Original article

INCIDENCE AND RISK FACTORS ASSOCIATED WITH ACUTE KIDNEY INJURY IN INTENSIVE CARE UNIT

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ABSTRACT: The study aims to identify the incidence, classification and risk factors for acute kidney injury in patients admitted to an intensive care unit. Descriptive documentary study with a quantitative approach, conducted from January to February 2016, based on the analysis of 114 medical records of hospitalized patients. The diagnosis was based on the criterion of the Acute Dialysis Quality Initiative. Incidence and the classification of acute kidney injury were assessed. Also, correlation was assessed using the Chi-square test ($p<0.05$) and Prevalence Ratio ($p<0.05$). The incidence rate of the disease is 44.7% (51 patients). Of these, most were at the risk class: 41% (20 patients). The development of disease is associated with changes in blood pressure levels, body fluid balance, inability of the kidneys to produce sufficient amounts of urine, and elevated blood urea and creatinine levels, and when complicated by the occurrence of acute respiratory diseases, mortality increases substantially. Strict monitoring of the identified factors is necessary, aiming at the early detection of acute kidney injury and decrease in mortality rates.
DESCRIPTORS: Acute kidney injury; Incidence; Risk factors; Intensive care unit; Health care.

INCIDÊNCIA E FATORES PREDISPONENTES DE INSUFICIÊNCIA RENAL AGUDA EM UNIDADE DE TERAPIA INTENSIVA

RESUMO: O estudo objetiva identificar incidência, classificação e fatores predisponentes de insuficiência renal aguda em pacientes internados em Unidade de Terapia Intensiva. Trata-se de estudo documental, descritivo, com abordagem quantitativa, realizado no período de janeiro a fevereiro de 2016, a partir da análise de 114 prontuários de pacientes internados. O diagnóstico deu-se conforme o critério da *Acute Dialysis Quality Iniciative*. Avaliou-se incidência e classificação da insuficiência renal aguda. Também foi avaliada correlação por meio do Teste Qui-quadrado ($p<0,05$) e Razão de Prevalência ($p<0,05$). A incidência da doença em estudo é de 44,7% (51), sendo a classificação risco a mais frequente com 41% (20). O desenvolvimento da doença está associado à alteração do nível pressórico, estado de hidratação, padrão de eliminação, aspecto urinário e de níveis séricos de ureia e creatinina, bem como diagnóstico de doenças respiratórias e a evolução para o óbito. Torna-se pertinente a manutenção da monitorização rigorosa dos fatores identificados, visando à detecção precoce da insuficiência renal aguda e redução de mortalidade.
DESCRITORES: Insuficiência renal; Incidência; Fatores predisponentes; Unidade de terapia intensiva; Assistência à saúde.

INCIDENCIA Y FACTORES PREDISPONENTES PARA INSUFICIENCIA RENAL AGUDA EN UNIDAD DE TERAPIA INTENSIVA

RESUMEN: Se objetivó identificar incidencia, clasificación y factores predisponentes para insuficiencia renal aguda en pacientes internados en Unidad de Terapia Intensiva. Estudio documental, descriptivo, de abordaje cuantitativo, realizado en enero y febrero de 2016, partiendo de 114 historias clínicas de internados. Diagnóstico establecido conforme criterio de *Acute Dialysis Quality Iniciative*. Se evaluó incidencia y clasificación de insuficiencia renal aguda. También se evaluó correlación mediante Test de Chi-cuadrado ($p<0,05$) y Razón de Probabilidades ($p<0,05$). La incidencia de la enfermedad es del 44,7% (51), siendo la clasificación de riesgo la más frecuente, con 41% (20). El desarrollo está asociado a niveles de presión, estado de hidratación, estándar de eliminación, aspecto urinario y de niveles séricos de urea y creatinina, y al diagnóstico de enfermedades respiratorias y evolución a fallecimiento. Resulta pertinente mantener monitoreo riguroso de los factores identificados, apuntando a la detección precoz de la insuficiencia renal aguda y reducción de la mortalidad.
DESCRIPTORES: Insuficiencia Renal; Incidencia; Causalidad; Unidades de Cuidados Intensivos; Prestación de Atención de Salud.

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INTRODUCTION

Acute kidney injury (AKI), known as the sudden loss of kidney function is characterized by fast decline in glomerular filtration rate and/or urine output, leading to inability to excrete nitrogen products and maintain the balance of body fluids and electrolytes[1]. AKI is a common complication in hospital settings, and its incidence varies according to the patient's clinical condition, being more evident in intensive care units (ICU), affecting 20 to 40% of hospitalized patients[2].

The high incidence of AKI in the ICU is related to the multiple diseases that cause the loss of the self-regulation capacity of the patients' organs. In this regard, the degree of impairment associated with AKI varies according to the etiology and severity of the primary disease, which poses a challenge to the implementation of therapeutic resources capable of providing clinical stability and prevent other complications[3].

Previous studies have shown a significant increase in the onset of this syndrome, whose incidence rates of 2-5% by 2002[4] rose to 5-30% or more, in 2014[5] in hospital environments, raising questions about the criteria used for the diagnosis, possible control and prevention of AKI.

The incidence of AKI varies according to the type of population studied, the different definitions and classification criteria used. These elements interfere significantly in the results obtained. AKI is often misdiagnosed due to the lack of accurate and effective criteria, which can have serious consequences[6]. AKI is closely related to a significant rise of 10 to 15 times in morbidity and mortality rates, resulting in the mobilization of large amounts of therapeutic resources[4].

There is a consensus that laboratory tests of creatinine and urea facilitate early diagnosis and prevention of complications[7]. Therefore, in this study, the patients who had changes in serum creatinine level (SCr) were diagnosed with AKI, and the levels of creatinine were classified as follows: Risk: an increase in SCr of 1.5 to 2 mg/dl; Damage: when serum creatinine values range between 2 and 3 mg/dl; Failure: SCr ranging between 3 and 4 mg/dl; and Loss: if serum creatinine is higher than 4 mg/dl[4]. Although the estimation of glomerular filtration rate by the Cockcroft-Gaut equation is also a parameter to define AKI[8], it was not used due to the impossibility to determine the accurate urine output and the weight of the subjects, which may have been one limitation of this study.

The justification for this study is the persistence of a high incidence of Acute Kidney Injuyry in ICU settings, despite recent technological advances, contributing to increase the morbidity and mortality of individuals affected by this condition during their ICU stay. Knowing the incidence and risk factors associated with the onset of this disease is key to the planning of the therapeutic plan, including actions that reduce complications and preserve lives. The study aims to evaluate the incidence, classification and risk factors for AKI in ICU patients.

METHODOLOGY

Descriptive documentary study with a quantitative approach, conducted from January to February 2016 based on the analysis of 114 medical records of patients admitted to the ICU of Hospital Regional Tibério Nunes, a public hospital of the state of Piauí, located in the city of Floriano, 240 km far from capital Teresina. It is a medium-complexity referral hospital for the entire Southern region of Piauí.

Inclusion criteria were patients aged 18 years or over admitted to ICU for more than 48 hours from December 2014 to May 2015 and who had AKI during treatment, detected in laboratory tests and/or by medical diagnosis. Exclusion criteria were: patients with a history of renal dysfunction who were on hemodialysis prior to admission to the ICU.

Data was collected in January and February of 2016, through a semi-structured form, containing the following questions: gender, age, smoking and drinking habits, diagnosis on admission, length of hospitalization, clinical evolution, blood glucose and blood pressure, urine output, urine color, oxygen therapy, use of mechanical ventilation, use of vasoactive drugs, changes in serum levels (creatinine, urea, sodium and potassium). Each medical record was analyzed for the aforementioned information.

The diagnosis of AKI was established according to the Acute Dialysis Quality Initiative (ADQI) that developed in 2002, a classification that proposes three categories with increasing severity criteria for AKI: Risk (class R), Injury (class I) and failure (class F), which are variables based on serum creatinine levels and diuresis, as well as two prognostic categories (Loss - L class and Final Stage class - Class E), a classification commonly defined by the acronym RIFLE[4].

The RIFLE classification was proposed to standardize the definition of AKI, establishing three levels related to the degree of severity of renal dysfunction, detected by the changes in the values of the glomerular filtration rate and/or serum creatinine levels. The information was stored in a database of the Statistical Package software for Social Sciences (SPSS) for Windows, version 20.0, and analyzed by descriptive statistics: absolute and relative frequency. The incidence of AKI was also calculated, and correlation was assessed using the Chi-square test ($p<0.05$) and Prevalence Ratio ($p<0.05$), with a 95% Confidence Interval.

The project was approved by the Research Ethics Committee of *Universidade Federal do Piauí*, under Statement no 1,385,032, obtaining the Term of Consent of Hospital Tibério Nunes Regional Hospital, the setting of the study.

RESULTS

The study involved the analysis of 114 records of ICU patients, of whom 44.7% (51) had AKI. Of this total, most were at the risk class: 41% (20) or damage class: 33% (17) for AKI, according to the RIFLE classification (Chart 1).

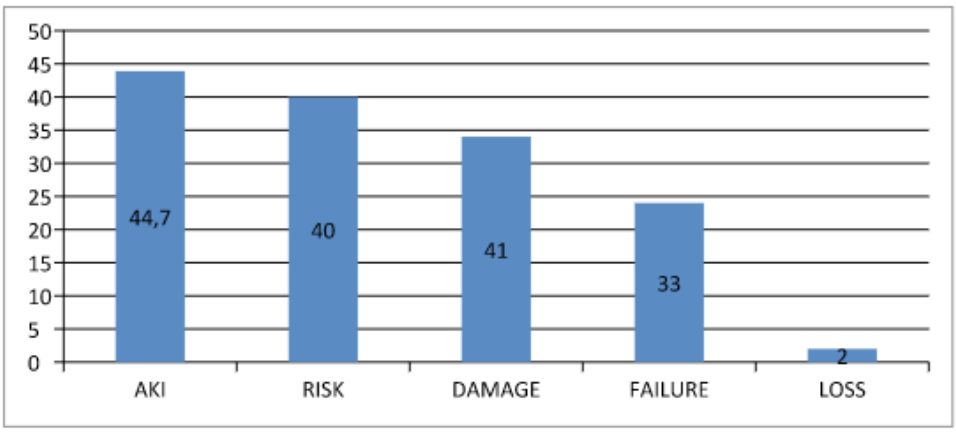

Chart 1 - Incidence of acute kidney failure in patients admitted to an intensive care unit. Floriano, PI, Brazil, 2015

Regarding the patients who developed AKI, 26 were male (47.3%) and 37 were elderly (44.6%), with very low incidence of smoking and alcoholism. The abovementioned variables showed no statistically significant association with or chance of development of AKI (Table 1).

Table 1 - Distribution of acute kidney injury according to social characteristics, habits and clinical conditions of patients in intensive care unit. Floriano, PI, Brazil, 2015 (continues)

Variable (n=144)	AKI		Not AKI		P	PR CI (95%)	
	n	%	n	%			
Gender					0.47		
Male	26	47.3	29	52.7		1,30	0.62-2.74
Female	24	40.7	35	59.3			

Age					0.90		
Elderly (> 60 years)	37	44.6	46	55.4		1.05	0.45-2.44
Adult (<60 years)	13	43.3	17	56.7			
Smoker					0.10		
Yes	09	31.0	20	69.0		0.48	0.19-1.18
No	41	48.2	44	51.8			
Drinker					0.60		
Yes	09	39.1	14	60.9		0.78	0.30-1.99
No	41	45.1	50	54.9			
Clinical diagnosis on admission					0.00*		
Respiratory	06	20.7	23	79.3		0,24	0,09-0,65
Others	44	51.8	41	48.2			
Length of hospital stay					0.34		
Above 7 days	16	38.1	26	61.9		0.68	0.31-1.49
Up to 7 days	34	47.2	38	52.8			
Progression to death					0.01*		
Yes	30	55.6	24	44.4		2.50	1.17-5.34
No	20	33.3	40	66.7			

Legend: n = absolute value; % = Relative value; P = value of the Chi-square test; PR = Prevalence Ratio; CI = Confidence Interval.

A clinical diagnosis of respiratory disease upon admission (p = 0.00) was significantly associated with the development of AKI, and this condition evolves to death (p = 0.01). Length of hospital stay is not associated with AKI (Table 1).

Abnormal blood pressure levels (p = 0.00), urine color (p = 0.00), body fluid balance (p = 0.00) and urinary output (p = 0.00) are health conditions significantly associated with the development of AKI, which are risk factors with different intensity levels (Table 2).

Table 2 - Distribution of acute kidney injury according to the health conditions of patients admitted to ICU. Floriano, PI, Brazil, 2015 (continues)

Variable (n=114)	**AKI**		**Not AKI**		**p**	**PRCI (95%)**	
	n	**%**	**n**	**%**			
Blood glucose level (n=104)					0.54		
Abnormal	40	44.9	49	55.1		0.71	0.23-2.13
Controlled (70 – 100 mg/dl)	08	53.3	07	46.7			
Blood Pressure level					0.00*		
Abnormal	32	59.3	22	40.7		3.23	1.48-7.03
Controlled (139 x 89 mmHg)	18	31.0	40	69.0			
Body fluid balance (n = 111)					0.00*		
Abnormal (dehydrated, edema, anasarca)	34	68.0	16	32.0		5.97	2.62-13.62
Controlled	16	26.2	45	73.8			
Urine output					0.00*		
Abnormal (anuria, oliguria, dysuria, polyuria)	39	75.0	13	25.0		13.90	5.62-34.37
Normal	11	17.7	51	82.3			
Urine color (appearance)					0.00*		
Abnormal (pyuria, hematuria, coluria)	37	62.7	22	37.3		5.43	2.40-12.28
Normal	13	23.6	42	76.4			

Oxygen therapy					0.63	
Yes	38	42.7	51	57.3	0.80	0.33-1.96
No	12	48.0	13	52.0		
Use of mechanical ventilation					0.66	
Yes	15	60.0	10	40.0	2.31	0.93-5.72
No	35	39.3	54	60.7		
Use of vasoactive drug (n = 113)					0.00*	
Yes	24	80.0	06	20.0	8.76	3.20-24.0
No	26	31.3	57	68.7		
Urea					0.00*	
Abnormal	44	55.0	36	45.0	5.70	2.12-15.28
Normal (10-45 mg / dl)	06	17.6	28	82.4		
Creatinine					0.00*	
Abnormal	50	89.3	06	10.7	0.10	0.05-0.22
Normal (0.6-1.3 mg / dl)	-	-	58	100.0		
Sodium (N = 113)					0.77	
Abnormal	40	44.9	49	55.1	1.14	0.45-2.84
Normal (135 - 145 mEq / L)	10	41.7	14	58.3		
Potassium (N = 113)					0.52	
Abnormal	22	47.8	24	52.2	46	1.27 0.60-2.71
Normal (3.5 - 5.5 mEq / L)	28	41.8	39	58.2	67	

Legend: n = absolute value; % = Relative value; P = value of the Chi-square test; PR = Prevalence Ratio; CI = Confidence Interval.

Abnormal glucose levels, oxygen therapy and use of mechanical ventilation are not related to the development of AKI. Likewise, changes in serum sodium and potassium levels in the studied population is not related to the development of AKI (Table 2).

The use of vasoactive drugs (p = 0.00) and abnormal serum levels of urea (p = 0.00) and creatinine (p = 0.00) were related to the development of AKI. However, the use of vasoactive drugs and abnormal serum levels of urea are serious risk factors, while serum creatinine levels are a positive factor (Table 2).

DISCUSSION

The present study found an incidence of 44.7% of development of AKI in ICU patients, while some studies found lower incidence such as 29%[9], 29.7%[10], 31.2%[2] and 35.7% [11], and one study obtained a higher incidence (76.5%)[12]. However, the finding demonstrates the high incidence of development of AKI because of the difficult and late diagnosis of the condition, presence of comorbidities and intense use of invasive procedures[10]. It also concerns a severe complication that worsens the prognosis of patients admitted to ICU.

Most hospitalized patients were at class I of RIFLE classification (Risk) during treatment, followed by class II (Damage), corresponding to 41.2% and 33.3% of the cases, respectively. Thus, the RIFLE classification may give different epidemiological results[13], directly related to mortality, i.e. the patient's risk of death increases according to the severity of their disease[14]. However, the RIFLE criteria, if used in "real time", allows an accurate description of the renal condition of patients and provides guidance to care in ICU[15].

The higher incidence of AKI development in male individuals is consistent with the findings of other studies[16-17]. Age did not have a significant relationship with the development of AKI. However, one study reported that more than 50% of individuals older than 60 years developed AKI during

hospitalization[18]. The average age of patients with renal failure was 63.43 years[16]. Old age is recognized as an independent predictor for the development of AKI [12,19-20].

Regarding smoking and alcohol consumption, there was low incidence of these habits and they were not related to the development of AKI, although one study reports smoking as a risk factor, particularly for patients who smoke more than 15 packs of cigarettes per year[21].

Smoking interferes with body weight gain and fat deposition in the retroperitoneal abdominal area. Also, association with the chronic use of moderate amounts of alcohol causes liver and renal necrosis, contributing to increased risk of kidney damage[22].

Among the main causes that lead to the development of AKI in ICU, infectious and obstructive processes, cardiovascular, respiratory and liver failures, hypovolemic shock, and a hospital stay for longer than seven days are worth mentioning[23]. In this study, the most frequent clinical diagnosis was respiratory disease, corroborating another study[16] while a hospital stay for longer than seven days was not significantly related to the development of AKI.

The development of pulmonary complications, such as edema, pleural effusion and infection is common in patients with kidney disease due to hemodynamic abnormalities involving increased volemia and high serum concentration of osmotically active substances[24].

There was a significant relationship between mortality rate in ICU patients and the development of AKI, which is a risk factor. Nonetheless, the mortality rate was lower than in other studies that reported mortality rates of 66% and 70%, respectively[9-10]. The incidence of AKI may be impacted by the unavailability of renal replacement therapy, that is, the fact that no patient had access to this therapeutic resource, which may have increased the number of deaths.

In the present study, most patients with abnormal glucose and blood pressure levels developed AKI, which is a risk factor for this condition, as demonstrated in another study[25]. The findings corroborate the literature, according to which hyperglycemia and hypertension are risk factors for kidney disease and mortality[18]. Therefore, control and monitoring of blood glucose and blood pressure levels are key strategies to prevent or reduce the progression of renal disease[25-26].

The high incidence of abnormalities such as inadequate body fluid balance and abnormal urine color of the patients showed a significant relationship with the development of AKI, being considered significant risk factors. The high incidence of abnormal urine output (observed in around 84.3% of the patients) was similar to the one found in a study with victims of polytrauma with AKI in ICU[19].

The main function of the renal and urinary systems is forming urine to eliminate waste products resulting from fluid and electrolyte degradation and regulation. Thus, renal failure impacts these parameters because they are directly related with renal function[18].

No relationship was found between the use of oxygen therapy, especially mechanical ventilation, and the development of AKI. However, these are therapeutic interventions to manage complications of renal disease[16], since abnormal lung function is a common complication in renal failure[24]. In patients with AKI, the strength of respiratory skeletal muscle is reduced resulting in inadequate ventilation, contributing to reduce lung capacity[27].

The use of vasoactive drugs has a significant relationship with the development of AKI, representing a serious risk factor for the referred condition. It is well known that the use of vasoactive drugs is an important risk factor for mortality in intensive care due to hemodynamic instability of patients, and vasoconstriction[28].

The parameters of normality of serum levels used in the present study were urea (10-45 mg/dl); creatinine (0.6-1.3 mg/dl); sodium (135-145 mEq/L); potassium (3.5 to 5.5 mEq/L. Values below or above these parameters were considered abnormal[5].

Significant changes in urea and creatinine levels of the patients were related to the development of AKI, the latter being more evident in this study. Urea levels were found to be negative (risk) factor and creatinine, a positive factor. In this regard, creatinine is a more sensitive indicator of renal function than urea, since urea is impacted by renal failure[29], but also by dietary protein intake, catabolism,

parenteral nutrition and certain medications (corticosteroids)[18].

Urea is the main nitrogen metabolite derived from degradation of proteins by the body, and 90% is excreted by the kidneys. On the other hand, creatinine is a breakdown product of creatine phosphate in muscle and is usually produced at a fairly constant rate by the body, depending on muscle mass[7].

The abnormal sodium and potassium levels of patients were not related to the development of AKI. Renal disorders are associated with fluid/electrolytic imbalance, requiring continuous monitoring. Among the fluid/electrolyte balance disorders in patients with kidney failure, hyperkalemia is the complication at highest risk for mortality[18].

Some limitations of this study included the short time frame (six months) for the selection of medical records and the study site (ICU), where hemodialysis was not available, and therefore where the development of AKI and the need for hemodialysis treatment increased the probability of progression to death.

CONCLUSION

The development of AKI in ICU patients is associated with abnormal blood pressure levels, body fluid/electrolyte balance, urine output, urine color and serum levels of urea and creatinine. Clinical diagnosis of pulmonary disease, use of vasoactive drugs and progression to death of people admitted to ICU are also related to the development of AKI.

The RIFLE criterion is an important tool for the early detection of renal failure and should be part of the regular monitoring of patients admitted to the ICU.

Therefore, strict monitoring and daily completion of a checklist of the aforementioned factors detected in ICU patients is suggested to ensure the early detection of AKI development and reduce mortality.

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