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Major Article

The impact of healthcare-associated infections on mortality in ICU: A prospective study in Asia, Africa, Eastern Europe, Latin America, and the Middle East

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Background: The International Nosocomial Infection Control Consortium has found a high ICU mortality rate. Our aim was to identify all-cause mortality risk factors in ICU-patients.
Methods: Multinational, multicenter, prospective cohort study at 786 ICUs of 312 hospitals in 147 cities in 37 Latin American, Asian, African, Middle Eastern, and European countries.
Results: Between 07/01/1998 and 02/12/2022, 300,827 patients, followed during 2,167,397 patient-days, acquired 21,371 HAIs. Following mortality risk factors were identified in multiple logistic regression: Central line-associated bloodstream infection (aOR:1.84; *P*<.0001); ventilator-associated pneumonia (aOR:1.48; *P*<.0001); catheter-associated urinary tract infection (aOR:1.18;*P*<.0001); medical hospitalization (aOR:1.81; *P*<.0001); length of stay (LOS), risk rises 1% per day (aOR:1.01; *P*<.0001); female gender (aOR:1.09; *P*<.0001); age (aOR:1.012; *P*<.0001); central line-days, risk rises 2% per day (aOR:1.02; *P*<.0001); and mechanical ventilator (MV)-utilization ratio (aOR:10.46; *P*<.0001). Coronary ICU showed the lowest risk for mortality (aOR: 0.34;*P*<.0001).
Conclusion: Some identified risk factors are unlikely to change, such as country income-level, facility ownership, hospitalization type, gender, and age. Some can be modified; Central line-associated bloodstream infection, ventilator-associated pneumonia, catheter-associated urinary tract infection, LOS, and MV-utilization. So, to lower the risk of death in ICUs, we recommend focusing on strategies to shorten the LOS, reduce MV-utilization, and use evidence-based recommendations to prevent HAIs.

INTRODUCTION

The goals of medicine encompass alleviating pain and suffering, promoting health and preventing disease, forestalling death, promoting a peaceful death, curing disease when possible, and caring for the incurable.[1] The International Nosocomial Infection Control Consortium (INICC) is dedicated to promoting these goals through the surveillance and prevention of health care-associated infections (HAIs) worldwide.[2] INICC is a multinational multicenter, prospective HAI research network, operating internationally since 2002.[3] Its main objective is surveillance of HAIs, and promoting evidence-based infection prevention practices to reduce the incidence of HAIs and their associated mortality.[2] INICC has published international reports providing data on HAIs and related mortality in 2006,[4] 2008,[5] 2010,[6] 2012,[7] 2014,[8] 2016,[9] 2019,[10] and 2021.[11] INICC found that the mortality rate in ICU patients without HAI it is 17.12% (95% CI 16.93-17.32), for those with 1 HAI is 30.15% (95% CI 27.70-32.77) to 48.21% (95% CI 45.57-50.96), and for those with 3 simultaneous HAIs it is 63.44% (95% CI 55.99-71.60).[11]

Regarding risk factors (RF) for in hospital all-cause mortality in ICUs, a study conducted in a Turkish ICU found that age, APACHE II score, invasive mechanical ventilation (MV), decreased serum albumin levels, and increased creatinine levels are independent death RFs.[12] A research in an ICU in Thailand identified Staphylococcus aureus infection, diagnosis of systemic inflammatory response, and having received adrenaline as independent mortality RFs.[13] An Indian study in ICUs observed that male gender was a mortality RF.[14] A Turkish research identified thrombocytopenia as a RF of ICU mortality.[15] An investigation conducted in Brazil identified HAI as a mortality RF.[16] Another Turkish study showed that use of central line (CL) is a significant mortality RF.[17] Similarly, a Northern Thai study of a tertiary-care university-based general surgical intensive care unit found that resistant organisms are mortality RF.[18]

The above mentioned studies have analyzed the impact of severity of illness scores, underlying diseases, age, gender, presence of HAIs, and a few others for in hospital all-cause mortality in ICUs. However, as of publication, no study has analyzed multiple countries from different continents simultaneously to identify RF for mortality in ICUs. Additionally, no study has been conducted prospectively over 24 years. To our knowledge no study has analyzed all the following variables simultaneously and their association with in hospital all-cause mortality in ICUs: Income per country according with World Bank (low, lower-middle, upper-middle, high),[19] hospital ownership (publicly owned facilities, not-for-profit privately owned facilities, for-profit privately owned facilities, university hospitals),[20] type of hospitalization (medical, surgical), ICU type (cardio-thoracic, coronary, medical, medical-surgical, neuro-surgical, neurologic, adult-oncology, pediatric-oncology, pediatric, respiratory, surgical, trauma, burn), device days (CL-days, MV-days, urinary catheter [UC]-days), device utilization ratio as a marker of severity (CL-utilization ratio, MV-utilization ratio, UC-utilization ratio).[21] The goal of the present study is to analyze the impact of these variables and others as RFs for in hospital all-cause mortality in ICUs.

METHODS

Study population and design

This multinational, multi-center, cohort, prospective study was carried out with patients admitted to 786 ICUs of 287 hospitals in 147 cities in 37 countries of Latin America, Asia, Africa, the Middle

East, and Eastern Europe throughout 24 years, between July 1st, 1998, and February 12th, 2022.

Surveillance of health care associated infections

The data was collected on each patient at the time of their ICU admission. From admission to discharge, infection prevention professionals (IPP) went to the bedside of each patient on a daily basis. All patients with or without HAIs admitted to an ICU were prospectively included in this investigation, and their data were collected from admission to discharge using the INICC Surveillance Online System (ISOS).[2,3] IPPs go with a tablet to the bedside of each hospitalized patient in the ICU, log in on ISOS, and upload the patient's data in real time.[2,3]

At the time the patient is admitted, this information includes details about the setting, including the country, city, hospital name, and type of ICU; as well as details about the patient, including age, type of hospitalization (surgical or medical), and use of invasive devices (CL, MV, UC, peripheral catheter).[2,3] IPPs upload information about a patient's invasive devices (CL, MV, UC, peripheral catheter), and positive cultures (blood cultures, urine cultures, respiratory samples), until the patient is released.[2,3]

In the case the patient has signs or symptoms of infection, an infectious diseases specialist approach the patient to determine the presence of an HAI (central line associated bloodstream infection [CLAB], ventilator associated pneumonia [VAP], catheter associated urinary tract infection [CAUTI], or other). According to the Centers for Disease Control and Prevention / National Healthcare Safety Network (CDC/NHSN), IPPs look at a patient's signs and symptoms, cultures, X-rays, and other described criteria to fulfill definitions of HAI.[22,23] When IPPs upload the result of a culture to the ISOS, the ISOS immediately shows a message to the IPP and leads the IPP to an online module of the ISOS to check all the criteria of CDC NHSN to confirm the presence of an HAI and kind of HAI (CLABSI, VAP, CAUTI, or other).[2,3]

ISOS checks device utilization (DU) on a daily basis. From admission to discharge, the ISOS sends messages to the IPPs when a bias on patient-days or use of devices is detected. If ISOS detects lack of use of any kind of device on any given day, it will send a message to IPP to remind him or her to upload missing devices or upload the discharge of the patient, because if the patient is hospitalized in ICU without any device in place, it is most probably because IPP forgot to upload to ISOS the use of devices, or forgot to upload to ISOS the discharge of the patient. That is, ISOS requests that IPPs investigate why a patient in an ICU has no devices in place,[2,3] This approach significantly reduces biases associated with DU, patient-days, and discharge conditions.[2,3]

Patients with missing data on their age or gender were excluded from this analysis. This study was approved by the Institutional Review Boards of the hospitals involved. The identities of patients and hospitals are kept confidential.

INICC surveillance online system

According to standard CDC/NSHN methods, HAI denominators are device-days collected from all patients as pooled data, without specifying each patient's characteristics or the number of device-days related to such patient.[22,23] INICC HAI surveillance is carried out through the use of an online platform, the ISOS, which includes CDC NHSN criteria and methods.[22,23]

ISOS also adds the collection of patient-specific data on all patients, with and without HAI, including several variables per patient.[2,3] Data from all patients admitted to the ICU, allow matching by various characteristics, serving to estimate RF for death.

Data collected through INICC's online surveillance system applies the latest CDC/NHSN criteria and methodology to diagnose HAIs, calculate HAI rates, and calculate DU ratio, among others.[22,23] Definitions of HAI used during surveillance were those published by CDC in 1991[22] and all their subsequent updates through 2022.[23]

Study definitions

World Bank country classifications by income level

The World Bank assigns the world's economies to four income groups—low, lower-middle, upper-middle, and high-income countries. The classifications are based on GNI per capita in current USD. Low income are those countries with gross national income (GNI) less than USD 1,045. Lower-middle income those with GNI from 1,046 to 4,095. Upper-middle income those with GNI from 4,096 to 12,695. High income those with GNI >12,695.[19]

Patient-day

A count of the number of patients in a patient care location during a defined time period.[21]

Device-utilization

DU was calculated as a ratio of device-days to patient-days for each location type. As such, the DU of a location measures the use of invasive devices and constitutes an extrinsic RF for HAI. DU may also serve as a marker for severity of illness of patients (ie severely ill patients are more likely to require an invasive device) which is an intrinsic RF for infection.[24]

Facility/institution ownership type

Publicly owned facilities owned or controlled by a governmental unit or another public corporation (where control is defined as the ability to determine the general corporate policy); ***not-for-profit privately owned*** facilities that are legal or social entities created for the purpose of producing goods and services, whose status does not permit them to be a source of income, profit or other financial gain for the unit(s) that establish, control or finance them; and, ***for-profit privately owned facilities*** that are legal entities set up for the purpose of producing goods and services and are capable of generating a profit or other financial gain for their owners.[20]

Intensive care unit: It is a nursing care area that provides intensive observation, diagnostic and therapeutic procedures for patients who are critically ill. An ICU excludes nursing areas that provide step- down, intermediate care or telemetry only. Specialty care areas are also excluded. The type of ICU is determined by the type of patients cared for in that unit according to the 80% Rule —which means 80% of the patients in a location are of a certain type. For example, if 80% of the patients in an area are patients receiving critical care for trauma, this area should be designated as an Inpatient Trauma Critical Care Unit. When an ICU houses roughly equal populations of medical and surgical patients (a 50/50 to 60/40 mix), it is called a medical-surgical ICU.[21]

Recorded data

Income group by World Bank country classifications by income level (low, lower middle, upper middle, high),[19] country name, city name, hospital name, hospital ownership (publicly owned facilities, not-for-profit privately owned facilities, for-profit privately owned facilities, university hospitals),[20] ICU type,[21] age, gender, device-days (CL-days, MV-days, UC-days),[21] DU ratio as a marker of severity of illness of patients (CL-utilization ratio, MV-utilization ratio, UC-utilization ratio),[24] patient-days/length of stay (LOS),[21] and acquisition of HAI according with CDC/NHSN definitions (CLABSI, VAP, CAUTI)[22,23] were recorded as independent variables. The evaluated outcome was in hospital all-cause mortality.

Statistical analysis

Surviving and deceased patients were compared using multiple logistic regression. Statistically significant variables were independently associated with an increased RF for mortality. The test statistic used was the Wald test, and the statistical significance level was set at 0.05. Calculated from the outputs of multiple logistic regression, adjusted odds ratios (aORs) and the corresponding 95% CIs of statistically significant variables were also reported. We used DU ratio as a marker for severity. We estimated independent variables independently associated with the outcome (death), adjusted for all confounders present in Table 1. All statistical analyses were performed using R software, version 4.1.3.

RESULTS

From July 1st, 1998 to February 12th, 2022, during the course of 24 years, a multinational, multicenter, cohort, prospective, surveillance study was conducted in 786 ICUs of 287 hospitals in 147 cities in 37 countries (Argentina, Bahrain, Brazil, Bulgaria, China, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, Egypt, El Salvador, India, Jordan, Kingdom of Saudi Arabia, Kosovo, Kuwait, Lebanon, Malaysia, Mexico, Mongolia, Morocco, Nepal, Pakistan, Palestine, Panama, Peru, Philippines, Poland, Romania, Slovakia, Sri Lanka, Thailand, Turkey, United Arab Emirates, Venezuela, and Vietnam) from Latin-America, Asia, Africa, Middle East, and Europe, currently participating in INICC.

Of all 287 hospitals, 121 (42.1%) were for-profit privately owned facilities, 115 (40.0%) were publicly owned facilities, 69 (24.04%) were academic, and the remaining 7 (2.43%) were not-for-profit privately owned facilities.

Among all 786 ICUs, 242 (29.44%) were medical-surgical, 138 (16.79%) were medical, 81 (9.85%) were pediatric, 76 (9.25%) were surgical, 75 (9.12%) were coronary, 47 (5.72%) were neuro-surgical, 27 (3.28%) were cardio-thoracic, 25 (3.04%) were neurologic, 23 (2.8%) were respiratory, 20 (2.43%) were trauma, 11 (1.34%) were pediatric-oncology, 11 (1.34%) were adult-oncology, and 10 (1.22%) were burn.

This is a cohort study, and length of participation of hospitals is variable. The length of participation of hospitals in INICC ranged from 1.17 to 227.53 months (Mean, 38.40; SD, 42.30). More participating hospitals' and patients' characteristics are shown in Table 1.

Table 1
Setting and patient characteristics
Data collected from 07/01/1998 to 02/12/2022, over 24 years, at 786 ICUs, of 287 hospitals, in 147 cities of 37 countries

Total patients, n (%)	300,827 (100%)
Survival status, n (%)	
Alive	256,935 (85.46%)
Death	43,728 (14.54%)
According with World Bank country classification by income level, n (%)	
Low	1 (2.7%)
Lower middle	11 (29.73%)
Upper middle	19 (51.35%)
High	6 (16.22%)
Number of patients admitted to ICUs of following kind of hospitals, n (%)	
For-profit privately owned facilities	125,771 (41.83%)
Publicly owned facilities	71,748 (23.86%)
University facilities	90,527 (30.11%)
Not-for-profit privately owned facilities	12,617 (4.2%)
Number of patients with medical hospitalization, n (%)	217929 (72.48%)
Number of patients with surgical hospitalization, n (%)	82734 (25.72%)
Number of patients admitted to following types of ICUs, n (%)	
Cardio-thoracic ICU	8,416 (2.8%)
Coronary ICU	27,349 (9.1%)
Medical ICU	33,281 (11.07%)
Medical-surgical ICU	182,098 (60.57%)
Neuro-surgical ICU	5,877 (1.95%)
Neurologic ICU	1,785 (0.59%)
Adult-oncology ICU	3,734 (1.24%)
Pediatric-oncology ICU	1,540 (0.51%)
Pediatric ICU	16,387 (5.45%)
Respiratory ICU	1,485 (0.49%)
Surgical ICU	15,784 (5.25%)
Trauma ICU	2,753 (0.92%)
Burn ICU	174 (0.058%)
Gender, n (%)	
Male	182,935 (60.84%)
Female	117,780 (39.16%)
Age, mean, SD	Mean = 52.15, SD = 23.93
CL-days, n, mean, SD	1,507,281; Mean = 5.01; SD = 10.83
MV-days, n, mean, SD	830,311; Mean = 2.76; SD = 7.15
UC-days, n, mean, SD	1,413,708; Mean = 4.70; SD = 7.84
CL-utilization ratio, mean, SD	Mean = 0.66; SD = 1.55
MV-utilization ratio, mean, SD	Mean = 0.28; SD = 0.66
UC-utilization ratio, mean, SD	Mean = 0.62; SD = 0.67
Patient-days, n	2,167,397
Average LOS, mean, SD	Mean = 7.21, SD = 9.43
CLABSI, n (%)	6,279 (29.38%)
VAP, n (%)	10,941 (51.2%)
CAUTI, n (%)	4,151 (19.42%)

CAUTI, catheter associated urinary tract infection; CL, central line; CLAB, central line associated bloodstream infection; ICU, intensive care unit; LOS, length of stay; MV, mechanical ventilator; PC, peripheral catheter; SD, standard deviation
UC, urinary catheter; VAP, ventilator-associated pneumonia;

Table 2
Mortality rate stratified per ICU type

ICU type	Number of patients, n	Number of patients dead, n (%), 95% CI
Respiratory ICU	1,511	467 (30.91%) 95% CI: (28.17-33.84)
Adult-oncology ICU	3,734	1,143 (30.61%) 95% CI: (28.86-32.44)
Medical-surgical ICU	182,148	30,871 (16.96%) 95% CI: (16.76-17.14)
Trauma ICU	2,754	404 (14.67%) 95% CI: (13.27-16.17)
Medical ICU	33,347	4,865 (14.59%) 95% CI: (14.18-15.00)
Neurologic ICU	1,789	228 (12.74%) 95% CI: (11.14-14.51)
Neuro-surgical ICU	5,881	651 (11.07%) 95% CI: (10.24-11.95)
Cardio-thoracic ICU	8,418	759 (9.02%) 95% CI: (8.39-9.68)
Surgical ICU	15,789	1,290 (8.17%) 95% CI: (7.73-8.63)
Pediatric ICU	16,392	1,322 (8.07%) 95% CI: (7.64-8.51)
Burn ICU	174	11 (6.32%) 95% CI: (3.16-11.31)
Coronary ICU	27,350	1,652 (6.04%) 95% CI: (5.75-6.34)
Pediatric-oncology ICU	1,540	84 (5.46%) 95% CI: (4.35-6.75)

ICU, intensive care unit; CI, confidence interval.

Mortality rates per ICU type are shown in Table 2**.** Mortality rates according to World Bank country classification by income level (lower-middle income, upper-middle income, and high income) and by facility ownership type (publicly owned facilities, for-profit privately owned facilities, university hospitals, not-for-profit privately owned facilities) are shown in Table 3.

Using multiple logistic regression, the following variables were identified as statistically significantly independently associated with death: acquisition of a CLABSI (aOR,1.84; 95% CI, 1.73-1.95; *P*<.0001); acquisition of a VAP (aOR,1.48; 95% CI, 1.41-1.55; *P*<.0001); acquisition of a CAUTI (aOR,1.18; 95% CI, 1.10-1.28; *P*<.0001); medical hospitalization instead of surgical (aOR,1.81; 95% CI, 1.75-1.86; *P*<.0001); longer stay (aOR,1.01; 95% CI, 1.01-1.02; *P*<.0001), showing an 1% rise on risk of death per day; female gender instead of male (aOR,1.09; 95% CI, 1.07-1.12; *P*<.0001); older age, rises 1% rise per year of age (aOR,1.012; 95% CI, 1.011-1.0124; *P*<.0001); longer use of CL rises 2% rise per CL-day (aOR,1.02; 95% CI, 1.01-1.02; *P*<.0001) and higher MV-utilization ratio (aOR, 10.46; 95% CI, 10.07-10.86; *P* <.0001). (See Table 4)

DISCUSSION

Although DU in INICC ICUs was similar to that reported in CDC-NHSN ICUs,[25] according to INICC last international report, the pooled CLABSI rate was higher (5.30 vs 0.8 per 1,000 CL-days), the VAP rate was also higher (11.47 vs 6.96 per 1,000 MV-days,) as was the CAUTI rate (3.16 vs 0.91 per 1,000 UC-days).[11] Different underlying reasons can explain this adverse situation, such as low rates of compliance with guidelines, low nurse-to-patient staffing ratios, over-crowding in ICUs, insufficient medical supplies, outdated technology, and lack of trained and experienced health care workers (HCW).[26,27] The previous INICC international report also found that the acquisition of one HAI increases mortality approximately 2-3times, however, should the patient present three HAIs simultaneously, mortality increases more significantly, reaching over 63%.[11]

The present study found an association of CLABSI, VAP, CAUTI, high income level of the country, for-profit privately owned facilities, medical hospitalization, patient-days, female gender, age, and MV-utilization ratio with death. On the other hand, we identified that the coronary ICU was the ICU with the lowest risk of death.

The present study found an association between acquisition of CLABSI and mortality, coinciding with previous findings, such as a Greek report which observed that the acquisition of a CLABSI was an independent death RF (OR, 1.76; 95% CI, 1.11-2.78; *P* =.015).[28] In addition, our study also found an association between the acquisition of VAP and mortality, as demonstrated by Wang, et al., showing a similar association.[29] Additionally a link between the acquisition of CAUTI and mortality was observed. This is consistent with assertions by Ylipalosaari, however these authors did not specify kind of HAI.[30]

Older age was also found to be associated with mortality in our study. A 1.2% rise on mortality per year of age was observed in our study. With logistic regression analyses, age (>60 years) (OR, 3.65; 95% CI, 1.48-9.0), was found to be significant risk factors for mortality in a Turkish study.[17]

Table 3
Mortality rate stratified per World Bank country classifications by income level and per Facility ownership type

	Number of patients, n	Number of patients dead, n (%), 95% CI
Lower-middle income		
Pooled	158,762	18,322 (11.54%) 95% CI: (0.1137-0.1171)
Publicly owned facilities	15,180	1,796 (11.83%) 95% CI: (0.1129 - 0.1239)
For-profit privately owned facilities	78,442	9,828 (12.53%) 95% CI: (0.1228 - 0.1278)
University hospitals	53,996	5,570 (10.32%) 95% CI: (0.1005 - 0.1059)
Not-for-profit privately owned facilities	11,144	1,128 (10.12%) 95% CI: (0.0954 - 0.1073)
Upper-middle income		
Pooled	103,043	18,129 (17.59%) 95% CI: (0.1734 - 0.1785)
Publicly owned facilities	23,587	3,755 (15.92%) 95% CI: (0.1541 -0.1644)
For-profit privately owned facilities	43,506	6,966 (16.01%) 95% CI: (0.1564 - 0.1639)
University hospitals	34,477	7,177 (20.82%) 95% CI: (0.2034 - 0.213)
Not-for-profit privately owned facilities	1,473	231 (15.68%) 95% CI: (0.1373 - 0.1784)
High income		
Pooled	37,776	7,169 (18.98%) 95% CI: (0.1854 - 0.1942)
Publicly owned facilities	32,913	6,096 (18.52%) 95% CI: (0.1806 - 0.1899)
For-profit privately owned facilities	2,785	405 (14.54%) 95% CI: (0.1316 - 0.1603)
University hospitals	2,078	668 (32.15%) 95% CI: (0.2975 - 0.3468)
Not-for-profit privately owned facilities	0	0

CI, confidence interval.

Table 4
Logistic regression analysis of risk factors associated with death

Variable	OR	95% CI	*P* value
CLABSI	1.84	1.73-1.95	<.0001
VAP	1.48	1.41-1.55	<.0001
CAUTI	1.18	1.10-1.28	<.0001
According with World Bank country classification by income level			
Lower-middle income country	1.31	1.07-1.59	.008
Upper-middle income country	1.96	1.61-2.39	<.0001
High income country	2.11	1.73-2.58	<.0001
Hospital ownership			
For-profit privately owned facilities	1.04	0.97-1.11	.3
Publicly owned facilities	0.85	0.79-0.91	<.0001
University facilities	0.96	0.90-1.03	.23
Medical Hospitalization	1.81	1.75-1.86	<.0001
ICU type			
Coronary ICU	0,34	0.18-0.64	<.0001
Pediatric ICU	0,57	0.30-1.07	.08
Surgical ICU	0,58	0.31-1.09	.09
Pediatric-oncology ICU	0,59	0.29-1.15	.12
Neurologic ICU	0,63	0.33-1.21	.17
Respiratory ICU	0,70	0.36-1.33	.28
Neuro -surgical ICU	0,71	0.37-1.35	.29
Cardio-thoracic ICU	0,80	0.42-1.52	.50
Medical-surgical ICU	0,83	0.44-1.57	.57
Medical ICU	0,85	0.45-1.61	.62
Trauma ICU	0,93	0.49-1.77	.83
Adult-oncology ICU	1,79	0.95-3.39	.07
Patient-days	1.01	1.01-1.02	<.0001
Gender, female	1.09	1.07-1.12	<.0001
Age	1.012	1.011-1.0124	<.0001
CL-days	1.02	1.01-1.02	<.0001
MV-days	0.97	0.96-0.97	<.0001
UC-days	1.00	1.00-1.01	<.0001
CL-utilization ratio	0.94	0.93-0.95	<.0001
MV-utilization ratio	10.46	10.07-10.86	<.0001
UC-utilization ratio	0.97	0.94-1.00	.03

CAUTI, catheter associated urinary tract infection; CI, confidence interval; CL, central line; CLABSI, central line associated bloodstream infection; ICU, intensive care unit; LOS, length of stay; MV, mechanical ventilator; OR, odds ratio; PC, peripheral catheter; UC, urinary catheter; VAP, ventilator-associated pneumonia;

The present study additionally found an association between the female gender and mortality. Coincidentally, Todorov et al. 2021 investigated the effect of gender on the likelihood of receiving intensive care in critically ill cardio- and neurovascular patients in a large nationwide Swiss cohort, and found the same association. They conducted a retrospective study of 450,948 adult patients with neuro- and cardiovascular disease admitted to all Swiss hospitals between 2012 and 2016. Overall, women had a lower likelihood of being admitted to an ICU than men, despite being more severely ill [odds ratio (OR) of 0.78 (0.76-0.79)]. ICU admission probability was lowest in women aged > 65 years (OR women:men 0.94 (0.89-0.99), *P*=.001). Despite having a more severe illness, women over 45 years of age had the same ICU admission probability as men in the same age group [OR women:men 1.03 (0.94-1.13)]. The odds of dying were significantly higher in women than in men per unit increase in Simplified Acute Physiology Score (SAPS) II (OR 1.008 [1.004-1.012]). In the care of the critically ill, this study suggests that women are less likely to receive ICU treatment regardless of disease severity. Underuse of ICU care was most prevalent in women under 45 years old.[31]

Moreover, an association was found between prolonged patient-days / LOS and mortality, consistent with a previous study analyzing epidemiology and risk factors for mortality in ICU patients, in which observed prolonged LOS was an independent RF in multivariate analysis (*P*<.01).[32]

Furthermore, this study found an association between invasive MV-utilization ratio and mortality. In a study analyzing incidence, RF, and associated mortality in a Turkish university hospital, with logistic regression analyses, MV (OR, 3.60; 95% CI, 1.05-12.39) was found to be a significant mortality RF.[17]

This study further observed an association between CL-days and mortality. We found a 2% increased mortality per CL-day, showing a similar association in a study analyzing RF and associated mortality in a Turkish university hospital, with logistic regression analyses, CL (OR, 7.85; 95% CI, 1.61-38.32) was found to be a significant mortality RF.[17]

The current study also observed that publicly owned facilities have a significantly lower risk of mortality than for-profit privately owned facilities or university hospitals. Regarding this association, Eggleston conducted a systematic review to examines what factors explain the diversity of findings regarding hospital ownership and quality. They found that ownership does appear to be systematically related to differences in quality among hospitals in several contexts. Those studies found for-profit and government-controlled hospitals to have higher mortality rates than their nonprofit counterparts.[33] Devereaux undertook a systematic review and meta-analysis of studies comparing the mortality rates of private for-profit hospitals and those of private not-for-profit hospitals. For each study, they calculated a relative risk of mortality for private for-profit hospitals relative to private not-for-profit hospitals. In the studies of adult populations, private for-profit hospitals were associated with an increased risk of death (relative risk [RR] 1.020, 95% confidence interval [CI] 1.003-1.038; *P*=.02). Their meta-analysis suggests that private for-profit ownership of hospitals, in comparison with private not-for-profit ownership, results in a higher risk of death for patients.[34] Regarding performance of publicly owned facilities in high income countries, Alatawi et al. in 2020 assessed the performance of publicly owned facilities in Saudi Arabia. They detected the sources of inefficiency and estimated the optimal levels of the resources that provide the current level of health services. They employed data envelopment analysis to measure the technical efficiency of 91 public hospitals. The assessment includes four inputs and six output variables taken from the Ministry of Health databases for 2017. They analyzed data from the Ministry of Health-affiliated hospitals in the Kingdom of Saudi Arabia. Findings identified 75.8% of public hospitals as technically inefficient. Small hospitals were more efficient than medium-sized and large hospitals. Hospitals in the central region were more efficient than those located in other geographical locations. More than half of the hospitals (62.6%) were operating sub-optimally in terms of scale efficiency. Performance analysis identified overuse of physicians' numbers and shortage of health service production as major causes of inefficiency. Most hospitals were technically inefficient and operating at suboptimal scale sizes, which indicates that many hospitals may improve their performance through efficient utilization of health resources to provide the current level of health services.[35]

Additionally, the present study found that high-income countries have a significantly higher risk of mortality than low or middle-income countries. This finding could be explained by the probably inadequate health care quality programs in those high-income countries participating in this study, as demonstrated by Alatawi et al. in 2020 analyzing the quality of health care in a high-income country.[35]

In addition, this study found that medical hospitalization has a significantly higher risk of mortality than surgical hospitalization. This could be explained by the fact that, on the one hand, patients admitted for planned surgical procedures have a less severe condition than those admitted for medical reasons, and thus, most of them are stable. But, on the other hand, when a medical patient is admitted to the ICU, they are rarely stable.[36]

Finally, the present study noted that patients admitted to coronary ICU have a significantly lower risk of mortality than patients hospitalized in any other kind of ICU. DU ratio, especially in the case of MV-utilization ratio, as a marker of severity of illness of patients, is

one of the lowest in coronary ICU,[25] and this could explain why coronary ICU is associated with the lowest risk of mortality.

As a conclusion, in the first instance, some of the mortality RFs identified in our study are unlikely to change, such as income level of the country, facility ownership, type of hospitalization, gender, and age. However, some RFs for death can be modified; acquisition of CLABSI, VAP, or CAUTI, LOS, and MV-utilization. As INICC has already shown, HAI rates in low- and middle-income countries are 3-5 times higher than in the US,[4-11] and therefore, there is room for improvement. So, to reduce the risk of death in ICUs, we recommend focusing on strategies to reduce LOS, reduce use of MV, and implement an evidence-based set of recommendations to prevent HAIs, such as those recently published by APIC/SHEA/IDSA.[37,38]

This study has several potential limitations. Firstly, this study is not representative of all hospitals in the world, as it is a surveillance system in which hospitals that wish to participate join voluntarily. Secondly, it is likely that the hospitals that decide to participate are those that have a better-quality program and surveillance and prevention of HAIs. Therefore, it is also likely that the rates of HAI shown in this study are lower than the actual rates found worldwide. Lastly, on he one hand, data regarding the severity of illness scores were not collected, which may contribute to identifying them as another RF for death, but, on the other hand, we adjusted the outcome to device utilization ratio as a marker for the severity of illness of patients.[24]

AUTHOR CONTRIBUTIONS

Rosenthal, V.D. was responsible for study conception and design, software development, technical support, drafting tutorials for surveillance process, training of data collectors, provision of study patients, data validation, data assembly, data interpretation, epidemiological analysis, drafting of the manuscript.

Zhilin Jin and Ruijie Yin contributed equally to building machine learning models and conducting statistical analysis, critical revision for important intellectual content, and final approval of the manuscript.

Yawen Lu has collaborated with the search for scientific references and the final approval of the manuscript.

Remaining authors were involved in the provision of study patients.

All authors were involved in critical revision of the manuscript for important intellectual content, and final approval of the manuscript.

IRB APPROVAL

An Institutional Review Board approved the study prior to data collection.

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