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ORIGINAL ARTICLE

ASSOCIATION OF ACUTE KIDNEY INJURY WITH CLINICAL OUTCOMES OF PATIENTS IN INTENSIVE CARE UNIT

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ABSTRACT
Objective: to evaluate the association of Acute Kidney Injury with the clinical outcomes of patients in the Intensive Care Unit.
Method: this is the clipping from a cohort study with a prospective view, carried out in a private intensive unit in the capital of Sergipe between October 2018 and July 2019. This was a convenience and non-probabilistic sample. The data were analyzed using the Kolmogorov-Smirnov tests; Fisher's exact test and t-Student through the Statistical Package for the Social Sciences.
Results: a total of 100 patients participated in the study, 29% had acute kidney injury, 62.1% were male and aged 70 ± 16 years. We evidenced an association between injury and infection (p=0.018), mechanical ventilation for more than 48 hours (p=0.016), death (p=0.010) and pressure injury (p=0.037).
Conclusion: The study will contribute to the early identification of kidney injury, promoting assistance with therapeutic planning to reduce the complications of the disease.

DESCRIPTORS: Intensive Care Units; Acute Kidney Injury; Epidemiology; Incidence; Patients.

ASOCIACIÓN DE LA LESIÓN RENAL AGUDA CON RESULTADOS CLÍNICOS DE PACIENTES EN UNIDAD DE TERAPIA INTENSIVA

RESUMEN:
Objetivo: evaluar la asociación entre la Lesión Renal Aguda y los resultados clínicos de los pacientes en Unidad de Terapia Intensiva. Método: se hizo una selección de datos de cohorte con visión prospectiva que se realizó en una unidad intensiva particular en la capital de Sergipe entre octubre de 2018 y julio de 2019. La muestra se hizo por conveniencia y no probabilística. Se analizaron los datos con pruebas de Kolmogorov-Sminorv; exacto de Fisher y t-Student por medio del Statistical Package for the Social Sciences. Resultados: 100 pacientes participaron del estudio: 29% presentaron Lesión Renal Aguda, siendo el 62,1% de estos del sexo masculino y edad de 70±16 años. Se evidenció asociación del agravio con infección (p=0,018), ventilación mecánica por más de 48 horas (p=0,016), muerte (p=0,010) y lesión por presión (p=0,037). Conclusión: El estudio ayudará en la identificación precoz de la lesión renal, contribuyendo al planeamiento para reducir las complicaciones de la enfermedad.
DESCRIPTORES: Unidades de Terapia Intensiva; Lesión Renal Aguda; Epidemiología; Incidencia; Pacientes.

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INTRODUCTION

Acute Kidney Injury (AKI) is a growing prevalent health issue among developed and developing countries, with high morbidity and mortality. It is considered a multifactorial syndrome, characterized by a decrease in renal function in less than 48 hours associated with an absolute increase in serum creatinine and a drop in urine output in 7 days[1].

To classify the disease, some protocols are employed, such as RIFLE - which refers to the acronyms Risk (risk of renal dysfunction); Injury (injury/damage to the kidney); Failure (renal function failure); Loss (loss of kidney function) and End-Stage Kidney Disease (end-stage kidney disease) - the Acute Kidney Injury Network (AKIN) and Kidney Disease Improving Global Outcomes (KDIGO), which define the increase in creatinine by urinary flow as a marker of renal dysfunction and classify patients at risk for developing AKI[2-4].

According to KDIGO, kidney injury may occur quickly and unexpectedly in three situations: I) when there is an increase of more than 0.3 mg/dL in the serum creatinine level over the baseline value in 48 hours; II) when there is an increase greater than or equal to 1.5 times the baseline value of serum creatinine in seven days; or III) when the urine output is reduced to below 0.5 mL/kg/h in 6 hours. According to this classification, there are three stages of dysfunction: stage 1 (risk), stage 2 (renal damage) and stage 3 (renal failure), according to the impairment of renal function, adopting the worst value of serum creatinine[5].

It is estimated that this injury can affect nearly 20 to 200 million of the general population, with 7% to 18% of patients being admitted to the hospital and of these, about 50% in critical units. The Intensive Care Unit (ICU) consists of one of these critical units designed to assist critically ill patients who have hemodynamic instability, requiring high complexity care, as well as high-tech resources and equipment for the intervention of critically ill patients[3,6-7].

Research carried out in a large public hospital in the Federal District showed a significant progression in the onset of AKI in the ICU, with incidence varying from 2 to 5% in 2002, increasing to 5 to 30% or more in 2014. In contrast, the hospital incidence was 3% to 5%[8].

It is important to analyze this data, since the degree of impairment caused by kidney injury directly impacts the patient's prognosis, requiring invasive interventions, such as dialysis treatment. Thus, a retrospective study carried out in an adult Brazilian ICU showed that, of the patients who progressed to AKI, 49% to 70% needed dialysis treatment and mortality ranged from 50% to 90%, and was often associated with time prolonged hospital stay[9].

Therefore, given the high incidence and high morbidity and mortality in the ICU, this study was carried out to help health professionals to detect the injury at an early stage with greater assertiveness, promoting assistance with therapeutic planning aimed at reducing the disease complications. Given the above, the objective of this research was to evaluate the association of AKI with the clinical outcomes of patients admitted to an ICU of a private hospital.

METHOD

This is the clipping from a cohort study with a prospective view linked to the project "Clinical Characterization, Severity Profile and Outcomes of Patients in Intensive Care

Units". The research was carried out in four hospitals in the state of Sergipe, but for this study, data from the ICU of a private hospital located in the capital of Sergipe were used, consisting of (20) clinical and (five) surgical beds, totaling 25 beds.

Data collection took place between October 2018 and July 2019, performed by Nursing students, for four hours on the afternoon shift, and three days of the week, as required by the institution.

This was a convenience and non-probabilistic sample. All patients admitted during the data collection period, aged over 18 years and with a minimum stay of 24 hours in the ICU, were included. Patients who were transferred to another unit/institution in the first 24 hours, who were discharged or died within the first 24 hours were excluded from the study.

For this purpose, a data collection instrument developed by the researchers was used, which addressed demographic data, clinical characteristics, support for admission to the ICU, exams performed, outcomes of the clinical condition, and KDIGO scores for AKI, the Sequential Organ Failure Assessment (SOFA), which aims to assess the extent and severity of organ dysfunction; the Simplified Acute Physiology Score III, which estimates the probability of death; the Charlson Comorbidity Index (CCI), which assesses comorbidity and the 10-year mortality prediction; and the Nursing Activities Score (NAS), which assesses the nurse's workload.

Patients were followed up throughout ICU stay, with a daily record by the instrument up to the seventh day of hospitalization, and at the time of discharge, transfer, or death. After discharge from the ICU, patients were followed up and their outcomes analyzed until they were discharged. The primary outcome was the onset of AKI up to the seventh day after admission to the ICU, based on the assessment of baseline creatinine and the use of KDIGO to classify the degree of injury. Secondary outcomes included: development of pressure ulcers (PU), acute myocardial infarction (AMI), stroke, infection, death, need for mechanical ventilation for more than 48 hours, need for dialysis or rehospitalization in ICU.

After data collection, the information was tabulated in the Excel 2010 program, and the Statistical Package for the Social Sciences (SPSS) program version 25.0 was used for analysis. The normality of the data was tested using the Kolmogorov-Smirnov test. Descriptive analyses of categorical data were performed in absolute and relative frequencies. Continuous variables were shown as means and standard deviations, or medians and interquartile ranges. The Chi-square test or Fisher's exact test were applied to verify if there were differences in the proportions of categorical variables between groups. The t-Student test was used to test the difference between continuous variables. The significance level was set at $p<0.05$.

To respect the ethical principles of those involved in the research, the study was approved by the Research Ethics Committee of the Universidade Federal de Sergipe under opinion No. 2,830,187, according to resolution 466/2012 of the National Health Council.

RESULTS

To answer the study's objectives, patients were divided into two groups: those who did not develop AKI (71% n = 71) and with the onset of AKI (29% n=9). In the univariate analysis of clinical and demographic characteristics, there was no significant difference between groups, except for baseline creatinine greater than 1.5 mg/dL (4.2%, three vs. 20.7%, six; p=0.016) and the presence of Chronic Obstructive Pulmonary Disease (COPD) (five 7% vs. 20.1%, six; p=0.048) and hypothyroidism (7%, five vs. 20.1%, six; p=0.048), being more frequent in the group with AKI when compared to those without AKI. Regarding admission support, patients who developed AKI had a higher frequency of using a central

venous catheter (22.5%, n=16 vs. 44.8%, n=13; p=0.026), as shown in Table 1.

Table 1 - Clinical and demographic characteristics of the study patients. Aracaju, SE, Brazil, 2019 (continues)

VARIABLES	AKI – n (%) n=71	EKI + n (%) n=29	p-value
Sex			
Male	32 (45,1)	18 (62,1)	0,123
Female	39 (54,9)	11 (37,9)	
Age, mean age ± SD	67± 20	70 ± 16	0,499
Origin			
Emergency Room	52 (73,2)	22 (75,9)	0,953
Operating Room	13 (18,3)	5 (17,2)	
Hospitalization	6 (8,5)	2 (6,9)	
Diagnostic by system			
Cardiovascular	22 (31)	7 (24,1)	0,719
Respiratory	12 (16,9)	7 (24,1)	
Neurological	10 (14,1)	2 (6,9)	
Infectious	10 (14,1)	3 (10,3)	
Digestive	6 (8,5)	5 (17,2)	
Renal	2 (2,8)	2 (6,9)	
History			
Previous surgery	33 (46,5)	11 (37,9)	0,435
AMI	12 (16,9)	3 (10,3)	0,543
Ex-Smoker	8 (11,3)	4 (13,8)	0,741
Stroke	5 (7)	4 (13,8)	0,441
Baseline creatinine >1.5	3 (4,2)	6 (20,7)	**0,016***
Comorbidities			
SAH	38 (53,5)	20 (69)	0,156
Diabetes Mellitus	20 (28,2)	10 (34,5)	0,532
Dyslipidemia	20 (28,2)	13 (44,8)	0,108
Arrhythmia	10 (14,1)	5 (17,2)	0,688
HF	8 (11,3)	2 (6,9)	0,719
COPD	5 (7)	6 (20,7)	**0,048***
Hypothyroidism	5 (7)	6 (20,7)	**0,048***
Pharmacological treatment on admission			
Noradrenaline	10 (14,1)	4 (13,8)	1
Dormonid	10 (14,1)	3 (10,3)	0,751
Fentanyl	9 (12,7)	5 (17,2)	0,55

Devices			
UC	24 (33,8)	11 (37,9)	0,695
CVC	16 (22,5)	13 (44,8)	**0,026**
Nasoenteral Tube	11 (15,5)	4 (13,8)	1
Orotracheal Tube	11 (15,5)	4 (13,8)	1
Drain	4 (5,6)	2 (6,9)	1
Nasogastric tube	3 (4,2)	3 (10,3)	0,352
Tracheostomy	2 (2,8)	2 (6,9)	0,577

Subtitles: Chi-square or Fisher's exact test p<0.05. AKI-: Absent Kidney Injury; EKI +: Existence of Kidney Injury; AMI: Acute Myocardial Infarction; SAH: Systemic Arterial Hypertension; HF: Heart Failure; COPD: Chronic Obstructive Pulmonary Disease; UC: Urinary Catheter; CVC: Central Venous Catheter.
Source: Authors (2019)

In the analysis of clinical outcomes, it was observed that patients who developed AKI had more infection (65.5%, n=19 vs. 39.4%, n=28; p=0.018), were for more than 48 hours under invasive mechanical ventilation (55.2%, n=16 vs. 29.6%, n=21 p=0.016), developed more PU (37.9%, n=11 vs. 18.3%, n=13 p=0.037) and had a higher mortality rate (44.8%, n=13 vs. 19.7%, n=14 p=0.037) when compared to those who did not develop AKI (Table 2).

Table 2 - Analysis of the association of the outcomes of patients with AKI. Aracaju, SE, Brazil, 2019

OUTCOMES	**AKI – n (%) (n=71)**	**EKI + n (%) (n=29)**	**p-value**
Infection, n (%)	28 (39,4)	19 (65,5)	**0,018**
HT, days, mean ± SD	23±21	26±21	0,540
MV> 48h, n (%)	21 (29,6)	16 (55,2)	**0,016**
Death, n (%)	14 (19,7)	13 (44,8)	**0,010**
PU, n (%)	13 (18,3)	11 (37,9)	**0,037**
LSICU, days, mean ± SD	12±14	15±14	0,327
Readmission, n (%)	11 (15,5)	3 (10,3)	0,752
Stroke, n (%)	9 (12,7)	1 (3,4)	0,273
AMI, n (%)	6 (8,5)	3 (10,3)	0,716

Subtitles: Chi-square or Fisher's exact test p<0.05. AKI-: Absent Kidney Injury; EKI +: Existence of Kidney Injury; HT: Hospitalization time; MV: Mechanical ventilation; PU: pressure ulcers; LSICU: Length of stay in the Intensive Care Unit; AMI: Acute Myocardial Infarction.
Source: Authors (2019)

Patients who developed AKI were classified according to severity by KDIGO and there was a higher prevalence of patients with KDIGO II (45% n=13), followed by KDIGO III nine (31%) and KDIGO I seven (24%). Given the greater degree of renal impairment, 19 (66%) of patients with AKI needed to undergo dialysis therapy.

DISCUSSION

The current study evidenced that, of the 100 patients analyzed, 29 (29%) developed AKI, and 19 (66%) required dialysis. AKI is a common clinical event among hospitalized patients, specifically, those admitted to the ICU, considered a predictable and preventable condition when risk factors are detected early [10].

The predominance of males (62.2%, n=18) among patients who developed AKI is confirmed by other studies[9,11]. Regarding the age of patients who developed AKI, a prospective observational study conducted in Sobral CE, showed a prevalence of elderly people, with an average of 47.6±22[12]. In this study, the mean age was 70±16, but there was no significant association between the mean age and renal impairment.

Most patients in this research came from the emergency room. These findings are similar to those found in the research carried out in an ICU in the state of Goiás, in which patients came from the Emergency Room (61%), followed by the Operating room (31%) and other units (8%). This occurs because of the severity of the patient's clinical condition, which causes these patients to be transferred from their unit to a higher complexity hospital unit[13].

The most frequent comorbidities were chronic diseases, such as Systemic Arterial Hypertension (SAH) and Diabetes Mellitus (DM). Another study[14] explains that chronic diseases are the main comorbidities related to AKI, with SAH being the most prevalent (38.9%) followed by DM (23.3%), with similarity to the finding of this study.

Renal injury caused by SAH is related to the degree of exposure of the renal microvasculature to blood pressure. If the self-regulatory protection interval is exceeded, glomerular hypertension occurs, resulting in kidney injury, such as stretching of the glomerular capillaries, hyperfiltration, endothelial dysfunction and increased glomerular protein filtration, glomerular collapse, with segmental necrosis and glomerulosclerosis[15]. As for DM, kidney injury results from high levels of glucose in the blood, causing damage to the kidney's blood vessels for its excretion[16].

In parallel, COPD and hypothyroidism were more frequent in patients with AKI (p=0.048). In a survey carried out in Italy[17], it was found that, among the patients with severe COPD, 354 cases (5%) developed AKI. In this context, the researchers explained that the relationship between COPD and renal dysfunction is still unclear, and COPD may be exacerbated by systemic inflammation or malnutrition, in associating with nephrotoxic drugs for the treatment of COPD, further worsening the risk of kidney dysfunction and death.

Regarding hypothyroidism, it was observed that this dysfunction decreases myocardial contraction, reducing the cardiac output increasing peripheral resistance. Consequently, there is a decrease in the glomerular filtration rate, leading to an increase in creatinine[18]. The actions of thyroid hormones are directly related to the onset of AKI, impacting the kidney's physiological function, the renal homeostasis of salt and water and the active tubular transport of sodium, potassium and hydrogen ions[19].

Concerning pharmacological treatment at the admission, the use of a vasoactive

drug, Noradrenaline, was observed in four (13.8%) patients. Similarly, it was observed in another study that the drug most used in the ICU was Noradrenaline[20]. In this context, it is imperative to consider its time of use and dose, since this medication causes an increase in vascular resistance, raising blood pressure, however, in the presence of hypovolemia or important shock, it can lead to decreased blood flow in the kidney, directly impairing renal function[9].

In the case of Dormonid, a correlation with the onset of AKI was observed due to its mechanism of renal excretion and its main metabolite to have a molecular weight that interferes with the glomerular mechanism[21]. Fentanyl, on the other hand, belongs to the class of synthetic opioids, fat-soluble, and has a balance with plasma approximately 12 hours after its use. It is metabolized in the liver, with a small percentage of the drug being excreted in the urine, therefore, safe for patients with renal failure[22].

About the use of devices at the time of admission, the use of a central venous catheter was greater for those patients who developed AKI (p=0.026). However, the research findings[23] in which medical records of users admitted to the ICU were analyzed, it was found that the use of devices showed an improvement in the patient's clinical condition, differing from the idea that the more devices used, the worse the prognosis.

The results of this research showed a negative impact of Mechanical Ventilation (MV) for the onset of the primary outcome. A possible explanation for this event may be what was observed in a cohort[24] that evaluated 27 patients in a public hospital in Brasília. The authors identified significant changes in cardiovascular hemodynamics in the association between prolonged use of MV with high positive end-expiratory pressure (PEEP), impacting the decrease in blood volume that reaches the kidney.

Similarly, sepsis is one of the main complications with a direct impact on the onset of kidney damage due to its pathophysiological mechanisms, involving excessive inflammatory and immune responses, which leads to dysfunction of cells and organs, contributing to death [25]. In this perspective, in a prospective cohort[26] carried out in the ICU of the Hospital do Servidor Público Estadual de São Paulo (HSPE/SP), to evaluate patients who stayed more than 48 hours in the ICU and developed AKI or Acute on Chronic Renal Failure (ACRF) and/or sepsis and to identify risk factors that could affect the evolution of those patients, the authors concluded that sepsis was the main factor associated with the incidence of AKI[26].

The high mortality of patients in the ICU is associated with complications during hospitalization. In this study, overall mortality in the ICU was 27%, however, when patients with AKI were evaluated, mortality was an event of almost half of this group (44.8%). Many of these patients required invasive support with the use of MV, nephrotoxic drugs and other invasive devices that promote hemodynamic control. However, as observed in other studies, some long-term therapeutic measures and without aseptic rigor can directly impact the patient's outcome, contributing to death[20].

In the analyzes carried out in current research, there was no relationship between the length of hospital stay and the onset of kidney injury (p=0.327). However, it was evidenced in another study[26] that, each day of stay in the critical unit, the chance of AKI increased by 33% and that the length of stay in the ICU was twice that of the other patients.

In this research, the distribution of AKI as to the degree of impairment showed a predominance of KDIGO II (45%), indicating kidney damage. It is suggested that this issue is noticed in advance and, in some cases, reversed when at admission, instruments are used to assess the severity in clinical practice.

Even though the ICUs have high technology and have trained professionals, it was observed that factors parallel to the employed therapy may result in AKI and compromise the clinical evolution of patients. Thus, the early identification of AKI is crucial to ensure a better prognosis for these patients.

As a study limitation, we can point to the sample size, considering it was a prospective cohort, a larger sample was expected. However, the amount presented is acceptable, because of the limited time and days for data collection established by the institution. Also, as it is a private institution ICU located in an urban area in the capital, it is not possible to generalize some sociodemographic data between the target population and the sample at issue.

CONCLUSION

The research contributed to the identification of the clinical and demographic profile of patients admitted to the ICU. A high incidence of kidney injury was observed, mainly in males and with a higher prevalence of KDIGO II. AKI was influenced by factors such as infection and the need for mechanical ventilation for more than 48 hours. Moreover, mortality was higher in patients who developed AKI.

This study contributed to health professionals identifying injury in advance with greater assertiveness, promoting assistance with therapeutic planning to reduce the complications of the disease.

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