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Original research

EARLY ACUTE KIDNEY INJURY IN SEPSIS AND SEPTIC SHOCK

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ABSTRACT

Background: *Acute kidney injury is one of the severe conditions in hospitalized patients. Acute kidney injury can develop early from admission, usually within the first 24 hours of ICU admission. In Vietnam, there have been limited studies monitoring the progression of acute kidney injury in the early stages. This study aims to investigate the incidence, severity, clinical, laboratory characteristics, and progression of acute kidney injury in patients with sepsis and septic shock within the first 48 hours.*

Methods: *This study is a cross-sectional descriptive analysis of 101 patients who are 15 or older and have been diagnosed with severe infection and septic shock. These patients were treated in the Intensive Care Unit of Hue Central Hospital. The patient had treatment in accordance with a standardized protocol while being closely observed. Samples were collected for diagnostic testing, and the patient's urine output and blood creatinine levels were diligently checked.*

Results: *The prevalence of acute renal injury (AKI) was 60.40%, with stage 1 accounting for 50.82% of cases, stage 2 accounting for 22.95%, and stage 3 accounting for 26.23%. The cohort of individuals diagnosed with AKI exhibited an advanced age, with a mean age of 60.72 ± 17.41 years, and predominantly consisted of male subjects. Patients diagnosed with acute kidney injury showed a statistically significant decrease in urine output and an increased incidence of shock ($p < 0.05$). Additionally, these patients demonstrated lower levels of Hct, blood pH, and bicarbonate while exhibiting higher levels of blood urea, blood creatinine, AST, ALT, total bilirubin, PCT, and blood lactate ($p < 0.05$) compared to individuals without AKI. Patients with AKI had significantly elevated SOFA and APACHE II scores compared to individuals without AKI, as indicated by statistical analysis ($p < 0.05$). Upon admission, a significant proportion of patients, precisely 81.97%, experienced the development of AKI. Furthermore, a observation was made about the prompt recovery of these patients within the initial 24 and 48 hours following admission.*

Conclusion: *The prevalence of AKI was accounted for 60.40%. Among the cases of AKI, stage 1 accounted for 50.82%, while stage 2 and stage 3 accounted for 22.95% and 26.23%, respectively. There were observed variations in urine output and rates of shock among individuals diagnosed with AKI. Additionally, SOFA and APACHE II scores were elevated. The percentage of AKI was 81.97% of patients upon their initial hospital admission, with a significant proportion seeing early recovery within the first 24 to 48 hours.*

Keywords: *Sepsis, septic shock, acute kidney injury, AKI, SOFA, APACHE.*

I. INTRODUCTION

Acute kidney injury (AKI) is one of the severe conditions in hospitalized patients, increasing the risk of short-term and long-term mortality, the risk of developing chronic kidney disease, and increasing the patient's treatment costs [1]. AKI can progress from the early stage of the disease course, upon admission. According to author Seung Seok Han, 90.3% of patients develop AKI in the early stage [2]. In their studies, Amanda and Sara B defined early AKI as AKI that develops within 48 hours of ICU admission [3,4]. In this stage, the first 24 hours play

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an important role. Bagshaw suggests that AKI often occurs within the first 24 hours of ICU admission [5]. Maria Plataki also reported that 61% of patients developed acute kidney injury within an average of 7.5 hours from the onset of septic shock [6].

In Vietnam, there have been limited studies monitoring the progression of AKI in the early stage. Therefore, we conducted a study to investigate the incidence, severity, some clinical and laboratory characteristics, and progression of AKI in patients with sepsis, septic shock within the first 48 hours.

II. MATERIALS AND METHODS

We conducted a cross-sectional descriptive study on patients who are 15 or older diagnosed with sepsis and septic shock in the Intensive Care Unit of Hue Central Hospital.

Patients who did not consent to participate or were diagnosed with chronic kidney disease were excluded.

Patients were examined clinically, their medical histories were recorded, laboratory tests were conducted, and intensive care treatment was administered. General information, clinical characteristics, and laboratory tests are included in the compilation of data. Upon hospital admission, urine output, and blood creatinine levels were measured at 24 and 48 hours. Treatment methods include antibiotics, vasopressors, and fluid management (intravenous fluids and oral consumption for the first 24 hours). APACHE II and SOFA indices were utilized to assess the severity of the disease.

Diagnostic criteria for severe sepsis and septic shock according to Sepsis-3 2016 [7].

The Sepsis-3 (2016) diagnostic criteria for sepsis and septic shock: Sepsis is defined as the presence of infection and multi-organ dysfunction (SOFA scale acute change 2 points) [7]. Septic shock is defined as sepsis accompanied by persistent hypotension necessitating vasopressors to maintain a mean arterial pressure of 65 mmHg and a serum lactate level of >2 mmol/L despite adequate volume resuscitation.

Early AKI (E-AKI) criteria is defined as acute kidney injury within 48 hours of ICU admission [4].

Diagnostic criteria for acute kidney injury according to KDIGO 2012.

Data were analyzed using SPSS 20.0 and Microsoft Excel 2010 to analyze data.

III. RESULTS

Through the study of 101 patients with sepsis and septic shock, the following conclusions were reached:

3.1. Incidence, severity, clinical and laboratory characteristics of acute kidney injury

The incidence of acute kidney injury within the first 48 hours was 60.4%, with stage 1 accounting for 50.82%, stage 2 accounting for 22.95%, and stage 3 accounting for 26.23%. Age distribution: most cases were over 65 years old (40.99%) and those aged between 40 - 65 (39.34%). In terms of gender, 72.13% were male.

Table 1: Clinical characteristics of acute kidney injury at admission

Parameter	AKI	Non-AKI	P
N	61	40	> 0,05*
Age (year)	60.72 ± 17.41	66,40 ± 18.06	> 0.05-#
Gender (male)	72.13%	52.50%	> 0.05*
Glasgow (score)	12.95 ± 3.50	13.30 ± 2.95	> 0.05#
Heart rate (beats/minute)	100.49 ± 21.14	100,20 ± 22,56	> 0.05#
MAP (mmHg)	71.95 ± 18.37	76.53 ± 17.57	> 0.05#
Days of fever before admission (days)	3,34 ± 4.81	3.98 ± 5.93	> 0,05#
Body temperature (°C)	37.91 ± 1.08	37.71 ± 0.82	> 0,05#

Parameter	AKI	Non-AKI	P
Urinary volume (ml/kg/h)	1.17 ± 0.67	1.46 ± 0.45	< 0,05[#]
Fluid volume in the first 24 hours (ml)	2719.7 ± 480.91	2805.0 ± 520.33	> 0,05[#]
Vasopressor use (%)	57.38	42.50	> 0,05[*]
Rate of septic shock (%)	50.82	27.5	< 0,05[*]

[*]Chi-square test; [#]Student T-test

Patients with AKI had a higher average age, with no significant differences in average age, gender, Glasgow score, heart rate, MAP, temperature, and days of fever compared to patients without AKI. The urine output volume of AKI patients was lower than that of patients without AKI, and this result was statistically significant with $p < 0.05$. The rate of vasopressor use and volume of fluid administered in the first 24 hours did not differ significantly between the two groups of patients. AKI patients had a higher rate of shock than those without AKI ($p < 0.05$).

Table 2: Laboratory results in the study cohort within 48 hours of ICU admission.

Parameter	AKI	Non-AKI	p
Hb (g/dl)	10.49 ± 2.86	11.22 ± 2.41	> 0.05
Hct (%)	29.79 ± 9.73	33.76 ± 7.28	< 0.05
WBC (x109/l)	29.79 ± 9.73	14.30 ± 8.28	> 0.05
PLT (x109/l)	177.82 ± 158.25	218.72 ± 125.35	> 0.05
Urea (mmol/l)	16.62 ± 13.00	6.94 ± 3.26	< 0.05
Blood creatinine (µmol/l)	281.42 ± 280.98	78.56 ± 29.22	< 0.05
AST (U/l)	277.11 ± 512.32	97.90 ± 100.27	< 0.05
ALT (U/l)	141.98 ± 257.71	59.44 ± 56.22	< 0.05
Bilirubin TP (µmol/l)	44.27 ± 54.16	22.09 ± 17.18	< 0.05
Blood pH	7.33 ± 0.14	7.44 ± 0.08	< 0.05
PaO2 (mmHg)	101.75 ± 57.18	85.91 ± 35.49	> 0.05
HCO3-(mmol/l)	18.14 ± 6.92	23.25 ± 8.00	< 0.05
PCT (ng/ml)	35.98 ± 40.73	20.33 ± 30.96	< 0.05
Lactate (mmol/l)	5.87 ± 5.11	2.97 ± 2.11	< 0.05

AKI patients had a mean Hb level of 10.49 ± 2.86 g/dL, an elevated white blood cell count of 29.79 ± 9.73 x109/L, a platelet count of 177.82 ± 158.25 x109/L, and a PaO2 level of 101.75 ± 57.18mmHg, with no significant difference compared to non-AKI patients. AKI patients had lower Hct, blood pH, and HCO3- levels and higher blood urea, creatinine, AST, ALT, Bilirubin TP, PCT, and lactate levels compared to non-AKI patients ($p < 0.05$).

Table 3: SOFA and APACHE II scores within 48hrs of ICU admission.

	AKI	Non-AKI	P
SOFA	9.56 ± 3.23	5.70 ± 3.22	< 0.05
APACHE II	15.90 ± 5.79	12.25 ± 4.60	< 0.05

AKI patients had higher SOFA and APACHE II scores compared to non-AKI patients

3.2. Investigation of the progression of acute kidney injury in patients with sepsis and septic shock in the first 48 hours

Table 4: Incidence and severity of acute kidney injury at different study time points.

AKI		Time		
		0h	24h	48h
Stage	Stage 1	28	21	14
	Percentage %	56.0	44.68	42.43
	Stage 2	10	14	6
	Percentage %	20.0	29.79	18.18
	Stage 3	12	12	13
	Percentage %	24.0	25.53	39.39
Total	N	50	47	33
	Percentage %	49.5	46.47	32.67

At the 0-hour time, stage 1 AKI was dominant with 56.0%, while stages 2 and 3 were roughly equivalent. At 24 hours, the proportion of stage 1 AKI decreased to 44.68%, while stages 2 and 3 increased (29.79%, 25.53%). By 48 hours, patients with stage 1 AKI remained high, but the percentage of stage 3 AKI increased significantly to 39.39%.

Table 5: Status of acute kidney injury at admission.

Time	Number	Percentage %
AKI	50	81.97
Non - AKI	11	18.03
Total	61	100

The majority of patients developed acute kidney injury at the time of admission to the intensive care unit, accounting for 81.97%, while a significant proportion did not progress to acute kidney injury (18.03%).

Table 6: Renal function progression in the First 24 Hours

Progression of acute kidney injury	Number	Percentage %
Onset of acute kidney injury	9	14.75
Increase in stage	7	11.48
Decrease in stage	3	4.92
Resolution of acute kidney injury	8	13.11

Progression of acute kidney injury	Number	Percentage %
No change	32	52.46
No acute kidney injury detected	2	3.28
Total	61	100

14.75% of patients started to develop acute kidney injury, 11.48% of patients progressed to a higher stage, while 4.92% had a decrease in stage, along with 13.11% of patients who had a resolution of acute kidney injury. Within the first 24 hours, up to 52.46% of patients had no change in the severity of acute kidney injury. A small percentage (3.28%) of patients did not have acute kidney injury at presentation.

Table 7: Progression of renal fucntion in the next 24 hours.

Progression of acute kidney injury	Number	Percentage %
Progress to acute kidney injury	2	3.28
Recurrence of acute kidney injury	2	3.28
Not recurrence of acute kidney injury	6	9.84
Increase in stage	3	4.92
Decrease in stage	5	8.20
Resolution of acute kidney injury	12	19.67
No change	31	50.81
Total	61	100

In the next 24 hours (from 24 to 48 hours), a small percentage of patients (3.28%) started to progress to acute kidney injury, along with the same percentage of patients experiencing a recurrence of acute kidney injury. 9.84% of patients who have recovered in the first 24 hours did not develop acute kidney injury. 4.92% of patients progressed to a higher stage of acute kidney injury, while the percentage of patients who regressed was 8.20%. 19.67% of patients ended up with this condition, and more than half of the patients had no change in the severity of acute kidney injury during this stage.

IV. DISCUSSION

4.1. Incidence, severity, clinical and laboratory characteristics of patients with acute kidney injury

The incidence of AKI was relatively high, at 60.40%. This incidence was higher than that reported by Rinaldo Bellomo and colleagues in 2017, where the AKI incidence was 22%, with a mortality rate of 38.2% [8]. J.R. Prowle's study reported an incidence of 39.4% [9]. According to Diem Ha Ngoc, the incidence of AKI in septic shock patients was 71.2% [10]. Huynh Quang Dai, Nguyen Truong Son recorded that 100% of patients with sepsis had acute kidney injury [11] [12].

Of the 61 AKI patients, 50.82% were in stage 1, 22.95% were in stage 2, and 26.23% were in stage 3. Ha Ngoc Diem reported that 46.5% of AKI patients were in stage 1, 33.3% were in stage 2, and 20.2% were in stage 3 [10]. Sang Heon Suh's study reported that 48.3% of patients were in stage 1, 31.8% were in stage 2, and 18.9% were in stage 3 [13].

We did not observe any differences in clinical characteristics between the two groups: Glasgow score, gender, age, heart rate, mean arterial pressure, number of fever days, body temperature at admission, and the rate of vasopressor use ($p>0.05$). Maria Plataki also reported no statistically significant differences in age, heart rate, and mean arterial pressure between the AKI and non-AKI groups, with a higher rate of vasopressor use in the AKI group, but this difference was not statistically significant [6]. However, author Sang Heon Suh found some statistically significant differences, precisely a higher average age and lower mean arterial pressure in the AKI group. Nevertheless, Sang Heon Suh also reported no differences in heart rate [13]. In the study by author Hakki Yilmaz, differences in age were observed [14]. Author Huynh Quang Dai did not report any differences in the rate of vasopressor use between AKI and non-AKI patients [11]. AKI patients may have a lower urine volume ($p<0.05$). Research of Xose Luis Perez Fernandez also reached a similar conclusion with $p < 0.05$ [15].

Septic shock was highly prevalent in AKI patients. Shigehiko Uchino reported that septic shock is the most common contributing factor to AKI (47.5%) [16]. Author Jiefeng Liu indicated that septic shock is an essential predictor of AKI (OR: 1.40; 95% CI: 1.13-1.72) [17]. Author Mukesh Sharma Paudel also reported this conclusion in their study [18].

We found no difference in hemoglobin, white blood cell count, and platelet count values between the AKI and non-AKI groups, while values of urea, blood creatinine, AST, ALT, total bilirubin, procalcitonin, and blood lactate were higher in the AKI group compared to the non-AKI group, and the Hct tended to be lower in the AKI group, and these differences were statistically significant ($p<0.05$). Author Hakki Yilmaz did not find any differences in AST, ALT, and total bilirubin levels, similar to our study, and the author did not find any differences in the number of platelets and white blood cells between the two groups [14]. Author Xose Luis Pérez Fernández reported that blood lactate levels were higher in AKI patients compared to non-AKI patients, but there was no difference in blood hemoglobin levels between the two groups [15]. Meanwhile, author Sang Heon Suh observed that the number of platelets and white blood cells in AKI patients was lower, and the author did not find any differences in total bilirubin and hematocrit levels [13]. Similarly, Maria Plataki also reported that in AKI patients, blood lactate and total bilirubin levels were higher than in non-AKI patients, and there were no differences in the results of platelet and white blood cell counts, but there was no difference in hematocrit levels [6]. Mukesh Sharma Paudel found that hematocrit levels were lower in AKI patients, but there were no differences in total bilirubin, blood urea, AST, and ALT levels [18].

AKI patients had higher average SOFA and APACHE II scores than non-AKI patients, and this difference was statistically significant ($p<0.05$). This result was similar to that of Mukesh Sharma Paudel, where the SOFA scores in the AKI and non-AKI groups were 9.2 ± 2.72 and 7.4 ± 2.57, respectively, and the APACHE II scores were 21.1 ± 6.60 and 16.4 ± 8.34, respectively ($p < 0.05$) [18].

These differences may be due to variations in research methods, criteria, research patients, or regional and national differences.

4.2. Progression of AKI in sepsis patients within the first 48 hours

Most patients developed AKI upon admission to the ICU, accounting for 81.97% of cases.

Within the first 24 hours, 14.75% of patients began progressing to AKI, 11.48% progressed to a higher stage, and 4.92% improved. In addition, 13.11% of patients recovered from AKI, and 52.46% showed no change in the severity of AKI. A small incidence (3.28%) of patients did not have AKI upon admission.

In the next 24 hours (from 24 to 48 hours after admission), 3.28% of patients began to progress to AKI, equivalent to the number of patients who had AKI recurrence. 4.92% of patients progressed to a higher stage of AKI, while the incidence of patients who had decreased stage was 8.20%. There were 19.67% of patients who recovered, and more than half of the patients showed no change in the severity of AKI during this period.

These results showed that AKI appears very early upon hospital admission, with many patients recovering within the first 24-48 hours. However, there were also a significant number of patients who worsened during this period, leading to a high incidence of AKI stage 3 cases within the first 48 hours. According to author Seung Seok Han, 90.3% of patients develop AKI in the early stage [2]. Author Maria Plataki also noted that 61% of patients progress to AKI on average 7.5 hours after the onset of septic shock [6]. Author Kristina H. Mitchell also found in her study that 95% of patients with AKI were diagnosed upon admission to the emergency department, and the remaining 5% developed AKI within the next 72 hours [19].

V. CONCLUSION

The incidence of AKI was 60.40%, including 50.82% in stage 1, 22.95% in stage 2, and 26.23% in stage 3. AKI patients may have lower urine output and a higher rate of septic shock. AKI patients also had lower Hct, blood pH, HCO3-, and higher blood urea nitrogen, creatinine, AST, ALT, total bilirubin, procalcitonin, and lactate levels than those without AKI ($p < 0.05$). The average SOFA and APACHE

II scores were higher in the AKI group than in the non-renal injury group.

AKI appeared very early after admission (81.97% of AKI patients), with many patients recovering within the first 24 and 48 hours (13.11% and 19.67%, respectively). However, a considerable number of patients also deteriorated during this period (11.48% in the first 24 hours, 4.92% between 24 and 48 hours), leading to a high incidence of stage 3 AKI within 48 hours (39.39%).

REFERENCES

1. Rodrigo E, Suberviolab B, Albines Z, et al. A comparison of acute kidney injury classification systems in sepsis. Nefrologia. 2016;3(1):530-534.
2. Han SS, Baek SH, Ahn SY, et al. Anemia is a Risk Factor for Acute Kidney Injury and Long-Term . Tohoku J. Exp. Med. 2015;16(3):287-295.
3. Ruth A., Basu R.K., Gillespie S., et al. Early and late acute kidney injury: temporal profile in the critically ill pediatric patient. Clinical Kidney Journal, 2022;15(2):311–319
4. Sara B, Monteiro JJ, Carvalho P, et al. Early vs late development of acute kidney injury and its prognostic relevance in ACS patients. European Heart Journal: Acute Cardiovascular Care. 2021;10(1):1
5. Bagshaw SM, George C, Bellomo R. Early acute kidney injury and sepsis: a multicentre evaluation, Critical Care. 2008;12(2):3-4
6. Plataki M. Predictors of Acute Kidney Injury in Septic Shock Patients: An Observational Cohort Study. Clin J Am Soc Nephrol.2016;6:1744-1751
7. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;3(2):2-3.
8. Bellomo R, Kellum JA, Ronco C, et al. Acute kidney injury in sepsis. Intensive Care Med. 20177(2):816-828.
9. Prowle J. Sepsis-Associated AKI. American Society of Nephrology.2018;13:339–342.
10. Ha Ngoc Diem, Nguyen Nhu Nghia, Pham Van Linh. Survey on acute kidney injury in septic shock patients at Can Tho Central General Hospital in 2017 - 2019. Can Tho Journal of Medicine and Pharmacy. 2019; 19:5-6.
11. Huynh Quang Dai. Acute kidney injury due to sepsis in the ICU. Medical Journal of Ho Chi Minh City.2021; 25(1):80-83.
12. Nguyen Truong Son. Survey on acute kidney injury in patients with sepsis at the Resuscitation Department of Cho Ray hospital. Medical Journal of Ho Chi Minh City. 2017;21(3):4-6.
13. Suh SH, Kim CS, Choi JS, et al. Acute Kidney Injury in Patients with Sepsis and Septic Shock: Risk Factors and Clinical Outcomes. Original Article. 2013;14(3):965-971.
14. Yilmaz H, Cakmak M, Inan O, et al. Can neutrophil–lymphocyte ratio be independent risk factor for predicting acute kidney injury in patients with severe sepsis? Renal Failure. 2015;8(3):225-229.
15. Fernández XLP. Sepsis associated Acute Kidney Injury: incidence, risk factors and continuous renal replacement therapies. Doctoral Thesis. 2019;39.
16. Uchino S, Kellum JA, Bellomo R, et al. Acute Renal Failure in Critically Ill Patients: A Multinational, Multicenter Study. JAMA. 2005;294(7):813-815.
17. Liu J. Rates, predictors, and mortality of sepsis associated acute kidney injury: a systematic. BMC Nephrology.2020;7(4):11-12.
18. Paudel MS, Wig N, Mahajan S, Pandey RM, et al. A Study of Incidence of AKI in Critically Ill Patients. Renal Failure. 2012;5(2):1217- 1222.
19. Mitchell KH. Resolution of Sepsis-Associated Acute Kidney Injury: Association with Emergency Department Fluid Management Patterns. Thesis Master of Science. 2017;6(2):17-18.