations that have reported that AKI is more frequently observed in septic patients (10). There are few studies on AKI in elderly patients admitted to ICU from developing countries. Research from India has shown that underlying sepsis, chronic illness, and presence of cardiac failure, were associated with AKI and poor outcome among the elderly population in a hospital-based study (11). In our study, we found most of the elderly AKI patients presented one or more concomitant diseases, like diabetes mellitus, cardiovascular diseases, and hypertension. Our finding was in

accordance with the study conducted by Pascual J et al (5).

Sepsis was the main cause of AKI in elderly patients (38%). This is similar to the studies carried on younger AKI patients in ICU. According to the literature, sepsis is a well-known risk factor for the development of AKI especially in developing countries occurring in approximately 19% of patients with sepsis, 23% of patients with severe sepsis, and 51% of patients with septic shock (12, 20). AKI associated with sepsis remains a major challenge in ICU due to its common occurrence, high treatment costs, and the unacceptable high mortality. There are few studies about the incidence and outcome of elderly patients with sepsis in ICU (13). The overall in-hospital mortality rate among critically ill patients is high, exceeding 50% and reaching 80%, depending on the clinical conditions, comorbidities, and need for replacement therapy. In accordance with other studies, we found that the mortality rate of the elderly AKI patients was 52.9% and higher than that of the elderly patients without AKI, which was 47%. Kohli et al, in their prospective study, found a high mortality rate of 61% in the elderly patients with AKI (aged >60 years) in a tertiary care center of India (14). The mortality rate in our study was higher in group who required RRT and in patients who had longer duration of stay in ICU as compared to those who did not receive RRT or were discharged early, these observations

were similar to the study done by Harbir et al. (15).

A number of studies had been conducted so far on different scoring systems to predict mortality. However, the comparison between the scoring systems shows differences in sensitivity and specificity. In a comparative study conducted by Fröhlich M et al in post-traumatic patients, SOFA score was sensitive in predicting the length of stay in ICU and showed the most balanced relation of sensitivity and specificity (16). Studies have also proved that SOFA score and APACHE II, scores are predictors of mortality in the elderly AKI patients and have good discriminative power for ICU and hospital mortality (17). Recently, the KDIGO criteria were developed to standardize the diagnosis of AKI and it gives a level of classification about AKI severity. In accordance with the previous literature, our study also showed a significant difference in AKI stage between the elderly non-survivors survivors (18). A high incidence of AKI among elderly AKI patients was detected and sepsis, diabetes, SOFA>11, higher APACHE II, and oliguria were identified as risk factors for AKI, serving as an explanation for the pathophysiology between AKI and its negative impact on short-term mortality (19).

CONCLUSION:

From our study we conclude;

HAAKI is a common clinical entity in the elderly population due to various factors. Development of HAAKI is associated with overall increased mortality in hospitalized patients, particularly in elderly. That the risk factors for AKI in elderly patients were SOFA>11 scores, higher APACHE II, the presence of sepsis, higher baseline creatinine and oliguria (<400 mL/day), requirement of dialysis, length of hospital stay. Underlying chronic illness, the presence of cardiac failure, and sepsis were associated with AKI and poor outcome among the elderly population. Sepsis was the main cause and diabetes was the main risk factor for elderly patients with AKI.

Conflict of interest: None

Funding source: Nil

References:

1. Chawla LS. Acute kidney injury leading to chronic kidney disease and long-term outcomes of acute kidney injury: the best opportunity to mitigate acute kidney injury? *Contrib Nephrol* 2011; 174: 182–190.
2. Sileanu FE, Murugan R, Lucko N et al. AKI in low-risk versus high-risk patients in intensive care. *Clin J Am Soc Nephrol*. 2015;10 (2):187–196.
3. Uchino S, Kellum JA, Bellomo R et al. Acute renal failure in critically ill patients. *JAMA* 2005; 294: 813–818.
4. Anderson S, Eldadah B, Halter JB et al. Acute kidney injury in older adults. *J Am Soc Nephrol* 2011; 22: 28–38.
5. Pascual J, Liano F. Causes and prognosis of acute renal failure in the very old. Madrid Acute Renal Failure Study Group. *J Am Geriatr Soc*.1998;46 (6):721–725.
6. Baraldi A, Ballestri M, Rapana R et al. Acute renal failure of medical type in an elderly population. *Nephrol Dial Transplant*. 1998;13 (Suppl 7):25–29.
7. Toma T, Abu-Hanna A, Bosman RJ. Discovery and inclusion of SOFA score episodes in mortality prediction. *J Biomed Inform*. 2007 Dec;40 (6):649-60.
8. Yu Gong , Feng Zhang, Feng Ding , Yong Gu. Elderly patients with acute kidney injury (AKI): Clinical features and risk factors for mortality. *Archives of Gerontology and Geriatrics*.54 (2012) e47–e51.
9. Medeiros P, Nga HS, Menezes P, Bridi R, Balbi AL, Ponce D. Acute kidney injury in septic patients admitted to emergency clinical room: risk factors and outcome. *Clin Exp Nephrol*. 2015;19(5):859–866.
10. Suh SH, Kim CS, Choi JS, Bae EH, Ma SK, Kim SW. Acute kidney injury in patients with sepsis and septic shock: risk factors and clinical outcomes. *Yonsei Med J*. 2013;54 (4):965–972.
11. Mahajan S, Tiwar S, Bhowmik D, Agarwal SK, Tiwari SC, Dash SC. Factors affecting the outcome of acute renal failure among the elderly population in India: a hospital based

- study. *Int Urol Nephrol*. 2006;38(2):391–396.
12. Silva E, Pedro MA, Sogayar ACB, et al. Brazilian sepsis epidemiological study (BASES study). *Crit Care*. 2004;8(4):R251–R260.
 13. Angus DC, Linde-Zwirbe WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. *Crit Care Med*. 2001; 29(7):1303–1310.
 14. Kohli HS, Bhat A, Aravindan SudK, Jha V, Gupta KL, Sakhuja V. Spectrum of renal failure in elderly patients. *Int Urol Nephrol*. 2006; 38(3–4):759–765.
 15. Harbir S Kohali, Madhu C, Bhaskaran, Thangamei Muthukumar: Treatment related acute renal failure in elderly: a hospital based prospective study. *NDT* 2000, 15:212-15.
 16. Fröhlich M, Wafaisade A, Mansuri A. Which score should be used for posttraumatic multiple organ failure?- Comparison of the MODS, Denver-and SOFA- Scores. *Scand J Trauma Resusc Emerg Med*. 2016 Nov 3;24 (1):130.
 17. de Mendonca A, Vincent JL, Suter PM, et al. Acute renal failure in the ICU: risk factors and outcome evaluated by the SOFA score. *Intensive Care Med*. 2000;26 (7):915–921.
 18. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO clinical practice guideline for acute kidney injury. *Kidney Int Suppl*. 2012;2:1–138.
 19. Chronopoulos A, Cruz DN, Ronoco C et al. Hospital-acquired acute kidney injury in the elderly. *Nat Rev Nephrol*, 2010 Mar;6(3):141-9.
 20. M. Sharma et al, Clinical Profile of Acute Kidney Injury in Intensive Care Unit: A Single Center Data of a developing nation. *Assam journal of Internal medicine* January 2017, 8-11