

Prevalence and factors associated with acute kidney injury in older adults hospitalized. A single-center observational study.

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Abstract

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Introduction: Acute kidney injury (AKI) is a persistent disorder that is a morbidity and mortality factor in hospitalized older adults. It is a public health problem associated with several factors, some modifiable.

Methods: Analytical cross-sectional study carried out in Cuenca in the HVCM emergency service from March 2018 to March 2020. The sampling was probabilistic, evaluating 200 older adults. The KDIGO (Kidney Disease: Improving Global Outcomes) criteria were used to determine and classify AKI. The data were analyzed with the SPSS v.20.0 program, using the prevalence ratio (PR) to measure association, with a 95% CI and statistical significance $P < 0.05$.

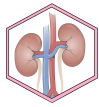
Results: The mean age was 80 ± 8.37 years, the female gender predominated, and the majority had a primary education level. The prevalence of AKI was 33%. Four out of ten older adults had AKI stage 3; more than half had high blood pressure and used nephrotoxicity. The associated factors were sepsis (PR 2.27; 95%CI 1.58- 3.27; $P = 0.0002$), dehydration (PR 1.73; 95%CI 1.18-2.54; $P = 0.006$), and diabetes mellitus (PR 1.58; 95% CI 1.07– 2.34 $P = 0.0181$).

Conclusion: Over a third of hospitalized older adults presented AKI; KDIGO stage 3 predominated and was associated with sepsis, dehydration, and diabetes mellitus.

Keywords:

MESH: Acute Kidney Injury, Aged, Frail Elderly, Epidemiology, Emergency Medical Services.

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Acute kidney failure (AKI) is defined as an abrupt decline in kidney function that occurs for seven days or less and is classified into three stages [1]. It is related to multiple etiologies in older adults: prerenal (volume depletion, hypoperfusion), renal (interstitial, tubular, glomerular, and vascular), and postrenal (obstructive). It is associated with several factors, such as acute pathologies (dehydration, obstructive uropathy, sepsis), chronic diseases (liver cirrhosis, diabetes mellitus, arterial hypertension), and the use of nephrotoxic drugs [2].

The prevalence of AKI is estimated to be increasing, and its impact on long-term health and healthcare costs has been increasing in recent years [3]. Furthermore, it is a preventable disease that is often underdiagnosed and acts as an individual factor of morbidity and mortality in hospitalized patients [4]. Comorbidities and aging contribute directly to the decline in kidney function, making this population more susceptible to developing AKI [5]. Silveira et al., in their meta-analysis, showed that the development of AKI was twice as high in older adults compared to young adults [6]; similar results were reported by Li Q. et al. in their study, where they also demonstrated a mortality of 42.5% at 90 days post-discharge [4]. Therefore, it is essential to prioritize the prevention of AKI and its early detection to reduce morbidity and mortality in older adults and reduce health costs.

Despite much information on this topic, no local data focus on aged people. Chávez et al., in their study in Latin America, affirm that there is a gap in information on the epidemiology of AKI [7]. Furthermore, the prevention and diagnosis of AKI in older adults do not receive adequate attention. Therefore, it is necessary to carry out local epidemiological studies in older adults to prevent and treat this pathology early.

The purpose of the present investigation was to determine the prevalence and factors associated with acute kidney injury in older adults hospitalized in the emergency room of a public reference hospital in Cuenca, Ecuador, during three years of follow-up.

Materials and methods

Study design

The study is an analytical cross-sectional observational study.

Scenery

The study was carried out in the emergency service of the Vicente Corral Moscoso Hospital of the Ministry of Public Health in Cuenca (VCMH), Ecuador. The study period was from March 1, 2018, to March 31, 2020.

Participants

Patients older than or equal to 65 years of age who were hospitalized in the institution's emergency department with a minimum of two

serum creatinine determinations were included. Patients with a history of CKD demonstrated by complementary studies or GFR <60 ml/min/1.73 m² SC calculated by the Modification of Diet in Renal Disease Study (MDRD) formula in the last three months or during hospitalization were excluded [1]. Patients with terminal illnesses were also excluded.

Variables

The variables studied were ranked in order:

- Dependents: acute kidney injury
- Moderators: age, gender, educational level, residence.
- Independent: nephrotoxic drugs, dehydration, sepsis, obstructive uropathy, diabetes mellitus, arterial hypertension and liver cirrhosis.

Data sources/measurements

The source was indirect. The information was collected in an electronic database created by the authors from the medical records found in the institution's archive. The biochemical measurements were part of the regular activity of the institution. They are carried out daily in the control studies and were collected from the institution's laboratory system.

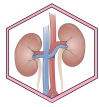
Definition of Acute Kidney Failure

AKI was defined based on the KDIGO criteria, with a serum creatinine value ≥ 1.5 times its baseline value in 7 days or increased creatinine ≥ 0.3 mg/dl in 48 hours. Baseline creatinine was the lowest value recorded in the last three months or during hospitalization. The criterion of diuresis reduction set out in the KDIGO guide was not taken into account because these are clinical records in which this value is not regularly specified. The history was reviewed to determine the presence of associated factors, and various validated scales detailed in Table 1 were used.

For future reproducibility purposes, the equipment, technique, and reagents used in the institution's laboratory to determine the values required in the study are detailed: creatinine, equipment: Roche Cobas c 501, technique: enzymatic method, kinetic Jaffé method. Data obtained from the VCMH clinical laboratory (2021). The reference value of serum creatinine for men was 0.7 to 1.2 mg/dl and 0.5 to 0.9 mg/dl for women.

Biases

To avoid possible interviewer, information, and memory biases, the leading researcher kept the data at all times with a guide and records approved in the research protocol. Observation and selection bias were avoided with the application of participant selection criteria. All clinical and paraclinical variables from the period already mentioned were recorded. Two researchers independently analyzed each record



in duplicate, and the variables were recorded in the database once their agreement was verified.

Table 1. Scales were used for the diagnosis of the factors studied.

Factors studied	Scales used
Dehydration	The Thompson et al. classification for dehydration in the older adult consists of 2 parameters: loss of body weight and signs and symptoms compatible with dehydration; according to these, it is classified as subclinical, mild, moderate, severe, or mortal.
Sepsis	The SOFA scale (score for assessment of failed organic sequential) consists of 6 parameters corresponding to an organ. Each organ is classified from normal until the dysfunctional organ with a score from 0 to 4; according to the score, it can estimate the Mortality rate: 2 points standard, 3 points 8% mortality, 4 points failure multiorgan, 12 either further points 80% of mortality, 15 points or more 90% of mortality.
Mellitus diabetes	The criteria of the ADA guide (American Association of Diabetes) 2019 consists of 4 parameters based on the elevation abnormal of glucose, the presence of one of which establishes the diagnosis.
Hypertension arterial	We took the guidelines of the practice clinic for treating hypertension arterial of the Ministry of Public Health of Ecuador 2019. It consists of 2 parameters according to the degree of systolic blood pressure and diastolic; it is classified as normal, normal high, hypertension grade 1, degree 2, and degree 3.

Study size

The sample consisted of patients admitted to the emergency service of VCMH between March 2018 and March 2020; a total of 3,360 older adults were obtained. To obtain the sample, we used the Sierra and Bravo formula used for prevalence studies with a finite universe (3360), based on the variable with the lowest prevalence of 16.7% of liver cirrhosis ($p=0.167$), $q=0.833$, $2=0.0025$ $\alpha \cdot Z^2=3.84$, with a 95% confidence interval and a margin of error of 5%. The formula is $N \cdot p \cdot q \cdot Z^2 / (N-1) \cdot \alpha^2 + p \cdot q \cdot Z^2$, resulting in 200 cases. The sample was chosen from the universe through probabilistic sampling with the systematic technique: the universe was divided for the sample, obtaining the number 16, and a random number was chosen between 1 and 16; it was the number 2 that was the first card revised, and subsequently, 2 points were added starting from the number 16. In this way, a random sample was obtained until the 200 patients who met the inclusion criteria were completed.

Quantitative variables

Descriptive and inferential statistics were used. The results were expressed on a scale of means and standard deviations. Categorical data such as sex are presented in proportions.

Statistical analysis

Noninferential and inferential statistics are used. For the descriptive analysis, measures of central tendency and dispersion were calculated according to the measurement scale of each of the variables. Qualitative variables are presented as absolute numbers and percentages; quantitative variables are presented as medians and standard deviations.

Inferential analysis: Two groups were formed. Group 1 patients had AKI, and Group 2 did not develop AKI. The factors between the groups were compared with the prevalence ratio (PR) with a confidence interval of 95%. The statistical package used was SPSS 20.0 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.).

Results

Study participants

Two hundred cases are analyzed.

General characteristics of the sample

The average age of the group was 80.1 ± 8.4 years. A third of the older adult population is between 75 and 84 years old. Women predominated at 64.5%. More than half of older adults live in urban areas (51.5%). A total of 59.5% of older adults had a primary level of education (Table 2).

AKI Prevalence

The prevalence of AKI was 33% (95% CI 26,233 – 39,767) (Table 3 and Figure 1). A quarter of older adults had AKI in stage 1, a third had AKI in stage 2, and 4 out of 10 older adults had AKI in stage 3. The present study estimates that 6 out of 10 older adults have high blood pressure and consumption of nephrotoxic drugs. One-third presented diabetes mellitus and dehydration, while a minority presented obstructive uropathy and liver cirrhosis.

Association analysis

A statistical association was determined between dehydration (PR 1.73; 95% CI: 1.18–2.54; $P=0.006$) and the development of AKI. Similarly, sepsis was a statistically significant risk factor (PR 2.27; 95% CI: 1.58–3.27; $P=0.0002$). There was also an association with diabetes mellitus (PR 1.58; 95% CI: 1.07–2.34; $P=0.0181$). No associations were found with obstructive uropathy, nephrotoxic drugs, arterial hypertension, or liver cirrhosis (Table 4).

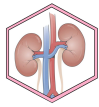
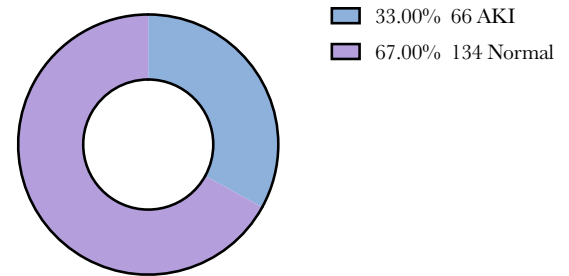


Table 2. Distribution of 200 older adults from the Vicente Corral Moscoso Hospital according to sociodemographic variables. Cuenca March 2018 to 2020.

n (200)	%	
Age*		
65 to 74 years	59	29.5
75 to 84 years	74	37.0
≥85 years	67	33.5
Sex		
Female	129	64.5
Male	71	35.5
Home		
Urban	103	51.5
Rural	97	48.5
Instruction		
None	73	36.5
Primary	119	59.5
Secondary	8	4.0

* Average: 80.1 DS ± 8.37

Figure 1. Prevalence of AKI in the study group.



Total=200

Table 3. Prevalence of AKI according to KDIGO stage in older adults at the Vicente Corral Moscoso Hospital. Cuenca March 2018 to 2020.

KDIGO	n (200)	%
Stadium 1	17	25.8
Stadium 2	twenty-one	31.8
Stadium 3	28	42.4

Table 4. Factors associated with AKI in older adults hospitalized at the Vicente Corral Moscoso Hospital.

Variables	With AKI n=66	Without AKI n=134	PR	CI (95%)	Value - P
	n (%)	n (%)			
Dehydrationon	27 (40.9%)	25 (18.7%)	1,735	1.18 – 2.54	0.0065
Uropathy Obstructive	4 (6.1%)	6 (4.5%)	1.22	0.55 – 2.69	0.4314
Sepsis	21 (31.8%)	13 (9.7%)	2,278	1.58 – 3.27	0.0002
Nephrotoxic	52 (78.8%)	91 (67.9%)	1,480	0.89 – 2.45	0.074
Diabetesmellitus	34 (51.5%)	27 (20.1%)	1,588	1.07 – 2.34	0.0181
Arterial hypertension	44 (66.7%)	80 (59.7%)	1,187	0.78 – 1.80	0.2532
Cirrhosishepatic	5 (7.6%)	6 (4.5%)	1,408	0.71 – 2.77	0.2762

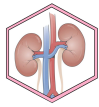
Discussion

The present study demonstrates that 33% of older adults studied presented with AKI. A similar prevalence in Taiwan was reported by Chao C. et al. in 2015, who determined a prevalence of 39% [8]. Likewise, in Mexico, Gaytán G. et al. found a prevalence of 39% in 2019; this is explained by the shared sociodemographic characteristics, sample size, and study population [9]. We can also mention greater exposure to polypharmacy, lower drug metabolism due to the

renal aging process, and concomitant chronic diseases predisposing to AKI [10].

When comparing the present study with data in Peru from Palacios et al., they observed a higher prevalence of 57.06% in patients hospitalized in clinics, and this increased to 88.14% in patients in the ICU, which could be justified by the inclusion of older adults with multiple serious pathologies included in their study [11].

In contrast, at the national and local levels, a lower prevalence of 6.63% was reported in Cuenca by Mogrovejo P. in UCI in 2014. This low prevalence may be due to the inclusion in half of the cases



of young patients with KDIGO stage 1, justifying the low prevalence [12].

Similarly, in China, Liu J. et al. 2018 reported a low prevalence of 1.61%; similar to the previous study, young adults were included, but AKI was higher in older people (1.61% vs. 1.40%; $P=0.045$) [13]. Pathophysiologically, with older age, the probability of presenting AKI increases due to senile nephrosclerosis that facilitates the development of AKI; therefore, AKI is less frequent in young patients [4].

According to the severity in the study by Silveira et al. in 2018, they reported similar results to the present study with a prevalence of advanced stage KDIGO-3 in 70.3% of older adults, KDIGO-2 in 20.6%, and KDIGO-1 in 9.1%; in addition, the more severe the AKI, the greater the probability of requiring RRT and in turn, these were risk factors for subsequent dialysis dependence [5]. In contrast, Chao C. et al. in 2015, in their study of older adults, identified that 51% presented stage 1, 25% presented stage 3, and 23% presented, less frequently, stage 2. However, they found a significant association between the advanced stage of KDIGO and the development of in-hospital complications such as infections (PR = 1.99, $P=0.08$) and hydroelectrolyte imbalance (PR = 7.1, $P < 0.01$) [8].

Therefore, although there is variation in the stage of AKI at hospital admission, the presence of more advanced stages predisposes older adults to the development of severe complications during their hospital stay, as confirmed by Okyere et al. in 2019, concluding that patients with KDIGO-3 are associated with less recovery of kidney function ($P = 0.002$). Therefore, the most appropriate conduct is to diagnose this pathology early and be alert to its presentation to initiate treatment and prevent complications [14, 15]. There are histological changes after an AKI episode despite complete renal function recovery. Bilateral renal ischemia followed by reperfusion favors the development of proteinuria, damage to the peritubular capillaries, and tubulointerstitial fibrosis. These alterations are more marked in advanced stages, from KDIGO [4].

Regarding associated factors, sepsis (PR 2.27; 95% CI: 1.58–3.27; $P = 0.0002$), dehydration (PR 1.73; 95% CI: 1.18–2.54; $P = 0.0065$), and diabetes (PR 1.58; 95% CI: 1.07–2.34; $P = 0.0181$) had a significant association. Sepsis is a factor that doubles the risk of developing AKI. In 2016, in Nicaragua, Téllez showed sepsis as the leading risk factor for AKI [16]. In China, Ge S. et al. in 2016 showed sepsis (PR 2.8, CI 2.01 - 3.9) and septic shock (PR 7.61, CI 6.07 - 9.56) as risk factors for higher mortality; this risk increases in adults over 80 years of age [10]. Funk I. et al. 2016 reported similar results, indicating sepsis as a frequent risk factor (38%) [11]. Pathophysiologically, sepsis produces the release of cytokines that amplify the inflammatory cascade, promote local thrombosis and induce tubular cell apoptosis, and increase oxidative stress and the formation of reactive oxygen species that inhibit oxidative phosphorylation and decrease oxygen delivery in the renal cell, making it susceptible to AKI [18].

Silveira et al., in 2018 in Brazil, identified dehydration as a high-impact factor for developing AKI and complications in older adults. When purchasing a study in Mexico conducted by Gaytán et al. in 2019, dehydration/hypovolemia (28.2%) was also identified as a risk

factor in older adults ($P = 0.002$), and Ge et al. in 2016 identified hypovolemia (PR 1.49, CI 1.2 – 1.85) [10, 17]. The ischemic process of prerenal and renal injury is the most frequent form that leads to the development of AKI (53%) [2, 6].

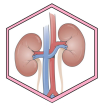
On the other hand, Pavkov M. et al. In 2018, in the United States, risk factors with a tendency to increase hospitalizations were evaluated, identifying that diabetes (40%) increased the risk of developing AKI four times ($P = 0.001$) and its complications, such as RRT [18]. Additionally, in 2016, Ge et al. identified diabetes as a significant risk factor (PR 1.94, CI 1.85 - 1.05) [10]. It should be remembered that CKD is ubiquitous in diabetic patients, favoring the establishment of AKI due to renal insults that cause acute tubular injury, decreased renal function, and chronic functional deterioration [19].

AKI was more frequent in those who consumed nephrotoxic drugs, 71.5% vs. 28.5%, compared to those who did not, with older adults being more susceptible. Despite not finding a statistical association, this could be explained by the type of population, since older adults with multiple pathologies may be affected by other factors not included in the study. In China, Ge S. et al. in 2016 stated that older adults have polypharmacy and therefore more significant exposure to nephrotoxic drugs (51.4%, $P < 0.001$); the majority consumed traditional medicine (33.8%), followed by the consumption of NSAIDs (29.2%) [10]. Locally, it can be compared with the study carried out by Rivera K. at the José Carrasco Arteaga Hospital in 2018, which showed the use of nephrotoxic drugs as the most frequent risk factor 73.6% ($P = 0.0020$) and high blood pressure 55.6% ($P = 0.0182$) with positive association [20].

AKI was seen more frequently in those with high blood pressure (62% vs. 38%), but no statistically significant association was identified. However, the relationship is established, as demonstrated by Liu J. et al. In 2018, in China, hypertension and cardiovascular diseases were reported as prevalent pathologies in older adults and were associated with a higher risk of AKI compared to young people (44.2% vs. 31.2%, $P < 0.001$; 16.1% vs. 4.6%, $P < 0.001$) [14]. Locally at the Rio Hospital in Cuenca in 2014, a frequency of 72.4% of arterial hypertension in patients with AKI was determined ($P < 0.05$) [12].

Obstructive uropathy (PR 1.22; 95% CI: 0.55–2.69; $P = 0.4314$) was a rare cause of AKI. Tejera et al. in Uruguay 2017 reported a statistical association in patients in the ICU ($P = 0.001$) [17]. This difference in epidemiology may be due to the severity of patients in critical units; for this reason, there was no such association in our study, as the patients were of lower complexity. The alteration of urinary flow requires establishing structural changes in the urinary tract due to obstruction; these alterations take time to affect the GFR and, therefore, a lower frequency of AKI [2].

Finally, liver cirrhosis was found less frequently (PR 1.40; 95% CI: 0.71–2.77; $P = 0.193$). Despite AKI being familiar to patients with liver disease, the small sample included few patients with cirrhosis, which could have influenced the statistical relationship. Other studies, such as that of Wong et al. in 2017, identified a high incidence (47%) of AKI in cirrhosis [19]. According to Correa et al., this incidence was more significant in decompensated cirrhosis in Uruguay [15].



Hepatorenal syndrome is produced by splanchnic vasodilation, decreased adequate blood volume, and renal perfusion; it activates the RAAS, favoring sodium and water retention and extra splanchnic vasoconstriction. This water retention leads to ascites and decreased renal perfusion, leading to a cycle that perpetuates AKI.

The present study demonstrated that epidemiological knowledge of AKI correlates with its detection, diagnosis, and timely treatment. The associated higher risk factors found in this study are very similar to studies worldwide, although there were many limitations in the study when collecting data retrospectively from clinical records. In addition to biases in collecting data from clinical records, associated factors that may need to be more detailed in the diagnoses may be omitted due to lack of time to take a good anamnesis in the emergency or because they are irrelevant as the primary admission diagnosis. By knowing the pathophysiological mechanism that leads to the development of AKI and the patients at higher risk of developing it, preventive measures can be carried out, such as hydration with crystalloids, avoiding the use of nephrotoxic medication, and optimizing infection control.

Conclusion

A third of the older adult population is between 75 and 84 years; 6 out of 10 are female, and most reside in urban areas with a primary education level. The prevalence of AKI in older adults hospitalized in the emergency department was over one-third. Of these, 4 out of 10 older adults presented AKI in stage 3, a quarter presented stage 1, and a third presented stage 2. It was found that 7 out of 10 older adults presented high blood pressure and consumption of nephrotoxic drugs. One-third presented diabetes mellitus and dehydration. A statistically significant relationship was found between AKI and sepsis, dehydration, and diabetes mellitus.

Abbreviations

NSAIDs: Nonsteroidal anti-inflammatory drugs.
AKI: Acute kidney injury.
RRT: renal replacement therapy.

Supplementary information

Supplementary materials have not been declared.

Acknowledgments

Does not apply.

Author contributions

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Carol Estefania Márquez Maldonado: Data curation, Formal analysis, Funding acquisition, Research, Methodology, Project management, Resources, Software, Writing – original draft.

Sonia Catalina Rivera Gonzalez: Conceptualization, Supervision, Validation, Visualization, Writing: review and editing.

All the authors have read and approved the final version of the manuscript.

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Studies and laboratory tests constituted the regular activity of the Emergency Department of the Vicente Corral Moscoso Hospital and did not constitute a cost for public service patients. None of the authors received funding for the present study. The authors paid the administrative expenses of the research.

Availability of data or materials

The data sets generated and analyzed during the current study are not publicly available due to participant confidentiality.

Statements

Ethics committee approval and consent to participate

The Bioethics Commission of the Faculty of Medical Sciences of the University of Cuenca approved the research project before carrying out the study.

All data obtained during the completion of this project were authorized for use by the teaching and research coordination of Vicente Corral Moscoso Hospital.

The handling of the data collected was always confidential, using codes instead of names.

The database and forms were managed solely by those directly responsible for the research, the project tutor, and the primary researcher and were used solely for research purposes.

Consent for publication

Not required for studies that do not publish patient photographs, tomography scans, or X-ray studies.

Conflicts of interest

The authors report having no conflicts of interest.

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