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# Epidemiology, patterns of care and prognosis of acute kidney injury in critically ill patients: A multicenter study in Argentina (The EPIRA study)

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ABSTRACT

*Background:* Acute kidney injury (AKI) is associated with high morbidity and mortality rates in the intensive care unit (ICU). In low- and middle-income countries (LMICs), epidemiological information about this condition is still scarce. Our main objective was to characterize its epidemiology, prognosis, and its treatment.

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Patterns of care
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*Methods:* This multicenter prospective cohort study included 1466 patients from 35 ICUs during 6 months in Argentina in 2018. Risk factors and outcomes in patients with and without AKI, and between AKI on admission ($AKI_{adm}$) and that developed during hospitalization ($AKI_{hosp}$) were analyzed.
*Results:* AKI occurred in 61.3% of patients (900/1466); 72.6% were $AKI_{adm}$ and 27.3% $AKI_{hosp}$. Risk factors were age, BMI, arterial hypertension, cardiovascular diseases, diabetes, SOFA, APACHE II, dehydration, sepsis, vasopressor use, radiocontrast, diuresis/h and mechanical ventilation. Independent predictors for AKI were sepsis, diabetes, dehydration, vasopressors on admission, APACHE II and radiocontrast use. Renal replacement therapies (RRT) requirement in AKI patients was 14.8%. Hospital mortality in AKI vs. non-AKI was 38.7% and 23.3% ($p < 0.001$); and in $AKI_{adm}$ vs. $AKI_{hosp,}$ 41.2% and 37.8% ($p = 0.53$).
*Conclusions:* ICU-acquired AKI has high incidence, complications and mortality. Risk factors for AKI and RRT utilization were similar to those described in other epidemiological studies. $AKI_{adm}$ was more frequent than $AKI_{hosp}$, but had equal prognosis.

## 1. Introduction

Acute kidney injury (AKI) is a common health problem and, in hospitalized patients, is associated with increased morbidity and mortality [1]. Each year, AKI develops in 13.3 million individuals globally; of these, 85% live in low- and middle-income countries (LMICS) and 1.4 million die annually [2,3]. The incidence of AKI is widely variable across different countries, depending on the settings (hospital vs. community-acquired AKI) and on the frequency of the associated different exposures and comorbidities. In LMICs, clinical presentation of AKI is related to location. In larger cities hospital-acquired AKI occurs more frequently and is associated with ICU admission, multiorgan disfunction, sepsis, nephrotoxic drugs, post-cardiovascular procedures, complex surgeries, and increasing age [3]. On the contrary, community-acquired AKI is more common in rural areas and usually affects young individuals with hypovolemia secondary to diarrhea and dehydration. Despite being a preventable, treatable, and reversible disease, AKI constitutes a burden on the weak health systems in these regions [3].

The lack of recognition, prevention and treatment of AKI is associated with scarce resources and inadequate healthcare structure and organization [4]. In South America, the available data on AKI are scarce [4,5]. Moreover, in Argentina, the impact of AKI developed in critically ill patients on outcomes has not yet been studied, which limits the possibility of drawing conclusions that could contribute to improving the evolution of these patients. For these reasons, from the Argentine Intensive Care Society (SATI) a prospective multicentric cohort study was launched, with the following objectives:

- To characterize the epidemiology, risk factors, clinical presentation, treatment, and outcomes of AKI in the ICU.
- To describe the differences between AKI present on ICU admission compared to AKI occurring during ICU stay.

## 2. Methods

### 2.1. Design

The Argentine Society of Intensive Care (SATI) organized a national, multicenter, prospective cohort study which included consecutive patients admitted to participating centers between 1st June and 1st December 2018.

Two local researchers were appointed per ICU, who were in permanent contact with the principal researchers of the study to solve any difficulty. They were also responsible for data integrity and uploading to a central database. Electronic, web-based, and paper forms were made available to each center to complete.

The institutional review board at each center approved the study, and written informed consent was obtained from all patients or surrogates.

### 2.2. Patients

We included patients over 18 years of age admitted to the ICUs during the study period.

Our exclusion criteria were the presence of chronic kidney disease (patients on chronic haemodialysis, or with an elevated creatinine measured within 3 months of ICU admission), AKI due to obstruction, patients who were readmitted to the ICU, and those who refused to sign the informed consent form.

### 2.3. Variables

The following variables were collected on ICU admission: age; gender; body mass index (BMI); Acute Physiology and Chronic Health Evaluation (APACHE) II and Sequential Organ Failure Assessment (SOFA) scores, comorbidities; and, for the first 24 h, fluid use (ml/day), type of fluid, and diuresis.

The following risk factors for AKI development were recorded: sepsis and septic shock (according to Sepsis-3 definitions) [6], arrythmia, burns, trauma, cardiac surgery with and without extracorporeal circulation, nephrotoxic drugs, contrast agents, dehydration, advanced age (>65 years), onco-hematological disease, diabetes mellitus, and anemia. Definitions are provided in Table S1.

During ICU hospitalization, the following events and complications were recorded: use of vasopressors and inotropes, including the type of drug used and its dose; intra-abdominal pressure; use of radiocontrast; mechanical ventilation (MV) support and development of acute respiratory distress syndrome (ARDS). Additionally, the requirement for renal replacement therapy (RRT), the method used (haemodialysis, hemofiltration, hemodiafiltration), and days of use were recorded.

The main outcome variable was hospital mortality. An additional objective was to identify the risk factors for AKI.

The following predetermined sub-groups were explored, according to the baseline creatinine defined by MDRD formula (Modification of diet in renal disease). MDRD baseline Creatinine refers to predefined creatinine according to age, sex and race [7,8,10].

-Non-AKI: no changes in the values of creatinine or diuresis.

-AKI: changes of creatinine from baseline already present on ICU admission or occurring during hospitalization in the ICU.

Patients were also stratified according to the KDIGO (Kidney Disease Improving Global Outcomes) 2012 guidelines scale for AKI [9,11]:

-KDIGO 1: serum criteria: creatinine ≥0.3 mg/dl or increases of 1.5 to 1.9 times the basal creatinine. Urinary criteria ≤0.5 ml/kg/h for ≥6–12 h.

-KDIGO 2: serum criteria: increases of 2 to 2.9 times basal creatinine. Urinary criteria: ≤0.5 ml/kg/h; ≥12 h.

-KDIGO 3: serum criteria: 3-fold increases in baseline creatinine or creatinine values ≥4.0 mg/dl or initiation of renal replacement therapy. Urinary criteria: ≤0.3 ml/kg/h for ≥24 h or 12-h anuria.

Additionally, the following predetermined sub-groups were explored:

-AKI admission ($AKI_{adm}$): modification of creatinine values or diuresis according to KDIGO guidelines scale on ICU admission, in relation to baseline creatinine estimated by MDRD.

-AKI hospitalization ($AKI_{hosp}$): modification of creatinine values or diuresis according to KDIGO guidelines scale occurring at ≥3 days after ICU admission.

The frequency of AKI was calculated as the number of patients who developed AKI regarding to the total population admitted to the ICU during the study period. We also reported the rate of $AKI_{adm}$ and $AKI_{hosp}$ for the entire AKI cohort.

The following characteristics of the participating centers were recorded: localization (city, province), type of hospital (public, private, social security; university-affiliated or not), number of hospital and ICU beds, type of ICU (medical, medical-surgical, medical-surgical-coronary care), number of ICU physicians, critical care specialists, residents), nurse-patient ratio (1:1–2, 1:3–4, 1:5–6), availability of RRT, type of RRT service, availability of urgent RRT, and types of RRT techniques.

### 2.4. Statistical analysis

Data are presented as proportions for categorical variables, mean and standard deviation or median and interquartile ranges [IQR 25–75%] for continuous variables. The comparisons were made with the $X^2$ or Fischer test, *t*-test or sum of ranks of Wilcoxon, as appropriate. Missing data were recorded and are provided in the Supplementary material. The main comparisons were made between patients who developed AKI and those who did not, and between $AKI_{adm}$ and $AKI_{hosp}$.

All tests were two-sided. A *p* value of <0·05 was considered statistically significant. Kaplan-Meier curves were constructed for patients with and without AKI; and for KDIGO stages. Differences were analyzed with the log-rank test.

To identify independent predictors of AKI development, variables differing between patients with and without AKI which had a *p* value <0.10 value of were tested into a multivariable logistic regression model.

We also sought to identify independent predictors of hospital mortality by means of logistic regression analysis.

Local investigators were contacted in case of missing data and possible errors. Figures were checked in the presence of extreme values.

Data were analyzed with Stata 14.0 (StataCorp LP, College Station, TX, USA).

## 3. Results

We included 35 ICUs located in 15 Argentine provinces (Table S2). A total of 1466 patients were admitted to the participant ICUs, of whom 61.3% (900/1466) had AKI (Fig. 1). Of these, 830 (92.3%) were diagnosed by an increase in serum creatinine and 70 (7.7%) by a decrease in 6 to12-hour urinary output. Epidemiological characteristics, risk factors, clinical variables are described in Table 1. Briefly, AKI patients were older and had higher BMI than those without AKI, albeit there were no differences between gender. Likewise, arterial hypertension, arrythmias, vasopressor use, sepsis, diabetes and dehydration were more frequent in the group with AKI.

Patients with AKI were more frequently admitted from the emergency room and general wards, and were more severely ill on admission, according to APACHE II and SOFA scores. KDIGO 1 was the most prevalent stage (Table 1). Vasopressor and inotropic administration and mechanical ventilation utilization were significantly more frequent in AKI patients during ICU stay, compared to patients without AKI (Table 2). In addition, severe forms of ARDS were more frequent in AKI patients. RRT was required in 134 patients (14.8%); intermittent

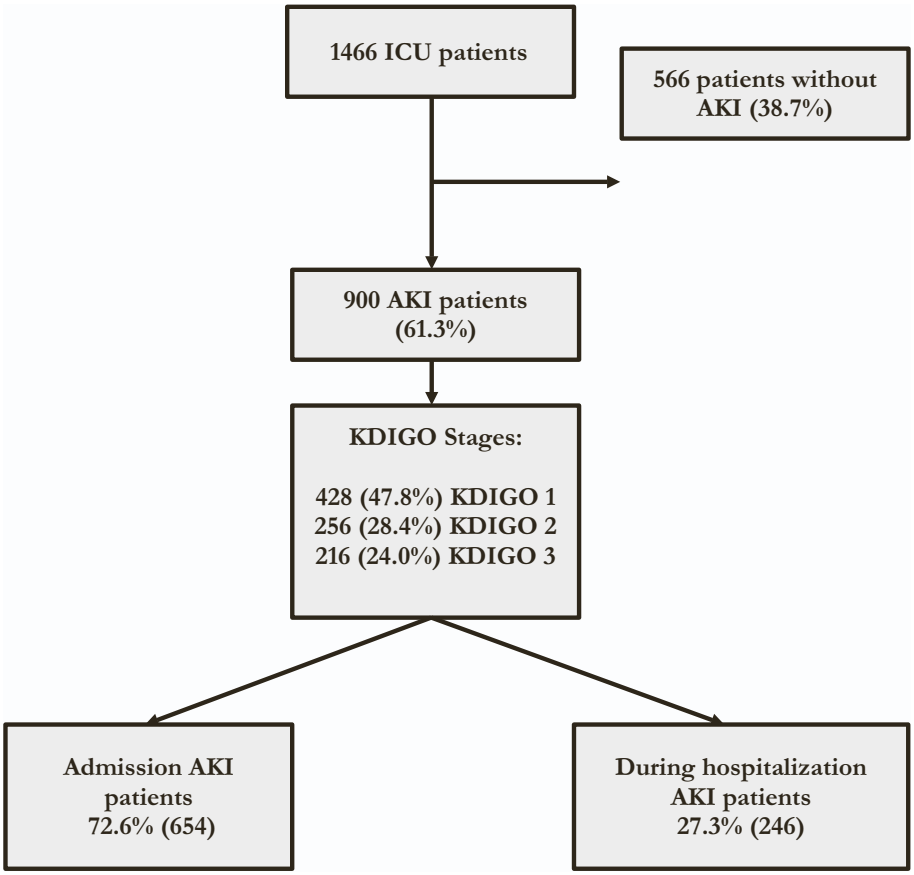


**Fig. 1.** Flowchart of the EPIRA study.

**Table 1**
Epidemiological and clinical characteristics of the entire group and of AKI and non-AKI patients.

| | All patients ($n = 1466$) | Patients with AKI $n = 900$ (61.3%) | Patients without AKI $n = 566$ (38.6%) | $p$ value |
|---|---|---|---|---|
| Age in years, mean (± SD) | 56.1 ± 20 | 57.8 ± 19 | 53.3 ± 20 | <0.001 |
| Age > 65 years (%) | 604 (41.2) | 408 (45.3) | 196 (34.6) | <0.001 |
| Female gender (%) | 632 (43.1) | 380 (42.2) | 252 (44.5) | 0.386 |
| Body mass index, median (IQR) (kg/m$^2$) | 26 [24–29] | 26 [24–29] | 26 [23–28] | <0.01 |
| Obesity (BMI ≥30 kg/m$^2$) (%) | 308 (21.0) | 216 (24.0) | 92 (16.2) | <0.001 |
| *Comorbid diseases* | | | | |
| Arterial hypertension (%) | 655 (44.7) | 442 (49.1) | 213 (37.6) | <0.0001 |
| Congestive heart failure (%) | 115 (7.8) | 73 (8.1) | 42 (7.4) | 0.632 |
| Coronary disease (%) | 109 (7.4) | 71 (7.9) | 38 (6.7) | 0.404 |
| Arrhythmias (%) | 87 (5.9) | 62 (6.9) | 25 (5.4) | 0.051 |
| Chronic obstructive lung disease (%) | 119 (8.1) | 70 (7.8) | 49 (8.7) | 0.548 |
| Chronic liver failure (%) | 53 (3.6) | 35 (3.9) | 18 (3.2) | 0.479 |
| *Risk factors of AKI* | | | | |
| Sepsis (%) | 480 (32.7) | 358 (39.8) | 122 (21.6) | <0.001 |
| Vasopressors at admission (%) | 541 (36.9) | 392(43.6) | 149 (26.3) | <0.001 |
| Burns (%) | 18 (1.2) | 10 (1.1) | 8 (1.4) | 0.609 |
| Cardiac surgery with extracorporeal support (%) | 25 (1.7) | 13 (1.4) | 12 (2.1) | 0.331 |
| Cardiac surgery without extracorporeal support (%) | 256 (17.5) | 150 (16.7) | 106(18.7) | 0.312 |
| Radiocontrast use before admission (%) | 122 (8.3) | 81 (9.0) | 41 (7.2) | 0.236 |
| Dehydration (%) | 256 (17.5) | 182 (20.9) | 74 (13.1) | <0.001 |
| Diabetes (%) | 274 (18.7) | 198 (22) | 76 (13.4) | <0.001 |
| Cancer (%) | 170 (11.6) | 97 (10.8) | 73 (12.9) | 0.217 |
| Anemia, (%) | 118 (8.1) | 65 (7.2) | 53 (9.4) | 0.412 |
| *Nephrotoxic drug utilization* | | | | |
| Angiotensin-converting enzyme inhibitor (%) | 44 (3.0) | 27 (3.0) | 17 (3.0) | 0.997 |
| Angiotensin-receptor antagonists (%) | 14 (0.9) | 8 (0.9) | 6 (1.0) | 0.743 |
| Chronic use of diuretics (%) | 115 (7.8) | 72 (8.0) | 43 (7.6) | 0.780 |
| Non-steroidal anti-inflammatory drugs (%) | 149 (10.2) | 86 (9.6) | 63 (11.1) | 0.331 |
| Previous antibiotic utilization (%) | 116 (7.9) | 72 (8.0) | 44 (7.8) | 0.876 |
| *Site of hospital admission* | | | | 0.043 |
| General ward (%) | 257 (17.6) | 168(18.7) | 89 (15.7) | |
| Emergency room (%) | 713 (48.6) | 452 (50.2) | 261 (46.1) | |
| Surgery room (%) | 364 (24.8) | 207 (23.0) | 157 (27.7) | |
| Other hospital (%) | 132 (9.0) | 73 (8.1) | 59 (10.4) | |
| *Clinical characteristics* | | | | |
| Diuresis in the previous 12 h in ml/h, median (IQR) | 62.5 [33−100] | 50 [25–100] | 75 [50–139] | <0.001 |
| Diuretics use 24 h previous (%) | 159 (10.9) | 118 (13.1) | 41 (7.2) | <0.001 |
| *Severity-of-illness scores* | | | | |
| Charlson scale, median (IQR) | 1 [0–3] | 1 [0–3] | 1 [0–3] | 0.139 |
| APACHE II score, mean (SD) | 16 ± 8 | 17 ± 8 | 14 ± 7 | <0.001 |
| SOFA score, median (IQR) | 4 [2–7] | 5 [3–8] | 3 [2–6] | <0.001 |
| KDIGO scores | – | | – | |
| Stage 1, (%) | | 428 (47.6) | | |
| Stage 2, (%) | | 256 (28.4) | | |
| Stage 3, (%) | | 216 (24.0) | | |
| Baseline creatinine in mg/dl, mean (SD) | 0.99 ± 0.15 | 0.99 ± 0.14 | 1.00 ± 0.15 | 0.086 |

Data are presented as n (%), median [interquartile range] o mean ± deviation standard. AKI: Acute.
Kidney Injury. APACHE II: Acute and Chronic physiological assessment score. SOFA: Sequential assessment of failure scale. MDRD: Diet modification kidney disease, KDIGO: Organization improving the global results of kidney disease.

haemodialysis was the most widely chosen technique (98%), while only 2% of the patients used continuous haemodialysis.

With respect to outcomes, AKI patients had higher ICU and hospital mortality (respectively 24.5% vs. 11.8%; and 38.7% vs. 23.2%; $p < 0.001$ for both comparisons) and longer duration of mechanical ventilation support and ICU stay, compared to patients without AKI. Hospital mortality according to KDIGO stages 1, 2 and 3 stages was 35.7% (152/426); 36.7%; (95/256) and 47.2% (102/216), respectively ($p = 0.03$, corrected for multiple comparisons).

Total fluid intake during the first 3 days was similar in AKI patients and in those without AKI ($p = 0.67$). However, Ringer lactate was more frequently administered in AKI than in patients without AKI during the first day (1200 ml [1000−2000] vs. 1000 ml [570–1500]; $p < 0.01$). Diuretics were more frequently used in AKI during the first 24 h than in patients without AKI (13.1% vs. 7.2%; $p < 0.001$).

As expected, after being admitted, diuresis during the first 24 h in patients with AKI vs. patients without AKI was different (1340 ml [700–2100] vs. 1600 ml [900–2200]; $p = 0.007$). Also, diuresis (ml/h) during the first 12 h was different 50 ml/h (25–100) vs. 75 ml/h (50–139); $p < 0.001$).

Of the 900 patients with AKI, 72.6% ($n = 654$) presented AKI on admission and 27.3% ($n = 246$) developed it at 6 ± 2.5 days of hospitalization. The only significant differences between both subgroups were higher BMI and radiocontrast utilization in AKI developed during hospitalization. Furthermore, the use of RRT was significantly higher in the last-mentioned group (Table 3).

Fig. 2 shows the Kaplan Meier curve of 30-day survival probability, where patients without AKI had higher probability of survival than AKI patients (log rank test; $p = 0.001$), and Fig. 3 shows the 30-day survival probability according to KDIGO stages (log rank test; $p = 0.08$).

Independently associated predictors of AKI identified by logistic regression were age, sepsis, diabetes, dehydration, radiocontrast use, vasopressor use on admission and APACHE II score (Table 4).

AKI, together with age, site of hospital admission, presence of sepsis, utilization of normal saline solution, APACHE II score and vasopressor use, acted as independent predictors of hospital mortality (Table 5).

With respect to ICUs' characteristics, 32 of the 35 participating ICUs

**Table 2**
Evolution, treatment, complications and outcomes.

| Variables | Patients with AKI $n = 900$ (61.3%) | Patients without AKI $n = 566$ (38.6%) | $p$ value |
|---|---|---|---|
| *Evolution and complications* | | | |
| RRT use (%) | 134 (14.8) | 0 | |
| ICU vasopressors use (%) | 287 (31.9) | 49 (8.7) | <0.001 |
| Norepinephrine(%) | 266 (97.4) | 46 (100) | 0.554 |
| Norepinephrine dose in ug/kg/min, median (IQR) | 0.3 [0.2–0.5] | 0.22 [0.1–0.4] | 0.082 |
| Inotropes (%) | 29 (3.2) | 3 (0.5) | <0.001 |
| Radio contrast use (%) | 45 (5.0) | 8 (1.1) | <0.001 |
| Mechanical ventilation (%) | 388 (43.1) | 102 (18.0) | <0.001 |
| ARDS (%) (Mild/moderate/severe) | 148/150/91 (38.1)/(38.6)/(23.4) | 58/33/11 (56.7)/(32.3)/(10.8) | <0.001 |
| *Fluid administration* | | | |
| Total fluid intake day 1 in ml, median (IQR) | 2074 [844–3465] | 2055 [860–3380] | 0.675 |
| Total fluid intake day 2 in ml, median (IQR) | 2732 [1600–3750] | 2665 [1305–3564] | 0.186 |
| Total fluid intake day 3 in ml, median (IQR) | 2470 [1245–3465] | 2381 [900–3200] | 0.273 |
| *Type of fluids* | | | |
| Normal saline solution in ml day 1 ($n = 1038$), median (IQR) | 1500 [750–2718] | 1562 [800–2750] | 0.326 |
| Normal saline solution in ml day 2 (ml) ($n = 1021$), median (IQR) | 1900 [1000–2964] | 2000 [1000−3000] | 0.655 |
| Normal saline solution in ml day 3 (ml) ($n = 941$), median (IQR) | 1755 [1000–2643] | 1700 [919–2600] | 0.332 |
| Lactate Ringer in ml at day 1 ($n = 341$), median (IQR) | 1200 [1000–2000] | 1000 [570–1500] | 0.007 |
| Lactate Ringer in ml at day 2 ($n = 270$), median (IQR) | 1000 [500–2000] | 1000 [600–1500] | 0.383 |
| Lactate Ringer in ml at day 3 ($n = 224$), median (IQR) | 1000 [500–2000] | 1000 [667–1500] | 0.393 |
| *Diuresis* | | | |
| Diuresis day 1 in ml, median (IQR) | 1340 [700–2100] | 1600 [900–2200] | <0.01 |
| Diuresis day 2 in ml, median (IQR) | 2100 [1400–2800] | 2045 [1440–2700] | 0.628 |
| Diuresis day 3 in ml, median (IQR) | 2200 [1500–3050] | 2200 [1550–2950] | 0.891 |
| *Results* | | | |
| ICU mortality (%) | 221/900 (24.5) | 67/566 (11.8) | <0.001 |
| Hospital mortality (%) | 348/900 (38.7) | 132/566 (23.3) | <0.001 |
| Length of mechanical ventilation in days, median (IQR) | 8 [5–15] | 7 [4–11] | <0.01 |
| Length of ICU stay in days, median (IQR) | 8 [5–16] | 7 [4–14] | <0.001 |
| Length of hospital stay in days median (IQR) | 19 [10−31] | 16 [10–29] | 0.342 |

Data are presented as n (%), median [interquartile range] o mean ± deviation standard; significance $p = 0.05$. AKI: Acute Kidney Injury. RRT: Renal replacement therapy. ug/kg/min: microgram/kg/min, ARDS: Acute Respiratory Distress Syndrome. ICU: Intensive Care Unit.

(91.4%) were located in big, provincial capital cities. Of note, 17 (48.6%) belonged to public hospitals, and 19 (54%) to university-affiliated-hospitals. All ICUs were situated in hospitals <500 beds, and mostly have 10–20 beds (49%). RRT was available in all, albeit with different intensity of support (some give 24/7; in other ICUs, RRT are available during 6–12 h, but are always on call. Other characteristics, human resources, and RRT utilization are shown in Table S3.

**Table 3**
Comparison between AKI present on admission vs. AKI developed during hospitalization.

| Variable | AKI on admission $n = 654$ (72.6%) | AKI during hospitalization $n = 246$ (27.3%) | $p$ value |
|---|---|---|---|
| Age (years), median (SD) | 58.1 ± 20 | 57.1 ± 19 | 0.498 |
| Age > 65 years (%) | 302 (46.2) | 106 (43.1) | 0.609 |
| Female gender (%) | 291 (44.5) | 89 (36.2) | 0.146 |
| BMI (kg/m$^2$), median (SD) | 27.2 ± 6.3 | 28.5 ± 8.3 | <0.01 |
| Obesity (%) | 149 (22.8) | 67 (27.2) | 0.27 |
| Sepsis prior to admission (%) | 258 (41.0) | 90 (36.6) | 0.427 |
| Diabetes (%) | 138 (21.1) | 60 (24.4) | 0.399 |
| Antibiotic previous use (%) | 55 (8.4) | 17 (6.9) | 0.494 |
| Diuretics previous utilization (%) | 94 (14.4) | 24 (9.8) | 0.106 |
| Days between hospital and ICU admission, median (IQR) | 1 [0–3] | 0 [0–1] | <0.01 |
| On-admission vasopressors (%) | 290 (44.3) | 102 (41.5) | 0.625 |
| Radiocontrast use (%) | 21 (3.2) | 24 (9.8) | <0.001 |
| ICU vasopressor use (%) | 34 (17.6) | 44 (25.6) | 0.136 |
| Serum creatinine day 1, median (IQR) | 1.3 [0.82–1.9] | 0.80 [0.70–1.0] | <0.001 |
| Serum urea day 1, median, (IQR) | 50 [33–89] | 35 [25–47] | <0.001 |
| Lactate Ringer volume day 1 (ml), median (IQR) | 1450 [1000–2000] | 1000 [500–2000] | 0.068 |
| Normal saline solution volume day 1 (ml), median (IQR) | 1500 [731–2740] | 1430 [800–2450] | 0.807 |
| Charlson scale, median (IQR) | 1 [0–3] | 2 [0–3] | 0.903 |
| APACHE II score, median (IQR) | 18 ± 8 | 17 ± 7 | 0.167 |
| SOFA score, mean (SD) | 6 ± 4 | 6 ± 5 | 0.999 |
| Renal replacement therapy utilization (%) | 31 (4.7) | 103 (41.9) | <0.001 |
| Mechanical ventilation utilization (%) | 231 (15.2) | 157 (63.8) | <0.01 |
| Hospital mortality (%) | 247 (37.8) | 101 (41.1) | 0.531 |

Data are presented as n (%), median [interquartile range] o mean ± deviation standard; significance p = 0.05. AKI: Acute Kidney Injury. APACHE II: Acute and Chronic physiological assessment score. SOFA: Sequential assessment of failure scale.

## 4. Discussion

This study represents the first report of the frequency, aetiology and outcomes of AKI in ICU patients in Argentina, an upper-middle income country. An AKI rate of 61.3% was observed, which is high in relation to the 25.4% to 42.4% reported in the only two epidemiological studies from South America, carried out in Uruguay and Brazil. [6,7]. Notwithstanding this, the global incidence reported varies from 35% to 65.8% [1,3-6,9]. Our high figures might be associated to the emphasis placed on the early recognition of AKI stage 1, which includes patients in whom minimal changes on serum creatinine occur. Urinary output, which usually alters earlier than serum creatinine, was utilized in only 7.7% of patients for AKI diagnosis. Since the use of urinary catheterization in a neighbor country with similar characteristics to Argentina -Brazil- is about 86.7% and 93.3%, factors other than the capacity of measurement of 6 to 12-h diuresis might explain the low rate of urinary output utilization to diagnose AKI [4,5]. A lack of alertness regarding

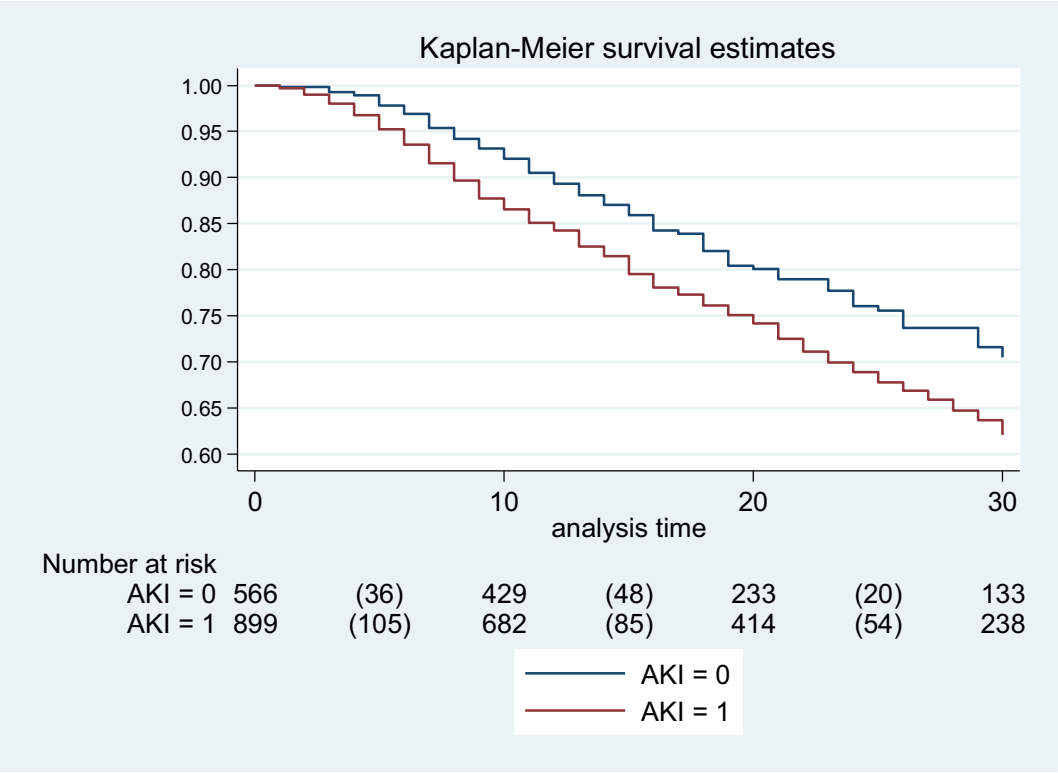


**Fig. 2.** Kaplan-Meier 30-day survival curve in AKI vs non-AKI patients.

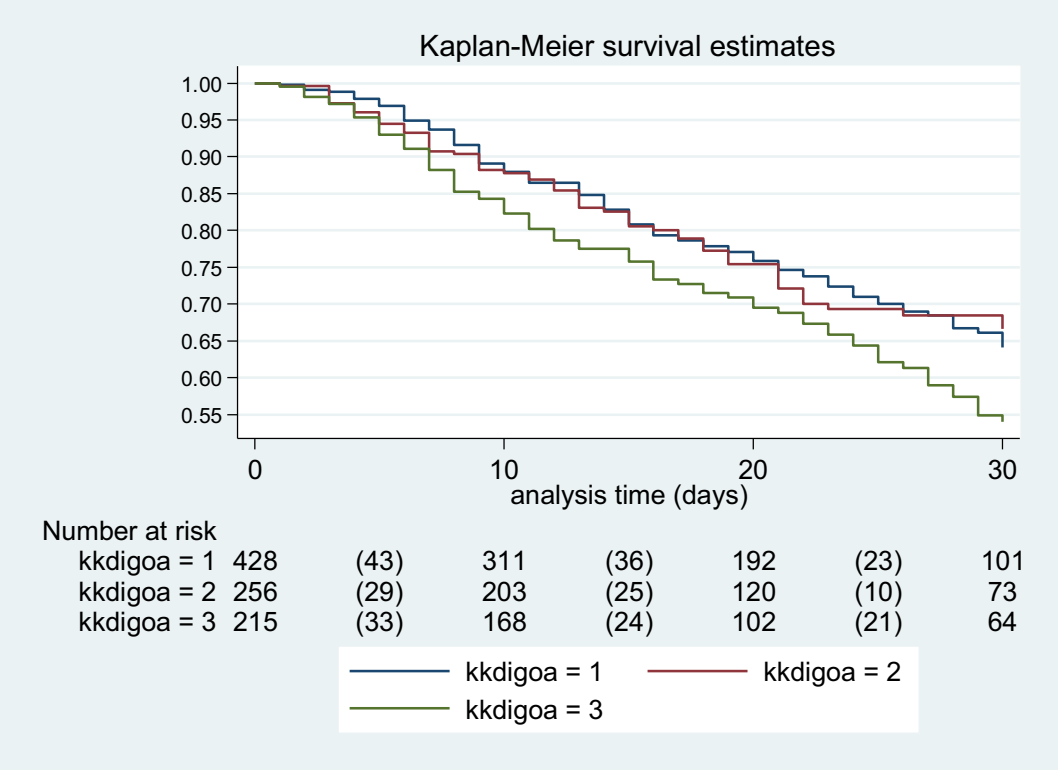


**Fig. 3.** Kaplan-Meier 30-day survival curve in AKI patients according to KDIGO scores.

the relevance of urinary output, or insufficient human resources to effectively monitor this crucial variable, might account for this shortfall.

AKI stage 1 frequency in our study was 47.6%, which is higher than in European epidemiological studies, such as the AKI-EPI and the FINNAKI studies [1,14]. However, this high frequency is similar to AKI Stage 1 reported by the two regional abovementioned studies (37.8% and 61.3%) [6,7].

Additionally, in LMICs, a high incidence of community AKI due to

**Table 4**
Independent predictors of AKI development.

| AKI | Odds ratio | Error Std. | P | [95% Conf. Interval] |
|---|---|---|---|---|
| Age | 1.01 | 0.00 | 0.022 | 1.001–1.013 |
| Sepsis | 1.81 | 0.24 | 0.000 | 1.402–2.345 |
| Diabetes | 1.45 | 0.22 | 0.017 | 1.070–1.964 |
| Dehydration | 1.38 | 0.22 | 0.041 | 1.013–1.879 |
| On-admission vasopressor use | 1.55 | 0.20 | 0.001 | 1.200–1.996 |
| APACHE II score | 1.03 | 0.01 | 0.000 | 1.017–1.051 |
| Radiocontrast use | 3.86 | 1.53 | 0.001 | 1.773–8.395 |
| Cons | 0.40 | 0.08 | 0.000 | 0.270–0.579 |

APACHE II: Acute and Chronic physiological assessment score.

**Table 5**
Independent predictors of hospital mortality in the entire population.

| Hospital mortality | Odds ratio | Error Std. | *P* | [95% Conf. Interval] |
|---|---|---|---|---|
| Acute kidney injury | 1.27 | 0.15 | 0.050 | 0.99–1.61 |
| Age | 1.01 | 0.03 | 0.000 | 1.01–1.02 |
| Site of hospital admission | 0.85 | 0.06 | 0.026 | 0.74–0.98 |
| Sepsis | 1.58 | 0.20 | 0.000 | 1.24–2.03 |
| Normal saline solution use | 1.67 | 0.22 | 0.000 | 1.30–2.16 |
| APACHE II score | 1.05 | 0.01 | 0.000 | 1.04–1.07 |
| On-admission vasopressor use | 1.73 | 0.24 | 0.000 | 1.32–2.28 |
| Cons | 0.61 | 0.02 | 0.000 | 0.03–0.11 |

hypovolemia associated to diarrhea has been reported [6,7]. Therefore, these situations may have contributed to these higher incidences in Latin-American epidemiological studies.

AKI most frequent causes were sepsis (39.8%) and dehydration (21%), consistent with a recently published cross-sectional study of 289 centres in 72 countries, in which rates of 39% and 46% were reported [17].

The risk factors independently associated with AKI were age, BMI, diabetes (22%), arterial hypertension (49.1%) and arrythmias (6.9%). All have been reported as independent risk factors for AKI development in ICU patients in large European, Latin-American and Asian studies [1,6,7,12-16]. Furthermore, these risk factors were associated with reduced renal functional reserve, compromised renal recovery and, therefore, the development of chronic kidney disease [18,19,20].

AKI patients recorded a higher use of vasopressors in comparison with patients without AKI (32% vs. 8.7%, $p < 0.001$). Norepinephrine was the vasopressor most frequently used (97%). Furthermore, vasopressor utilization on ICU admission, a surrogate of hypotension, was an independent factor for the development of AKI. Norepinephrine administration has been shown to improve renal perfusion pressure in patients with septic shock [20,21]. However, in this group of patients, there are no studies showing a reduction in RRT requirement [20]. The use of inotropics was low when compared to the AKI-EPI study (3.2% vs. 10.4%) [1].

AKI patients required mechanical ventilation more frequently. Although its utilization was lower than that reported in large epidemiological studies, the association with AKI development remains [1,6,7,12-16]. A recently published systematic review also showed that mechanical ventilation requirement was associated with an increased risk of AKI development [22,23].

ICU stay was longer in patients with AKI, compared to patients without AKI. In general, this variable is related to disease severity and mechanical ventilation requirement [1,6,7,12-16].

Among the patients with AKI, 47.6% belonged to the KDIGO 1 category, while 28.4% and 24% belonged to KDIGO 2 and KDIGO 3, respectively. Unlike epidemiological studies in Europe and Asia, we observed a high incidence of KDIGO stage 1 [1,12-16]. Regarding more severe stages, incidences are similar to regional epidemiological studies [6,7,16]. Recently, it has been shown that the incidence of AKI and its stages depend on basal creatinine [24]. The basal creatinine on admission might vary and significantly modify the incidence of AKI, especially when it is calculated rather than measured [25]. In addition, diuresis collection can be inaccurate, especially when it is collected hourly [24]. The differences in basal creatinine estimation might account for the discrepancies found between epidemiological studies.

Of the KDIGO stage 3 patients, 14.8% required RRT. Between 15 and 20% of the ICU admitted patients will require RRT and its use constitutes an independent risk factor of ICU morbidity and mortality [26]. As a recent Latin-American survey, which included 246 RRT units from 14 countries showed, the most used RRT technique is intermittent haemodialysis (97%) [16]. By contrast, recent Asian and European studies report a high use of continuous therapies [1,6,12,13]. Notwithstanding its wide utilization, continuous RRT has not shown an advantage in terms of survival [26-28].

Many studies have reported AKI-associated mortality in the ICU [1,6,7,12-16]. In developed countries, an ICU mortality between 25 and 30% was described (28.8% for NEFROINT study and 24% for AKI-EPI) [1,15]. In LMICs, AKI mortality figures reported are heterogeneous and ICU mortality is not always informed. Studies of AKI from South America which included ICU patients have reported hospital mortalities ranging from 25.7% to 42.2% [6,7], while reports from Africa and Asia have shown 28-day and 30-days mortality of 22.5% and 44.1%, respectively [29,30].

We reported an AKI mortality of 38.7%, without differences between AKI on admission vs. AKI developed in the ICU (38,7% vs. 41.1% $p = 0.342$). Moreover, consistently with previous studies, we observed an association between AKI development and mortality risk [1,6,12-16]. However, these differences might be due to a delay in consultation and/or lack of recognition of AKI by physicians. All in all, our findings are similar to other reports, which have emphasized the differences between LMIC and HICs [17,32].

With respect to the timing of AKI development, AKI developed during hospitalization was less frequent (26.7% vs. 72.3% on admission; $p < 0.001$); its prevalent risk factors were BMI and utilization of radiocontrast, and required higher RRT (76.9% vs. 23.1%, $p < 0.001$). Yet patients that require radiocontrast administration are probably sicker and hence might have concomitant risk factors leading to nephrotoxicity, such as shock, dehydration, nephrotoxic antibiotics, and others. Mortality, however, was similar in the two groups (37.8% vs. 41.2%, $p = 0.531$). Studies assessing prognosis of these two conditions are scarce. An African multicentre study of 527 patients reported an AKI incidence at admission of 39.7%, and of 37.4% during hospitalization [29]. As in our cohort, both conditions had the same risk of death (HR 2.74 [1.45–5.17] vs. 2.14 [1.02–4.48]; $p = 0.41$) [29]. Not unsurprisingly, given the severity of the condition, AKI also acted as an independent predictor of hospital mortality, similar to the findings of other researchers [12,34].

Recently, a retrospective Canadian study involving 815 patients with COVID-19 has shown a higher incidence of AKI on admission than during hospitalization, reporting a higher risk of death in the latter condition (OR: 5.28 [2.60–10.73] vs. 7.87 [4.35–14.23] [31,33]. However, this study has some limitations since it only included patients with COVID-19. Our results are consistent with pre-existing studies which found no differences between mortality in AKI present on admission and during hospitalization in COVID-19 populations. [33,35] Finally, given that there is scarce information about the differences and prognosis of these two subgroups of AKI, our study adds up to the knowledge on the issue. We hope our findings will contribute to raise awareness of this condition in the community by increasing recognition of risk factors for AKI, but also in healthcare venues, to improve AKI management and outcomes.

Our study has some limitations. First, participation was voluntary so there might be some degree of selection bias. Most ICUs were located in

big, capital cities, therefore the information about AKI frequency and RRT availability occurring in ICUs in smaller cities might be underestimated. However, our cohort includes at least one centre of each geographical region of Argentina, and the information about physical and human resources and RRT availability is comparable to that of a study about organizational issues and resources recently performed in Latin America [36]. Second, we estimated baseline creatinine according to KDIGO 2012 guidelines from the MDRD table due to the difficulties having the real usual creatinine. This may have over or underestimated the different AKI stage categories. Third, due to the intensity of data upload, it was not possible to calculate variables after 7 days of hospitalization in patients in whom AKI had been diagnosed. Four, this study did not collect data about kidney recovery or long-term results.

The strengths of this study reside in its prospective, multicentre design that included 35 ICUs and thus provides real-life information about AKI in critically ill patients. Likewise, we obtained a general view about RRT utilization in a LMIC. In addition, our study also focuses on patients who developed AKI during hospitalization, a population which was not frequently evaluated in previous epidemiological studies. Finally, it is the first study that informs mortality associated with AKI in Argentine ICUs.

## 5. Conclusion

The main finding of this study is the high incidence of AKI of patients admitted to the ICU. Compared to those who did not develop AKI, AKI patients were more severely ill on admission and developed more complications, which was reflected in their higher mortality, mechanical ventilation requirement and longer duration of mechanical ventilation and of ICU stay. Although AKI already present on admission was more prevalent than that developed during hospitalization, no major clinical differences were observed between both subgroups.

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## CRediT authorship contribution statement

**Paolo Nahuel Rubatto Birri:** Conceptualization, Methodology, Investigation, Formal analysis, Project administration, Funding acquisition, Data curation, Supervision, Writing - original draft, Writing - review & editing. **Roberto Giannoni:** Conceptualization, Validation, Resources, Visualization, Data curation, Investigation, Project administration, Supervision. **Mariano Furche:** Conceptualization, Validation, Resources, Visualization, Data curation, Investigation, Methodology. **M. Nahra:** Investigation, Data curation, Resources. **M. Arce Gallardo:** Investigation, Data curation, Resources. **Gabriela Segui:** Investigation, Data curation, Resources. **Santiago Ilutovich:** Investigation, Data curation, Resources. **Matias Olmos:** Investigation, Data curation, Resources. **Pilar Birri:** Investigation, Data curation, Resources. **Maria Romano:** Investigation, Data curation, Resources. **Patricia Ayala:** Investigation, Data curation, Resources. **Veronica Petrochelli:** Investigation, Data curation, Resources. **Luis Huespe:** Investigation, Data curation, Resources. **David Banegas:** Investigation, Data curation, Resources. **Alejandro Gomez:** Investigation, Data curation, Resources. **Graciela Zakalik:** Investigation, Data curation, Resources. **Fernando Lipovestky:** Investigation, Data curation, Resources. **Juan Pablo Montefiore:** Investigation, Data curation, Resources. **Cayetano Galletti:** Investigation, Data curation, Resources. **Carlos Pendino:** Investigation, Data curation, Resources. **Mariana Vera:** Investigation, Data curation, Resources. **Sebastian Mare:** Investigation, Data curation, Resources. **Laura Bergallo:** Investigation, Data curation, Resources. **Gabriela Fernandez:** Investigation, Data curation, Resources. **Maria Luz Campassi:** Investigation, Data curation, Resources. **Fernando Ríos:** Investigation, Data curation, Resources. **Pablo Saul:** Investigation, Data curation, Resources. **Pablo Bonsignore:** Investigation, Data curation, Resources. **Beatriz Gallardo:** Investigation, Data curation, Resources. **Mirta Gimenez:** Investigation, Data curation, Resources. **Elisa Estenssoro:** Supervision, Conceptualization, Methodology, Formal analysis, Project administration, Writing - review & editing.

## Declaration of Competing Interest

None.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2023.154382.

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