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Adverse events as key risk factors for in-hospital mortality in intensive care units

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Abstract

Introduction Intensive care units (ICUs) represent high-risk environments for adverse events (AEs). Preventing these events requires a solid understanding of their epidemiology based on standardized and validated methodologies. The aim of this study was to quantify AEs using the established Harvard Medical Practice Study (HMPS) methodology, identify associated factors, and analyze their prognostic impact on critically ill patients.

Materials and methods A multicenter observational study with a cross-sectional design was conducted in 26 hospitals across the Community of Madrid on a single, specified day in May 2019. Following the HMPS methodology and using its standardized instruments, clinical records were reviewed in two phases: (1) an AE screening phase and (2) a confirmation and characterization phase for cases with positive screenings. A multivariate logistic regression model was developed to identify variables associated with the presence of AEs, and the association between AEs and in-hospital mortality was assessed using an explanatory model adjusted for potential confounders.

Results A total of 458 patients were included, of whom 125 (27.3%; 95% CI: 23.4 to 31.6) had ≥ 1 AE. The following antecedents were associated with the presence of AEs: pressure ulcer (PU), hypoalbuminemia, mechanical ventilation, central venous catheter, surgical intervention and sensory deficit. Among the AEs found, 44.6% were health care-associated infections (HAIs). In-hospital mortality among patients with AEs was twice that observed in patients without AEs (OR: 2.15; 95% CI: 1.10–4.25).

Conclusions The presence of AEs was associated with a two-fold higher risk of in-hospital mortality. Among the identified AEs, HAIs were the most frequent and had the highest mortality. Designing and implementing bundles of measures adapted to the individual risk of presenting AEs in the ICU emerges as the next step in the development of strategies to reduce the prevalence of AEs.

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Introduction

Adverse events (AEs) related to health care are among the leading challenges to patient safety, as they involve unintended harm resulting from the care provided. AEs refer to injuries attributable to medical management and may occur with or without error; in contrast, medical errors represent failures in the process of care that may or may not result in patient harm [1]. Several studies have estimated that the prevalence of AEs in hospitalized patients ranges from 3.2% to 23.6% [2, 3], with these figures varying according to patient comorbidities and the care setting. AEs rarely arise from a single cause; instead, they result from a multifactorial interplay between latent system failures, patient factors and individual errors, shaped by organizational, environmental, and human factors.

In this context, intensive care units (ICUs) represent an environment of particular vulnerability to AEs. The complexity of critically ill patients—combined with the use of invasive procedures, polypharmacy, and advanced technologies—creates conditions prone to errors in care [4]. Consequently, the ICU is the hospital setting with the highest prevalence of AEs, estimated to range between 15% and 51% [5–7], with medication-related AEs occurring twice as frequently as in other units [8, 9]. To factors such as organ failure, the need for higher levels of care, advanced age, the number of invasive procedures performed (including intubation, catheterization, and drainage), admission to a surgical service, elevated APACHE scores, and ICU readmission [8–10]. Moreover, experiencing AEs in the ICU has negative consequences for both patients and the health system, including increased mortality, prolonged hospital stays, and higher economic costs [11–13].

Further epidemiological characterization of adverse events in ICUs is essential to identify priority areas and to develop proactive strategies that anticipate errors before they occur. To achieve this, the use of AE measurement tools with a high degree of validity and reliability is crucial. Among the different strategies employed in patient safety, the methodology providing the strongest level of evidence is that developed by Brennan et al. in the Harvard Medical Practice Study (HMPS) [14], which is based on a two-phase retrospective medical record review: an initial screening phase with high sensitivity (84%) and negative predictive value (92%) for AE detection, followed by a second confirmation phase with acceptable inter-rater reliability ($\kappa = 0.61$) [15]. This methodology has been used in large-scale studies measuring AEs in various regions, such as the United Kingdom, Australia, Spain, Ireland and Latin America [16–19]. The results have been used by the WHO to estimate the burden associated with AEs and for the preparation of their current recommendations [20].

However, most studies on AEs in the ICU do not use the HMPS methodology and are based on questionnaires developed from an expert consensus (the Delphi method) [21, 22] or use the Global Trigger Tool [12], thus yielding greatly variable results, making reliability and comparability difficult. In this context, the aim of the present study was to analyze the frequency and distribution of AEs in all ICUs in the same administrative region using the standardized and validated HMPS methodology [15]. The specific objectives of the study are 1) to identify the variables associated with the appearance of AEs in critically ill patients, 2) to determine the main types of AEs that affect patients admitted to the ICU, and 3) to analyze the clinical impact of AEs and evaluate their association with in-hospital mortality.

Materials and methods

Study design

Multicenter cross-sectional observational study. All patients admitted to ICUs of various care profiles in 26 public hospitals in the Community of Madrid, Spain, were included (16 medical ICUs, 6 surgical critical care units, 4 neonatal ICUs, and 6 pediatric or mixed units). The cross-sectional assessment was conducted on a single, specified day in May 2019.

Phases of the study

The study was developed within the framework of the Safety Study in Hospitals of the Community of Madrid (ESHMAD) [23], following the HMPS methodology, which involved two phases of medical record review:

1. **Screening phase:** An adaptation of the *Screening Review Form* was used [24] to detect possible adverse events (AEs) and collect basic epidemiological variables. Records that met at least one screening criterion were considered positive screenings, indicating a potential AE that requires further review. Records that did not meet any criteria were considered negative screenings and were excluded from the second phase.
2. **Confirmation and classification phase:** Patients with positive screening results were individually assessed using the *Modular Review Form 2* (MRF2) [24] at hospital discharge (or at 30 days if the patient was still hospitalized) to confirm, classify and characterize the AEs.

Prior to the execution of the ESHMAD, all participating hospitals received training in patient safety and in the application of the assessment tools to ensure high-quality data collection. This training consisted of several sessions, beginning with a comprehensive theoretical overview of patient safety principles and detailed instructions on the

use of the assessment tools followed by practical exercises to standardize reviewer evaluations. All the sessions were conducted by experienced patient safety professionals. Full details of the study design, training procedures, and data collection process are described in Valencia-Martín et al. [25]

Study variables

The main variables were the presence AEs and in-hospital mortality. AEs were defined according to the World Health Organization framework as any incident occurring during medical care that results in harm to the patient, including injury, suffering, disability, or death. Accordingly, AEs were not limited to events arising from negligence or error [18, 26]. To assess the likelihood that the event was attributable to healthcare, the MRF2 Likert-type scale was used, which assigns scores from 1 to 6, with 1 indicating “minimal evidence that medical management caused the harm” and 6 indicating “definite evidence that medical management was the cause of the harm”. According to the HMPS methodology and the previous validation of the MRF2, those with a score ≥ 4 were considered to have a confirmed AE [15, 24, 27].

Variables related to AEs, such as type (following the classification provided by the MRF2), were collected [27]. Categories were mutually exclusive, and severity was assessed following the definitions of the WHO Taxonomy [1], the *Point Prevalence Survey of the European Center for Disease Control* [28], and previous studies based on the HMPS [15, 29]. Severity was classified as mild, moderate, or severe based on their impact on patient care and outcomes. Mild AEs were those that caused minimal or no additional intervention or monitoring. Moderate AEs required additional treatment, tests, observation, or temporary prolongation of hospitalization but did not result in permanent harm. Severe AEs involved significant consequences, such as permanent harm, life-threatening events, major surgical intervention, or the need for life support. The time of onset of each AE during hospitalization was documented, as well as its impact on health care or additional days of hospitalization. The impact on healthcare was evaluated individually for each AE using the MRF2 questionnaire. For each event, reviewers assessed whether it affected healthcare and, if so, classified the impact as: healthcare not affected; required observation or monitoring; required an additional test; required medical treatment or rehabilitation; required an additional surgical intervention; or required life support. This approach allowed multiple AEs and their respective impacts to be recorded independently for the same patient.

In addition, the following demographic and clinical variables of the patients were recorded: sex, age, total hospital stay, surgical history, type of ICU and level of

complexity of the hospital. A history of relevant comorbidities (cardiovascular diseases, neoplasms, COPD, immunodeficiencies, liver cirrhosis, hypoalbuminemia, pressure ulcers [PUs], mobility limitations, sensory deficits, renal failure, neutropenia, obesity and active smoking [etc.]) was included [29, 30], as well as factors related to invasive procedures in clinical practice (the presence of peripheral or central venous catheters, mechanical ventilation and bladder catheterization at the time of screening).

The complete definitions of the variables, criteria and categories can be found in the Supplementary Material (Tables S1 and S2).

Statistical analysis

Descriptive analyses were performed according to the presence or absence of AEs. For quantitative variables, the mean and standard deviation were reported when the data were approximately normally distributed, while the median and interquartile range were used for variables with non-normal distributions. Categorical variables were summarized using proportions. AE characteristics are described according to the outcome of the patient (discharge vs. death). For bivariate analysis, the Mann-Whitney U test and the chi-square test were used. Values of $p < 0.05$ were considered significant.

Variables associated with the presence of AEs in the ICU were identified using a multivariate unconditional logistic regression model, with AEs as the dependent variable. All candidate variables were initially considered for inclusion. A stepwise selection procedure was then applied, in which variables were sequentially entered or removed based on a significance threshold of $p \leq 0.05$. Variables not meeting this criterion were excluded, resulting in a parsimonious final model that retained only those factors significantly associated with AEs.

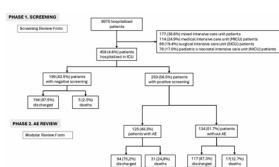
Finally, the association between the presence of AEs and in-hospital mortality was evaluated using an explanatory logistic regression model, adjusting for confounding variables (those that modified the crude association by more than 10%). The results of the analysis of confounding factors can be found in the Supplementary Material (Table S3).

Results

Sample

A review of the hospitalization episodes of 458 patients revealed 177 patients hospitalized in mixed ICUs (38.6%), 114 patients hospitalized in medical ICUs (24.9%), 89 patients hospitalized in surgical ICUs (19.4%) and 78 patients hospitalized in the neonatal or pediatric ICU (17.0%). Among these patients, 259 (56.5%) had ≥ 1 positive screening, and 125 (48.3%) ultimately had ≥ 1 AE during hospitalization (Fig 1), with a total of 166 AEs,

Fig. 1 Flow chart diagram. AEs: adverse events. MRF2: modular review form 2. ICU: intensive care unit



corresponding to a prevalence of 27.3% of patients with ≥ 1 AE in the total sample (95% confidence interval [95% CI]: 23.4 to 31.6).

Table 1 shows the main characteristics of the sample. The mean age was 52.1 (SD 27.1) years, and 62.7% of the patients were men. Most admissions were urgent (72.3%) and in high-complexity hospitals (72.9%). Overall, 51.5% of patients underwent surgery before the onset of AEs; and 83.0% had one or more clinical instrumentation factors. During hospitalization, 53 patients (11.6%) died.

The mean age of patients who experienced ≥ 1 AE was higher than that of patients who did not experience an AE (59.7 years vs. 49.3; $p < 0.001$). In addition, there was a higher incidence of AEs in patients with a previous surgical intervention (34.3% vs. 19.8%; $p < 0.001$), in patients with a greater number of comorbidities (36.9% in patients with ≥ 3 comorbidities vs. 8.5% in patients without comorbidities; $p < 0.001$) and in patients with a greater number of clinical instrumentation factors (34.8% in those with $\geq$ three vs. 8.5% in those with one; $p < 0.001$). Among the patients who died, 58.5% had ≥ 1 AE, whereas this figure was 23.2% for patients who did not die ($p < 0.001$).

Multivariate model of AEs

Table 2 shows the results of the association between clinical and therapeutic factors and the risk of developing

Table 1 Demographic characteristics of the total sample and according to the presence of AEs

	Total N = 458 [†]	Patients with AEs N = 125	Patients without AEs N = 333	p
Age (years), mean (SD)	52.1 (27.1)	59.7 (24.1)	49.3 (27.7)	$p < 0.001$
Sex				
Women, n (% by row)	171 (37.3) [†]	44 (25.7)	127 (74.3)	$p = 0.563$
Men, n (% by row)	287 (62.7)	81 (28.2)	206 (72.7)	
Type of admission				
Scheduled, n (% by row)	124 (27.1) [†]	36 (29.0)	88 (71.0)	$p = 0.259$
Urgent, n (% by row)	331 (72.3)	87 (26.3)	244 (73.7)	
Surgical intervention				
Yes, n (% by row)	236 (51.5) [†]	81 (34.3)	155 (65.7)	$p < 0.001$
No, n (% by row)	222 (48.5)	44 (19.8)	178 (80.2)	
Type of ICU				
Mixed ICU, n (% by row)	177 (38.6) [†]	63 (35.6)	114 (64.4)	$p < 0.001$
Medical ICU, n (% by row)	114 (24.9)	19 (16.7)	95 (83.3)	
Surgical ICU, n (% by row)	89 (19.4)	31 (34.8)	58 (65.2)	
Pediatric ICU, n (% by row)	78 (17.0)	12 (15.4)	66 (84.6)	
Type of hospital				
Low complexity, n (% by row)	24 (5.2) [†]	8 (33.3)	16 (66.7)	$p = 0.345$
Medium complexity, n (% by row)	100 (21.8)	32 (32.0)	68 (68.0)	
High complexity, n (% by row)	334 (72.9)	85 (25.5)	249 (74.5)	
Comorbidities				
Absence, n (% by row)	71 (15.5) [†]	6 (8.5)	65 (91.5)	$p < 0.001$
1, n (% by row)	75 (16.4)	15 (20.0)	60 (80.0)	
2, n (% by row)	79 (17.3)	18 (22.8)	61 (77.2)	
≥ 3 , n (% by row)	233 (50.8)	86 (36.9)	147 (63.1)	
Clinical instrumentation factors				
Absence, n (% by row)	26 (17.0) [†]	8 (30.8)	18 (69.2)	$p < 0.001$
1, n (% by row)	71 (15.6)	6 (8.5)	65 (91.5)	
2, n (% by row)	108 (17.2)	23 (21.3)	85 (78.7)	
≥ 3 , n (% by row)	253 (50.2)	88 (34.8)	165 (65.2)	
Discharge				
Yes, n (% by row)	53 (11.6) [†]	31 (58.5)	22 (41.5)	$p < 0.001$
No, n (% by row)	458 (88.4)	94 (23.2)	311 (76.8)	

[†]Percentages by column

ICU: intensive care unit; AE: adverse event; p: p value

Table 2 Associations between clinical and therapeutic factors and the risk of AEs

	Total (N=458)	Patients with AEs (N=125)	OR	95% CI	p Value
Age					
per year (mean)	52.1	60.7	1.01	1.00 to 1.02	p=0.012
Surgical intervention					
No	222 (48.5)	44 (19.9)	1.00	NA	
Yes	236 (51.5)	81 (34.3)	1.76	1.07 to 2.91	p=0.027
Risk factors					
Pressure ulcer	48 (10.5)	28 (58.3)	2.73	1.38 to 5.43	p=0.004
Hypoalbuminemia	119 (26.0)	47 (39.5)	2.30	1.40 to 3.30	p=0.012
Mechanical ventilation	179 (39.1)	70 (39.1)	2.02	1.23 to 3.25	p=0.005
Central venous catheter	309 (67.5)	92 (29.8)	1.90	1.03 to 3.72	p=0.040
Sensory deficit	80 (17.5)	32 (40.0)	1.85	1.04 to 3.31	p=0.036
Peripheral venous catheter	315 (68.8)	65 (20.6)	0.53	0.31 to 0.91	p=0.022

AE: adverse event; OR: odds ratio, p: p value

≥1 AE. The greatest association was observed with a history of PUs (odds ratio (OR) [95% CI]: 2.73 [1.38 to 4.43], versus absence), followed by a history of hypoalbuminemia (OR [95% CI]: 2.30 [1.40 to 3.30], versus absence), mechanical ventilation (2.02 [1.23 to 3.25], versus absence) and surgical intervention (1.76 [1.07 to 2.91], versus absence). Unlike the other factors, the presence of a peripheral venous catheter was associated with a lower risk of AEs (0.53 [0.31 to 0.91]).

Types and impacts of AEs

Table 3 shows the frequency and distribution of AEs among all patients and among those who died. A total of 125 patients had ≥1 AE, resulting in a total of 166 AEs. Of the total number of AEs, 44.6% (74) were health care-associated infections (HAIs), 28.3% (47) were procedure-related AEs, 12.7% (21) were care-related AEs related to care, and 9.6% (16) were medication-related AEs.

Among HAIs, the most frequent type was pneumonia (31.1% of HAIs), followed by surgical site infection (20.3%). Among the total number of patients who died (53), 15.1% had pneumonia, and 5.7% had surgical site infections. Among the procedure-related AEs, hemorrhages or hematomas accounted for 34% of the total and 12.5% of the total number of patients who died. Among the care-related AEs, the most frequent AE was PUs (85.7% of the total), whereas heart failure and other cardiovascular diseases (acute myocardial infarction (AMI), pulmonary thromboembolism (PTE), cardiovascular accident (CVA) or deep vein thrombosis (DVT)) accounted for 18.7% of the medication-related AEs (Table 3).

76.5% of AEs were classified as moderate or severe, and 96.4% required some type of additional care, including observation or monitoring, additional tests or procedures, medical treatment, rehabilitation, or life support. Among patients who died, 36% experienced at least one

severe AE, and in 63.2% of cases, the AE resulted in an increased hospital stay of five to nine days (Table 3).

Association between the presence of AEs and patient death

Patients with ≥1 AE had a fourfold greater risk of in-hospital mortality (OR: 4.27; 95% CI: 2.35 to 7.77). Adjustment for confounding factors (those that modified the association more than 10%) included the number of intrinsic risk factors, coma status, and a history of PUs, urinary catheterization, peripheral vascular catheterization, central vascular catheterization and mechanical ventilation, which reduced the strength of the association, although the risk of in-hospital mortality among patients with ≥1 AE remained double that for patients without AEs (OR: 2.15; 95% CI: 1.10 to 4.25) (Table 4, Fig 2).

Discussion

This study aimed to assess the prevalence of AEs in critically ill patients and to evaluate their association with in-hospital mortality. Our findings show that AEs are highly frequent in the ICU setting and are strongly associated with patient outcomes. Among the 458 patients admitted to 50 ICUs with different care profiles, nearly three out of ten experienced at least one AE. In-hospital mortality was 11.6%, higher than that reported in conventional hospital wards [31] and the presence of ≥1 AE was associated with a twofold increase in the risk of death after adjusting for confounding factors (OR [95% CI] 2.15 [1.10–4.25]). Using the HMPS methodology, three out of five patients who died had ≥1 AE, a proportion higher than that reported in ICU populations by Nilsson et al. [32] or by Zegers et al [33], who reported prevalence rates of 19.5% and 10.7%, respectively. The higher prevalence of AEs observed in our study likely reflects a combination of methodological and sample-related factors.

Table 3 Frequency and distribution of AEs

	Total AEs (N=166)	Total patients (458)	Patients who died (53)	p
Type of AE				
HAI	74 (44.6)	59 (12.9)	20 (37.7)	
<i>Pneumonia</i>	23 (31.1)	23 (5.0)	8 (15.1)	
<i>Surgical site infection</i>	15 (20.3)	15 (3.3)	3 (5.7)	
<i>Device-associated bacteremia</i>	10 (13.5)	10 (2.2)	2 (3.8)	p=0.204
<i>Sepsis or septic shock</i>	9 (12.2)	9 (2.0)	1 (1.9)	
<i>Urinary tract infection</i>	2 (0.3)	2 (0.4)	1 (1.9)	
<i>Other</i>	13 (17.6)	12 (2.6)	7 (13.2)	
Procedure-related AE	47 (28.3)	34 (7.4)	7 (13.2)	
<i>Bleeding or hematoma</i>	16 (34.0)	13 (2.8)	2 (3.8)	
<i>Injury to an organ</i>	7 (14.9)	7 (1.5)	1 (1.9)	
<i>Suture dehiscence</i>	5 (10.6)	5 (1.1)	2 (3.8)	p=0.733
<i>Pneumothorax</i>	5 (10.6)	5 (1.1)	1 (1.9)	
<i>Others</i>	14 (29.8)	13 (2.8)	3 (5.7)	
Care-related AE	21 (12.7)	14 (3.1)	1 (1.9)	
<i>Pressure ulcers</i>	18 (85.7)	18 (3.9)	2 (3.8)	p=0.039
<i>Other</i>	3 (14.3)	3 (0.7)	1 (1.9)	
Medication-related AE	16 (9.6)	12 (2.6)	2 (3.8)	
<i>AMI, PTE, CVA or DVT</i>	3 (18.7)	2 (0.4)	2 (3.8)	
<i>Heart failure</i>	3 (18.7)	2 (0.4)	1 (1.9)	
<i>Bleeding, epistaxis, hematomas</i>	2 (12.5)	2 (0.4)	1 (1.9)	p=0.448
<i>Neurological disorders</i>	2 (12.5)	1 (0.2)	1 (1.9)	
<i>Other</i>	6 (37.6)	5 (1.1)	3 (5.7)	
Other AEs	8 (4.9)	6 (1.3)	2 (3.8)	
Severity				
<i>Mild</i>	39 (23.5)	35 (7.6)	9 (17.0)	
<i>Moderate</i>	55 (33.1)	47 (10.3)	10 (18.9)	p=0.647
<i>Severe</i>	69 (41.6)	58 (12.7)	19 (35.8)	
Additional health care due to AE				
<i>Health care was not affected</i>	6 (3.6)	6 (1.3)	2 (3.8)	
<i>Required observation/monitoring</i>	1 (0.6)	1 (0.2)	1 (1.9)	
<i>Required an additional test</i>	5 (3.0)	5 (1.1)	2 (3.8)	p=0.193
<i>Medical treatment or rehabilitation</i>	77 (46.4)	63 (13.8)	17 (32.1)	
<i>Additional surgical intervention</i>	22 (13.3)	21 (4.6)	2 (3.8)	
<i>Life support</i>	55 (33.1)	48 (10.5)	15 (28.3)	
Days of additional hospitalization due to AE				
<i>Stay did not increase</i>	5 (3.0)	5 (1.1)	18 (34.0)	p=0.562
<i>1–4 days</i>	45 (27.1)	40 (8.7)	1 (1.9)	
<i>5–9 days</i>	105 (63.2)	82 (17.9)	6 (11.3)	
<i>≥10 days</i>	11 (6.6)	11 (2.4)	14 (26.4)	

In total, 125 patients presented ≥ 1 AE, with a total of 166 AEs. Patients who presented >1 AE were included in both categories; thus, the total number of patients with each type of AE may not coincide with the sum of the different types of AEs in that category

Methodologically, the use of a highly sensitive detection tool, rigorous training and calibration of reviewers, and the inclusion of all identified AEs—regardless of severity—enhanced detection rates. In terms of the sample, our study included a large and diverse group of hospitals with varying levels of care and patient case-mix, increasing the likelihood of identifying AEs compared with studies with smaller or more homogeneous populations. Although this may limit direct comparability with studies using less sensitive tools or narrower samples, these

factors together provide a comprehensive and systematic assessment of AEs in the ICU setting.

Additionally, 4 out of 10 AEs detected were classified as severe, increasing to 5 out of 10 among patients who died. This frequency is higher than that reported in previous studies, which estimated the prevalence of severe AEs between 12.8% and 22.8% [33, 34], and aligns with other studies indicating that the rate of severe AEs is up to seven times greater in patients who die during hospitalization [34]. Given that previous evidence considers

Table 4 Associations between in-hospital mortality and adverse events in the ICU

Crude association between the presence of ≥ 1 AE and in-hospital mortality	N	OR	95% IC	p value
Absence	333	1.00	NA	
Presence	125	4.27	2.35 to 7.77	$p < 0.001$
Adjusted association between the presence of ≥ 1 AE and in-hospital mortality*	N	OR	95% IC	p value
Absence	333	1.00	NA	
Presence	125	2.15	1.10 to 4.25	$p = 0.026$

* Model adjusted for the number of intrinsic factors, coma, PUs, urinary catheter, peripheral vascular catheter, central vascular catheter and mechanical ventilation.

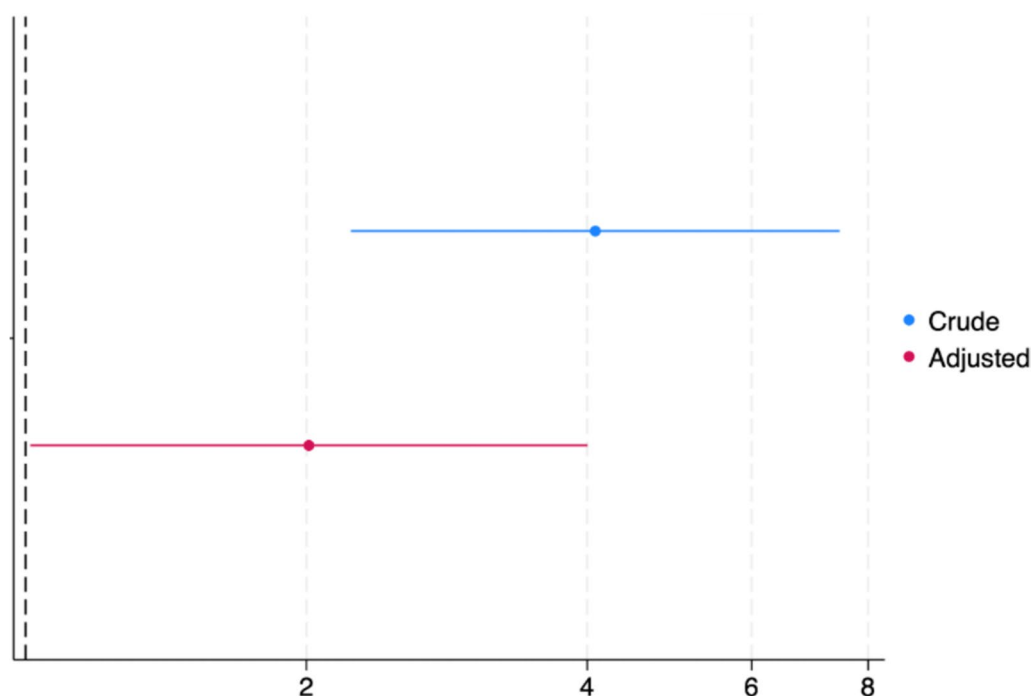
50% of AEs preventable [35, 36], these findings highlight the potential impact of AE prevention strategies on improving patient safety in the ICU, reinforcing its role as a strategic element in reducing mortality.

The most frequent type of AE detected were HAIs, followed by procedure-related AEs, care-related AEs, and medication-related AEs. This differs from the findings of longitudinal studies, which revealed that AEs related to medication were the most frequent AEs [4, 22]. The cross-sectional design may have led to an overestimation of HAIs and procedure related AEs because since both are associated with a prolonged hospital stay. Similarly, the impact of HAIs highlights the importance of

their prevention [11, 16]. Among the patients who died, approximately 40% had HAIs, and 1 in 7 had procedure related AEs.

The high prevalence and impact of HAIs in ICUs can be explained by the clinical complexity of these patients, who often require the use of invasive devices that predispose them to complications such as ventilator-associated pneumonia (VAP) or catheter-associated bloodstream infections [8, 12]. In addition, in our sample, HAIs were the AEs that were most strongly associated with in-hospital mortality. Among them, pneumonia stood out for its high mortality, a finding that is consistent with the results of a study by Johnstone et al., who reported that VAP was associated with an increased risk of in-hospital mortality of between 30% and 80%, depending on the definition used [37]. Similarly, another study revealed that the risk of death doubled in patients with nosocomial pneumonia in the ICU (OR: 2.1 to 2.7), adjusting for severity and comorbidities [38].

The magnitude of HAIs in the ICU is known and has motivated various initiatives to mitigate their impact. In the Spanish context, the National Health System, in collaboration with the Spanish Society of Intensive Medicine and the Spanish Society of Intensive Nursing, has promoted the development of *Project Zero*, which is part of the country's patient safety strategy [1]. This project includes *Bacteremia Zero*, *Pneumonia Zero*, *Resistance Zero* and *UTI Zero*. Its implementation, which is based on numerous preventive measures, has reduced the

**Fig. 2** Crude and adjusted ORs for death during hospitalization and the presence of ≥ 1 AE

frequency of HAIs by up to 50%, has decreased mortality and has improved safety culture [39].

Since AEs arise from a multifactorial interaction between latent system failures—such as organisational culture, communication processes, workflow design, or lack of resources—and patient-related factors—including comorbidity, severity of illness, and exposure to high-risk interventions—along with active human errors, it is essential to understand how these patient-related factors interact with the care system to shape vulnerability to harm [40]. Preventive strategies should therefore combine system-level interventions with targeted measures adapted to the epidemiological risk profile of patients, alongside the implementation of evidence-based safety bundles that integrate multiple coordinated actions. Thus, our multivariate model identified older patients undergoing a previous surgical intervention and with a history of hypoalbuminemia, PUs, sensory deficit, mechanical ventilation and central venous catheter as risk profiles. These findings offer a comprehensive perspective of the epidemiology of AEs in the ICU and coincide with the results of previous studies. In a 2020 study in Canada, Sauro et al. reported an association between the presence of AEs and surgical intervention, mechanical ventilation, a high APACHE score and the presence of two or more comorbidities [8]. In other studies, multiorgan failure, previous comorbidities, longer ICU stays and increased NEMS scores were identified as factors associated with the presence of AEs [9, 10, 13]. Among clinical instrumentation factors, one study revealed that 10% of AEs were associated with the presence of vascular ports and catheters (including accidental removal) [7].

In this regard, our results provide a detailed view of the epidemiology of AEs by using a model with 23 epidemiological variables, allowing for more precise identification of at-risk patients. These findings support the development of targeted bundles of interventions tailored to the risk profiles of patients, as a strategy to reduce the prevalence of AEs in ICU. The evidence shows that the application of sets of structured measures is effective, as indicated by improvements in adherence to the guidelines for the prevention of surgical wound infections or with the implementation of protocols for the safe use of catheters and probes [41]. Similarly, organizational and cultural factors—team coordination, effective communication and continuous training—increase the effectiveness of these interventions [9]. A recent study from 2023 revealed that a higher proportion of certified nurses with specific training in critical care at the time of admission was associated with a lower probability of AEs [42]. It is also important to emphasize the need for a proactive approach to address the underlying causes of errors that can lead to AEs [43]. Preventive measures must therefore be tailored to the specific context in which they are

applied, taking into account patient characteristics, types of procedures performed and centre-specific factors such as workload, staff turnover, and safety culture. This approach enhances the relevance and feasibility of preventive measures and increases the likelihood of achieving meaningful reductions in AE incidence.

Our study has certain limitations. First, its cross-sectional design does not allow the establishment of causal relationships; thus, the findings should be interpreted as an association. However, this design offers significant advantages, as it not only allows for more efficient case review but also demonstrates high sensitivity for detecting serious AEs or those that prolong hospital stay—precisely the outcomes we aimed to analyze in detail to inform the implementation of prevention strategies [16]. Another possible limitation of our study lies in the fact that we analyzed all the participating ICUs together, despite the fact that they have different characteristics. However, this also provides relevant advantages, since it provides results that are more generalizable and applicable to a larger population of critically ill patients. Besides, although all hospitals were from a single administrative region, which may limit generalizability to other healthcare systems or regions with different organizational structures, the inclusion of 50 ICUs from 26 hospitals increases the representativeness of the sample and enhances both the internal and external validity of the findings. Furthermore, the study relied on retrospective review of medical records, which may be subject to missing or incomplete information. In particular, some AEs may not have been documented, potentially leading to underestimation of their true incidence. Although electronic health records provided structured and consistently organized data, supported by automated laboratory, diagnostic, and discharge reports, and represent the most feasible and accessible method, we acknowledge that this approach has inherent limitations that may affect the completeness and accuracy of the information collected. Finally, while the two-stage HMPS methodology may potentially undercount AEs by not reviewing negative screenings from the first stage, we maintained this approach to ensure comparability with other studies using this well-established method. Moreover, the Screening Review Form (SRF), with its high sensitivity and negative predictive value, minimizes the impact of this limitation [44]. One of the greatest strengths of our study is the use of the standardized and validated HMPS methodology, complemented with WHO definitions for AEs and ECDC for HAIs, thus providing an additional degree of quality in the results. Finally, the consideration of 23 risk factors in the analyses ensured a comprehensive approach and may facilitate the design of preventive *bundles* adapted to the individual risk of each patient as a strategy to reduce the prevalence of AEs in the ICU.

Future research with longitudinal designs should evaluate the effectiveness of interventions based on this approach.

Conclusion

ICUs represent a critical environment in patient safety because of the high prevalence of AEs, which are associated with a significant increase in in-hospital mortality, even doubling it.

Among the identified AEs, HAIs were the most frequent and those associated with higher mortality; procedure-related AEs were the second most frequent. Almost all of the AEs required some type of assistance or additional intervention, providing evidence of their high clinical and care impacts.

The risk profile identified corresponds to older patients and patients with a history of surgery, hypoalbuminemia, PUs, mechanical ventilation, sensory deficit or a central venous catheter. These findings support the need to design and implement preventive measures adapted to patients according to the presence of these risk factors to optimize the prevention of AEs and reduce their impact on in-hospital mortality and on the care burden.

Future research should evaluate the effectiveness of this approach in longitudinal studies, integrating strategies that increase the culture of safety and training of professionals to maximize patient safety in the ICU.

Supplementary Information

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Additional file 1

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Author contribution

MRR contributed to the conceptualization and design of the study, the analysis and interpretation of data, manuscript writing, and data visualization. DSJ participated in the conceptualization, data collection, manuscript writing, critical review, and project supervision. CDA played a key role in the critical review, project management, and final approval of the manuscript. JVG collaborated in data collection, manuscript writing, critical review, supervision, and project management. PMN and BPA were responsible for analysis and interpretation of data, critical review, and data visualization. Lastly, JMA was involved in the conceptualization, critical review, supervision, project management, and final approval of the manuscript.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Declarations

Ethical approval and consent to participate

This study was approved by the Ethics Committee of Ramón and Cajal University Hospital (reference 057/19).

Consent for publication

Informed consent was not needed, since the study met the exemption criteria established in Regulation (EU) 2016/679 (General Data Protection Regulation, RGPD), including the absence of direct intervention, the complete anonymization of the data and the relevance of the research to public health.

Competing interest

The authors declare no competing interests.

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References

1. World Health Organization(WHO). International Classification for Patient Safety Statement of Purpose. [cited 1 de marzo 2025]. Available in: http://www.who.int/patientsafety/taxonomy/ICPS_Statement_of_Purpose.pdf.
2. Bates DW, Levine DM, Salmasian H, Syrowatka A, Shahian DM, Lipsitz S, et al. The safety of inpatient health care. *N Engl J Med*. 2023;388:142–53.
3. De Vries EN, Ramrattan MA, Smorenburg SM, Gouma DJ, Boermeester MA. The incidence and nature of in-hospital adverse events: a systematic review. *Qual Saf Health Care*. 2008;17:216–23.
4. Merino P. Epidemiology of adverse events in intensive medicine units. *Medicina Intensiva (English Edition)*. 2025;49:32–9.
5. Ahmed AH, Giri J, Kashyap R, Singh B, Dong Y, Kilickaya O, et al. Outcome of adverse events and medical errors in the intensive care unit: a systematic review and meta-analysis. *Am J Med Qual*. 2015;30:23–30.
6. Garrouste-Orgeas M, Flaatten H, Moreno R. Understanding medical errors and adverse events in ICU patients. *Intensive Care Med*. 2016;42:107–9.
7. Merino P, Alvarez J, Martin MC, Alonso A, Gutierrez I, SYREC Study Investigators. Adverse events in Spanish intensive care units: the SYREC study. *Int J Qual Health Care*. 2012;24:105–13.
8. Sauro KM, Soo A, Quan H, Stelfox HT. Adverse events among hospitalized critically ill patients: a retrospective cohort study. *Med Care*. 2020;58:38.
9. Valentin A, Capuzzo M, Guidet B, Moreno RP, Dolanski L, Bauer P, et al. Patient safety in intensive care: results from the multinational Sentinel Events Evaluation (SEE) study. *Intensive Care Med*. 2006;32:1591–8.
10. Valentin A, Schiffinger M, Steyrer J, Huber C, Strunk G. Safety climate reduces medication and dislodgement errors in routine intensive care practice. *Intensive Care Med*. 2013;39:391–8.

11. Forster AJ, Kyeremanteng K, Hooper J, Shojania KG, Van Walraven C. The impact of adverse events in the intensive care unit on hospital mortality and length of stay. *BMC Health Serv Res*. 2008;8:259.
12. Aikawa G, Ouchi A, Sakuramoto H, Ono C, Hatozaki C, Okamoto M, et al. Impact of adverse events on patient outcomes in a Japanese intensive care unit: a retrospective observational study. *Nurs Open*. 2021;8:3271–80.
13. Cantor N, Durr KM, McNeill K, Thompson LH, Fernando SM, Tanuseputro P, et al. Increased mortality and costs associated with adverse events in intensive care unit patients. *J Intensive Care Med*. 2022;37:1075–81.
14. Unbeck M, Schildmeijer K, Henriksson P, Jürgensen U, Muren O, Nilsson L, et al. Is detection of adverse events affected by record review methodology? An evaluation of the “Harvard Medical Practice Study” method and the “Global Trigger Tool.” *Patient Saf Surg*. 2013;7:10.
15. Brennan TA, Hebert Lie AR, Localio AR, Newhouse JP. Incidence of adverse events and negligence in hospitalized patients. *N Engl J Med*. 1991. <https://doi.org/10.1056/nejm199102073240604>.
16. Aranaz Andrés JM, Limón Ramírez R, Aibar Remón C, Gea-Velázquez De Castro MT, Bolúmar F, Hernández-Aguado I, et al. Comparison of two methods to estimate adverse events in the IBEAS study (Ibero-American study of adverse events): cross-sectional versus retrospective cohort design. *BMJ Open*. 2017;7:e016546.
17. Vincent C, Neale G, Woloshynowych M. Adverse events in British hospitals: preliminary retrospective record review. *BMJ*. 2001;322:517–9.
18. Wilson RM, Runciman WB, Gibberd RW, Harrison BT, Newby L, Hamilton JD. The quality in Australian health care study. *Med J Aust*. 1995;163:458–71.
19. Connolly W, Raftar N, Conroy RM, Stuart C, Hickey A, Williams DJ. The Irish National Adverse Event Study-2 (INAES-2): longitudinal trends in adverse event rates in the Irish healthcare system. *BMJ Qual Saf*. 2021;30:547–58.
20. Global patient safety action plan 2021–2030: towards eliminating avoidable harm in health care. Geneva: World Health Organization; 2021. Licence: CC BY-NC-SA 3.0 IGO. [citado 4 de enero de 2024]. Disponible en: <https://www.who.int/teams/integrated-health-services/patient-safety/policy/global-patient-safety-action-plan>.
21. Garrouste-Orgeas M, Timsit JF, Vesin A, Schwebel C, Arnodo P, Lefrant JY, et al. Selected medical errors in the intensive care unit: results of the IATROREF study: parts I and II. *Am J Respir Crit Care Med*. 2010;181:134–42.
22. Danielis M, Bellomo F, Farneti F, Palese A. Critical incidents rates and types in Italian Intensive Care Units: a five-year analysis. *Intensive Crit Care Nurs*. 2021;62:102950.
23. Valencia-Martín JL, Vicente-Guijarro J, San Jose-Saras D, Moreno-Nunez P, Pardo-Hernández A, Aranaz-Andrés JM. Prevalence, characteristics, and impact of adverse events in 34 Madrid hospitals. The ESHMAD study. *Eur J Clin Invest*. 2022;52:e13851.
24. Woloshynowych M. Case record review of adverse events: a new approach. *Qual Saf Health Care*. 2003;12:411–5.
25. Valencia-Martín JL, Martín-Delgado J, Pardo-Hernández A, Vicente-Guijarro J, Requena-Puche J, Aranaz Andrés JM. The Study on Safety in Hospitals in the Region of Madrid (ESHMAD) design: screening and analysis of incidents and adverse events. *J Healthc Qual Res*. 2021;36:231–9.
26. World Health Organization (WHO). Patient Safety. [citado 24 de enero de 2025]. Available in: <https://www.who.int/es/news-room/fact-sheets/detail/patient-safety>.
27. Agency for Healthcare Research and Quality. Guide to Patient Safety Indicators. 2003. vAvailable from: https://qualityindicators.ahrq.gov/downloads/modules/psi/v31/psi_guide_v31.pdf.
28. European Centre for Disease Prevention and Control. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals, 2022–2023. LU: Publications Office; 2024 [citado 18 de agosto de 2024]. Disponible en: <https://data.europa.eu/doi/https://doi.org/10.2900/88011>.
29. Aranaz-Andrés JM, Aibar-Remon C, Vitaller-Burillo J, Requena-Puche J, Terol-García E, Kelley E, et al. Impact and preventability of adverse events in Spanish public hospitals: results of the Spanish National Study of Adverse Events (ENEAS). *Int J Qual Health Care*. 2009;21:408–14.
30. Woo SA, Cragg A, Wickham ME, Villanyi D, Scheuermeyer F, Hau JP, et al. Preventable adverse drug events: descriptive epidemiology. *Br J Clin Pharmacol*. 2020;86:291–302.
31. Lenti MV, Croce G, Brera AS, Ballesio A, Padovini L, Bertolino G, et al. Rate and risk factors of in-hospital and early post-discharge mortality in patients admitted to an internal medicine ward. *Clin Med*. 2023;23:16–23.
32. Nilsson L, Pihl A, Tågsjö M, Ericsson E. Adverse events are common on the intensive care unit: results from a structured record review. *Acta Anaesthesiol Scand*. 2012;56:959–65.
33. Zegers M, De Bruijne MC, Wagner C, Hoonhout LHF, Waaijman R, Smits M, et al. Adverse events and potentially preventable deaths in Dutch hospitals: results of a retrospective patient record review study. *Qual Saf Health Care*. 2009;18:297–302.
34. Haukland EC, Mevik K, Von Plessen C, Nieder C, Vonen B. Contribution of adverse events to death of hospitalised patients. *BMJ Open Qual*. 2019;8:e000377.
35. Zanetti ACB, Dias BM, Bernardes A, Capucho HC, Balsanelli AP, Moura AAD, et al. Incidence and preventability of adverse events in adult patients admitted to a Brazilian teaching hospital Jayadevappa R, editor. *PLoS One*. 2021;16:e0249531.
36. Vlayen A, Verelst S, Bekkering GE, Schrooten W, Hellings J, Claes N. Incidence and preventability of adverse events requiring intensive care admission: a systematic review. *J Eval Clin Pract*. 2012;18:485–97.
37. Johnstone J, Muscedere J, Dionne J, Duan E, Rochwerf B, Centofanti J, et al. Definitions, rates and associated mortality of ICU-acquired pneumonia: a multicenter cohort study. *J Crit Care*. 2023;75:154284.
38. Fagon JY, Chastre J, Vuagnat A, Trouillet JL, Novara A, Gilbert C. Nosocomial pneumonia and mortality among patients in intensive care units. *JAMA*. 1996;275:866–9.
39. Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias. Seguridad del paciente crítico Evaluación de los proyectos Zero 2023 [cited 27 August 2025]. Available in: https://seguridaddelpaciente.sanidad.gob.es/informacion/publicaciones/2024/docs/Seguridad_del_paciente_critico_Evaluacion_de_Los_PZ_2023.pdf.
40. Vincent C, Irving D, Bellandi T, Higham H, Michel P, Staines A, et al. Systems analysis of clinical incidents: development of a new edition of the London Protocol. *BMJ Qual Saf*. 2025;34:413–20.
41. Liu Z, Dumville JC, Norman G, Westby MJ, Blazeby J, McFarlane E, et al. Intra-operative interventions for preventing surgical site infection: an overview of Cochrane Reviews. *Cochrane Database Syst Rev*. 2018;2018:CD012653.
42. Ross P, Hodgson CL, Illic D, Watterson J, Gowland E, Collins K, et al. The impact of nursing skill-mix on adverse events in intensive care: a single centre cohort study. *Contemp Nurse*. 2023;59:3–15.
43. Global Patient Safety Action Plan 2021–2030: Towards Eliminating Avoidable Harm in Health Care. 1st ed. Geneva: World Health Organization; 2021. 1 p.
44. Brennan TA, Localio RJ, Laird NL. Reliability and validity of judgments concerning adverse events suffered by hospitalized patients. *Med Care*. 1989. <https://doi.org/10.1097/00005650-198912000-00006>.

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