Original research

Acute renal failure in patients hospitalized in the intensive care unit in Ibague Clinic 2016-2017

Factores asociados a la insuficiencia renal aguda en pacientes hospitalizados en la unidad de cuidados intensivos de la Clínica Ibagué, 2016-2017

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Abstract

Objective: To establish the association of acute renal failure with demographic and clinical factors in patients hospitalized in an intensive care unit in a Colombian city. **Methods:** Analytical case-control study whose source of information was the patient´s clinical history, in a sample of 130 cases and 184 controls; the cases were about patients older than 18 years, who had a glomerular filtration rate higher than 60 ml/min and who fulfilled the AKIN criteria. With the independence test, it was established the effect of the factors of interest on the result (case-control), with the Odds Ratio (OR) as a measure of the association with its 95% confidence interval. The logistic regression allowed to control the presumable variables of confusion.

Results: The average age of patients was 62.2 years (SD-16.7 years) with a predominance of men from the urban area and where hypertension stood out in 52.2% of them. On admission, 55.7% had coronary syndrome and 40% developed acute renal failure (ARF); 84.6% of the patients were in stage I according to the AKIN classification. The administration of saline in the first 24 hours of admission increased the possibility of ARF 1.8 times compared to those who received Ringer´s lactate (OR 1.8 CI (95% OR: 1.2-2.8), adjusting for other variables.

Conclusion: The administration of Ringer´s lactate decreases the development of acute renal failure; also, age of the patient and if it came from the postoperative period, were the factors that were related to the presence of kidney disease.

Key words: Acute renal failure, treatment, intensive care, risk factors (Source: Decs)

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Resumen

Objetivo: establecer la asociación de la insuficiencia renal aguda con los factores demográficos y clínicos en pacientes hospitalizados en la unidad de cuidados intensivos en Colombia.

Métodos: estudio analítico de casos y controles cuya fuente de información fue la historia clínica del paciente, en una muestra de 130 casos y 184 controles; pacientes mayores de 18 años, que tenían una tasa de filtración glomerular mayor de 60 ml/min y que cumplían los criterios AKIN (*Acute Kidney Injury Network*). Con la prueba de independencia se estableció el efecto de los factores de interés sobre el desenlace (caso-control), con el Odds Ratio (OR) como medida de asociación con su intervalo de confianza del 95 %. La regresión logística permitió controlar las variables presumibles de confusión.

Resultados: la edad promedio de los pacientes fue de 62,2 años (DE=16,7 años), hombres provenientes de la zona urbana y donde la hipertensión sobresalió en el 52,2 % de ellos. Al ingreso, el 55,7 % presentó síndrome coronario y el 40 % desarrolló insuficiencia renal aguda (IRA); el 84,6 % de los pacientes estaba en el estadio I, según la clasificación AKIN. La administración de solución salina al 0,9 % en las primeras 24 horas de ingreso incrementó la oportunidad de IRA 1,8 veces, con respecto a los que se les administró lactato de ringer (OR=1,8 IC (95 % OR: 1,2-2,8), ajustando las demás variables.

Conclusión: La administración de lactato Ringer disminuyó el desarrollo de la insuficiencia renal aguda. La edad de los pacientes y sus antecedentes posoperatorios, fueron los factores que se relacionaron con la presencia de IRA. **Palabras clave:** insuficiencia renal aguda, tratamiento, cuidados intensivos, factores de riesgo (Fuente: DecS)

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Introduction

Acute renal failure (ARF) is known as an alteration that predisposes to a decrease in the capacity of the kidneys to eliminate waste products, in a short period of time, associated with a hydroelectrolytic imbalance and that occurs in approximately 7% of all hospitalized patients and in 28-35% of those admitted to intensive care units (ICU).[1] Serum creatinine and glomerular filtration rate (GFR) have been universally accepted as the determining methods for the diagnosis of ARF,[2] especially the second one, that is reflected through its deterioration with the consequent impairment in the acid-base and hydroelectrolytic balance.[3] The presence of ARF increases mortality to 36% in intensive care units, while perioperative and posttraumatic mortality remains high, greater than 50%, largely due to its association with sepsis and multiple organ failure; the predictors of mortality due to ARF are: advanced age, previous alteration of the health status with organic dysfunction, hospitalization prior to admission to the ICU, onset of the ARF after admission to the ICU, sepsis, oliguria and the severity of the disease upon admission, assessed by scores such as SAPS or APACHE. The survival of the patient is more related to the underlying disease and its severity than to the presence of renal dysfunction;[1] the development of ARF in a hospital environment continues to be associated with a poor prognosis of survival. Some observational studies have evaluated the risk factors associated with the development of ARF: an American cohort, with about 150,000 surgical interventions, found that being a man, being over 56 years old, having suffered from heart failure (cardiac dysfunction with LVEF > 40%), hypertension (blood pressure values > 130/90 mmhg), diabetes (glycemia > 200 mg/dl and/or glycosylated hemoglobin > 6.4), anemia (hemoglobin <10 mg/dl), ascites (fluid in the abdominal cavity), sepsis (infectious focus with life-threatening organ dysfunction),[4] coronary syndrome (angina, acute myocardial infarction) intraperitoneal or emergency surgery, and serum creatinine higher than 1.2 mg/dL, are the most relevant risk factors, evidencing that the presence of 6 or more of these factors increases the incidence of ARF by 10%. Other risk factors that have also been assessed are: presence of infection, acute respiratory or circulatory failure, antecedent of cirrhosis or hematologic neoplasms, obesity, peripheral vascular disease, chronic obstructive pulmonary disease (COPD)[5] (determined by spirometry FEV1 < 80%) and high risk surgery. Responding to the problem that relates acute renal failure with socio-demographic and clinical characteristics such as patient antecedents and diagnosis of admission to the ICU of a Colombian clinic, will serve to improve the management protocols of the diagnoses studied and thus achieve an optimal care, which would reduce the risk of developing acute renal failure; the above is the foundation for the following research question: What are the factors associated with the development of acute renal failure in patients hospitalized in the intensive care unit of a Colombian clinic between May 2016 and October 2017?

Materials and methods

It was conducted a retrospective, observational, analytical case-control epidemiological study, which allowed to establish the association of the factors related to the development of ARF in patients hospitalized in the ICU of the *Clínica Ibagué*, in the period from May 1, 2016 to October 31, 2017. This type of study compares a group of individuals who suffer from a disease that are called «cases» (with ARF), with a group of individuals who do not suffer from it that are called «controls or witnesses» (without ARF). This allows the estimation of likelihood ratios or Odds Ratios (OR), as a measure of the association. The analysis strategy consists in comparing the exposure of patients with ARF with the exposure of those who do not present it (without ARF); it is assumed that the factor studied, which is considered associated with the disease should be present more frequently in the cases of disease than in the controls.

The sources of information were secondary, the clinical records of the medical institution, and their collection was done using the instrument «Checklist to determine the association factors in the development of acute renal failure.» The observation unit was the medical records of the patients who were

hospitalized in the ICU in the stipulated period of time, and the unit of analysis was the referred patients, taking into account the inclusion and exclusion criteria. For the inclusion it was required, both for cases and for controls, that the patients were over 18 years old, with a date of admission to the clinic within the indicated times, that they had a glomerular filtration rate greater than or equal to 60 ml/min calculated by the CKD-EPI formula **-for the cases-**, and less than 60ml/min **-for the controls-**, and that met the definition of acute renal failure according to the AKIN criteria during their hospital stay, for the cases, and that they did not comply with them, for the controls. For both study groups, patients with an antecedent of chronic kidney disease recorded in the clinical history and/or with ultrasound changes of chronic kidney disease documented during their hospital stay were excluded. To minimize selection bias, the study was carried out exclusively in the institution mentioned; with respect to the control of information bias, data collection was carried out by the researchers, who had received previous training to avoid inconsistencies in the process of obtention of the data; confounding biases were controlled through the construction of a multivariate logistic regression model, through which the measure of the association of each independent variable was analyzed, controlling the other variables that entered into the model. For the determination of the sample size, it was used the proper expression for a case-control study with Yates correction according to Machin;[6] for this, it was considered a 95% confidence, a power of 84%, an expected OR of 2.2, a ratio of exposure to the factor, septic shock, in the cases, of 49.5%, value corresponding to the upper limit of the confidence interval obtained from the study by Uchino, et al.,[7] a ratio of exposure to the factor, in controls, of 30.822% and the combination of the two ratios, P_M($P_M = \frac{(P_1 + r X P_2)}{(r+1)}$ (with r representing one control for each case). The sample obtained was 260 patients, discriminated in 130 cases and 130 controls, but given the facilities and support provided by the institution for the collection of information, the number of controls was expanded to 184, i.e., the final sample size was 130 cases and 184 controls, that is, 314 patients. In the statistical analysis, tables with absolute and relative frequencies were constructed for the qualitative variables; and the classical summary measures, mean, median, standard deviation (SD), minimum and maximum) were calculated for the quantitative variables. In the bivariate analysis, the Chi Square test of independence or Fisher 's test were used to find association or independence between the outcome (case-control) and the factors of interest, with criteria of biological plausibility, considering as a measure of epidemiological association the Odds Ratio (OR), which was accompanied by its respective 95% confidence interval. In the multivariate analysis, an explanatory logistic regression model was constructed in order to establish the relationship between the factors of interest and the outcome, controlling for presumable confounding variables. Statistical procedures were carried out in the SPSS software version 22, licensed to the University of Tolima. The definitive model was that whose independent variables were significant. According to Resolution 8430 of 1993, the research conducted was classified as a research without risk because secondary sources of information were used, prior authorization from the management of the institution, respecting Resolution 1995 of 1999, recognizing the rules that govern this document. The institution endorsed the development of the research through its ethics committee.

Results

Of the 314 data analyzed, the average age of the patients who entered the ICU of the *Clínica Ibagué* during the period between May 1, 2016 and October 31, 2017 was 62.2 years (SD = 16.7 years) with a minimum age of 18 years and a maximum age of 93 years, the most frequent data being 54 years. Regarding the sex, 65.3% corresponded to men, with an average age of 60.2 years (SD = 16.5 years), while in the case of women it was 34.7% with an average age of 59 years (SD = 16.9 years). As for the place of origin, 68.2% came from the urban area. It is noted, regarding the place of origin, that significant volumes of patients were referred from institutions of first and second level of complexity, so that 100% of patients of the rural area corresponded to referrals (Table 1).

Table 1. Demographic characteristics of the patients admitted to the ICU of the *Clínica Ibagué* between May 1, 2016 and October 31, 2017.

Characteristic category (n=314)		N	%	95% CI
Age				
	<= 48	51	16,2	12,1 20,4
	>48	263	83,8	79,6 87,9
	Total	314		
Sex				
	Men	205	65,3	59,9 70,7
	Woman	109	34,7	29,3 40,1
	Total	314		
Place of origen				
	Urban	212	68,2	63,0 72,7
	Rural	99	31,8	27,3 37,0
	Total	311*		

* No information was obtained from 3 patients about their place of origin.

With regard to the clinical characteristics of the patients admitted to the ICU during the study period, it was observed that arterial hypertension occurred in 52.2%, followed by COPD with 19.8% and diabetes with 17.8%. As for the admission diagnosis, it was evidenced that coronary syndrome was the most prevalent with 55.7%, followed by the postoperative period, 12.4%, sepsis, 9.2%, and heart failure, 3.8% (Table 2); it was known that 84.6% were found in stage I, 11.5% in II, and 3.8% in III, according to the AKIN classification (Table 2).

It was observed that in the cases and in the controls men prevailed, 66.2 % vs. 64.7 %, respectively, over women, 33.8% vs. 35.3%; note that the chance of developing kidney disease is greater than 10 % in men, although this difference was not statistically significant, OR=1.1 (95% CI 0.7-1.7). When the antecedents of the patients were considered, the cases of ARF were more prevalent in those who did not present hypertension, diabetes mellitus, anemia and COPD, in contrast to those who presented only hypertension predominant in the controls. Patients with hypertension, diabetes mellitus and COPD, had a greater chance of developing ARF by 10%, 30% and 40% than those who did not present such diseases, although without statistical significance (p> 0.05, in all cases). With respect to the diagnosis of admission, when a patient presented coronary syndrome, the chance of developing ARF increased 1.1-fold in relation to the patient who did not present this syndrome, but without evidence of significant association (95% CI 0.7-1.8); similarly, the ARF was increased twice in those patients with heart failure and in 20% in those who presented sepsis, although these associations were clinically but not statistically relevant, OR = 1.1 (95% CI 0.7-1.8) and OR = 1.2 (95% CI 0.5-2.5); Those patients whose diagnosis of admission was not in the postoperative period increased their chance of ARF 1.7-fold, a result with clinical but not statistical significance, OR=1.7 (95% CI 0.8-3.5) (Table 3).

125 cases with ARF (of 130 cases) and 11 controls without ARF (of 184) were found in the study when they were related to the administration of crystalloids in the first 24 hours, 43.2% of those who received 0.9% saline solution had 1.5-fold greater chance to develop acute renal failure than those who received Ringer lactate, with a statistically significant association (95% CI: 1.0-2.5 p = 0.071). It is important to clarify two aspects: for the selection of controls they were required to have a glomerular filtration rate lower than 60 ml/min according to the AKIN formula, which implied that they could receive Ringer lactate or 0.9% saline solution in the first 24

Table 2. Clinical characteristics of the patients admitted to the adult ICU of the *Clínica Ibagué* between May 1, 2016 and October 31, 2017.

Characteristic (n=314)	Category	n	%	95% CI
Comorbidities				
Hypertension	Si	164	52,2	46,5 57,6
	No	150	47,8	42,4 53,5
Diabetes	Si	56	17,8	13,4 22,0
	No	258	82,2	78,0 86,6
COPD	Si	62	19,7	15,3 24,5
	No	252	80,3	75,5 84,7
Admission diagnosis				
Coronary syndrome	Si	175	55,7	50,0 61,1
	No	139	44,3	38,9 50,0
Heart failure	Si	12	3,8	1,9 6,1
	No	302	96,2	93,9 98,1
Postoperative period	Si	39	12,4	8,9 16,6
	No	275	87,6	83,4 91,1
Sepsis	Si	29	9,2	6,1 12,7
	No	285	90,8	87,3 93,9
AKIN classification*	Estadio I	110	84,6	78,5 90,8
	Estadio II	15	11,5	6,9 17,7
	Estadio III	5	3,8	0,8 7,7

* Only for the controls.

hours; the second aspect, the obtained value of OR, 1.5, has the aggravating fact of being crude or unadjusted for confounding variables, a problem that is solved in the multivariate analysis shown in Table 4.

An explanatory logistic regression model was constructed, with an outcome of interest, the ARF (control case), where those independent variables that had a joint influence on the development of ARF in patients hospitalized in the ICU were considered. The independent variables that in the bivariate analysis presented a p-value of less than 0.25 in the tests of association with acute renal failure (Hosmer-Lemeshow criterion) were chosen as candidate variables to enter in the model. Simple logistic regression models were constructed with each of the independent variables and the Nagelkerke coefficient was obtained in each of them; then, for the construction of the multivariate model, the variables that initially presented a higher Nagelkerke coefficient were entered one by one and the significance of each of them in the model was assessed with the p-value. The final model was the one whose independent variables were significant. It was also decided, with statistical criterion, to categorize the variable age according to the mode and the arithmetic mean into three categories, namely, <54, 54.1-62.1 and 62.2-93

Table 3. Clinical characteristics of the patients who entered the adult ICU of the *Clínica Ibagué*, according to the development of acute renal failure between May 1, 2016 and October 31, 2017.

Characteristic	Case (n=130)	Control (n=184)	p	OR	95% CI OR	
	n (%)	n (%)				
Sex						
Men	86 (66,2)	119 (64,7)	0,786	1,1	0,7	1,7
Woman*	44 (33,8)	65 (35,3)				
Antecedents						
Hypertension						
Yes	70 (53,8)	94 (51,4)	0,665	1,1	0,7	1,7
No*	89 (59,7)	60 (40,3)				
Diabetes mellitus						
Yes	26 (20,0)	30 (16,3)	0,399	1,3	0,7	2,3
No*	104 (80,0)	154 (83,7)				
Anemia						
Yes	1 (8)	8 (4,3)	0,061	0,2	0,0	1,4
No*	129 (99,2)	176 (95,7)				
COPD						
Yes	30 (23,1)	32 (17,4)	0,213	1,4	0,8	2,5
No*	100 (76,9)	152 (82,6)				
Diagnosis of admission						
Coronary sindrome						
Yes	75 (57,7)	100 (54,3)	0,557	1,1	0,7	1,8
No*	55 (42,3)	84 (45,7)				
Heart failure						
Yes	7 (5,4)	5 (2,7)	0,245	2,0	0,6	6,6
No*	123 (94,6)	179 (97,3)				
Postoperative						
Yes	12 (9,2)	27 (14,7)	0,15	0,6	0,3	1,2
No*	118 (90,8)	157 (85,3)				
Sepsis						
Yes	13 (10,0)	16 (8,7)	0,694	1,2	0,5	2,5
No*	117 (90,0)	168 (91,3)				

* Reference category.

years. According to the multivariate model, with respect to the type of crystalloid, it was identified that the administration of 0.9%saline solution in the first 24 hours of admission increased the chance of acute renal failure 1.8 times with respect to those who received Ringer lactate, also in the first 24 hours (OR = 1.8 (95% CI OR: 1.2-2.8), adjusting it according to the other variables. It was also

Table 4. Indicator of the magnitude of the association between the type of crystalloid administered within the first 24 hours and the development of acute renal failure between May 1, 2016 and October 31, 2017.

Factor	Case	control	P		
	n (%)	n (%)			
Type of crystalloid within the first 24 hours					
0.9% saline solution	54(43,2)	57(32,9)	0,071	1,5	1,0 2,5
Ringer lactate	71(56,8)	116(67,1)			
Total	125*	173*			

* No information from 5 patients with ARF and 11 patients without ARF was obtained when it was related to the type of crystalloid administered in the first 24 hours.

observed that the chance of ARF in patients who were between 54.1 and 62.1 years old was 2.5 times higher compared to those patients who were between 62.2 and 93 years, adjusting for the rest (OR = 2.5 (95 CI% OR 1.4- 2.4) and although in patients under 54 years of age the chance of renal failure increased 1.6 times compared to patients between 62.2 and 93 years old, these differences were not significant (p=0.174). Regarding the pathology of admission, the postoperative period, it was noted that, in relation to the reference category, not postoperative, the chance of renal failure decreased by 60%, holding fixed the other variables. The variables that constituted the model explained the variability in renal failure in 10.3 %. The goodness-of-fit test supported the relevance of the explanatory model, p = 0.926. It should be noted that the difference found in the OR of the crystalloid type in Table 4 with respect to Table 5, reveals that, if these variables had not been controlled, the association measure would be underestimated, 1.5 vs. 1.8, that is, the indicated factors confused the association between the type of crystalloid and ARF (Table 5).

Table 5. Joint factors associated with the development of acute renal failure in patients admitted to the ICU at the *Clínica Ibagué*, between May 1, 2016 and October 31, 2017

Variables	Coefficient	Standard error	p	OR	95 % C.I. for OR	
					Lower	Lower
Type of crystalloid*						
0.9% saline solution	0,59	0,23	0,009	1,8	1,2	2,8
Age*						
Age (54.1-62.1)	0,92	0,29	0,001	2,5	1,4	4,4
Age (≤54)	0,47	0,35	0,174	1,6	0,8	3,2
Postoperative*						
Yes	0,52	0,21	0,015	0,6	0,4	0,9

* The reference categories are Ringer lactate, age between 62.2 and 93 years and non-postoperative.

Discussion

ARF is one of the complications that most often occur in patients hospitalized in the ICU; therefore, the results of this study are of great relevance, since they support, with scientific criteria, that the factors that are associated with the ARF, resemble the findings of similar studies, both in national and international literature. It was found that the highest percentage of cases occurred in men with a mean of 62.2 years with a minimum age of 18 years and a maximum age of 93 years, from the urban area, results that are consistent with those derived from the study of epidemiology of acute renal injury and chronic kidney disease in the intensive care unit of 2017;[8] in the same way, when the clinical variables were considered, the highest percentage of ARF was evidenced in those who presented as admission pathology heart failure with co-morbidity of COPD, results that are consistent with proxies such as chronic heart and/or respiratory disease, predisposing for the development of ARF according to Tejara, et al.[8] Regarding the AKIN variable, the present study showed that stage I was the most frequent, represented by 35% (110 patients), followed by stage II with 4.8% (15 patients) and stage III with 1.6% (5 patients), results consistent with the research *Clasificaciones de la insuficiencia renal aguda*, (Classifications of acute renal failure),[9] where it was shown that stage I was the most frequent and stage III was associated with the initiation of renal replacement therapy.

The study found that the type of crystalloid influenced the development of the ARF; it was identified that the administration of 0.9% saline solution in the first 24 hours of admission increased the chance of ARF 1.8 times with respect to those who received Ringer lactate, also in the first 24 hours (OR = 1.8 95% CI; OR: 1.2-2.8); taking into account that the study conducted by Zampieri et al.,[10] was focused on the reduction of mortality; in addition, in the study, the type of fluid and the amount that affects renal function in critically ill patients, demonstrated that solutions rich in sodium and chloride could trigger afferent arteriolar vasoconstriction through tubuloglomerular feedback, which supported, once again, the use of Ringer lactate over 0.9% saline in critically ill patients.[10] Also, the findings of this study keep an affinity with the results found in the study «Association between the choice of the type of crystalloid IV and hospital mortality among critically ill adults and with sepsis», which ratifies the importance of administering Ringer lactate crystalloid, due to its electrolytic composition and because its chlorine content is closer to plasma and more physiological, which decreases hyperchloremia and metabolic acidosis and therefore the risk of ARF.

Other studies, such as the study conducted by Zampieri, et al.[11] have reported a greater development of ARF in those patients who, due to their comorbidities, were managed with crystalloid of the type of 0.9% saline solution, added to the systemic commitment given by the underlying pathologies and the increased morbidity of the patients in the ICU, Ringer lactate is associated with the reduction of mortality and less acute kidney injury in critically ill patients. In 2016, one study compared the mortality associated with the different fluids administered during hospitalizations, among them, 0.9% and 0.45% saline, dextrose 5%, hydroxyethyl and Ringer lactate, evidencing that the probability ratio for mortality with 75% ringer lactate versus 25% Ringer lactate was 0.50 (95% CI, 0.32-0.79; p <0.001). An analysis of the principal components suggested that the infused volume of Ringer lactate and 0.9% saline had opposite effects on the outcome, favoring Ringer lactate with an estimate of lower hospital mortality for every 31 patients treated with balanced fluids instead of saline solution at initial resuscitation in sepsis[12] Finally, although this work demonstrated that the type of crystalloid, the age and the postoperative period were associated with ARF, the other factors considered had clinical relevance but not statistical significance.

It is concluded that, since the development of ARF in patients managed with Ringer lactate decreases significantly with respect to those managed with 0.9% saline solution, the main recommendation in intensive care units is the management of the patient with ARF with Ringer lactate in order to minimize the presentation of this event.

The main limitations of the study were due to the fact that, first, the institution from where the data was collected is a clinic specialized in the treatment of patients with pathologies of traumatic origin, which limited the obtention of variables mentioned in the literature as sepsis, the cause of admission to the ICU, cardiovascular insufficiency, liver cirrhosis, respiratory failure, chronic heart failure, hypertension, heart disease, peripheral vascular disease, diabetes mellitus, jaundice, hemodynamic instability and anemia; in addition, the Clinic has agreements for the management of patients in ICU with only two of the EPS (health promoting entities) established in the region, which are not representative of the population of the city. This work is intended to be considered a theoretical reference support for future research related to the development of acute renal failure with the objective of minimizing the short, medium and long-term repercussions that this event entails.

Conflict of interest

The authors refer they do not have any conflict of interest.

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Ethical responsibilities

Protection of people and animals

The authors declare that no experiments were performed on human beings or animals for this research.

Data confidentiality

The authors declare that they have followed the protocols of their workplace on the publication of patient data.

Right to privacy and informed consent

The authors declare that patient data do not appear in this article.

Contribution of the authors

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