

Original Article

Multinational prospective study of incidence and risk factors for central-line–associated bloodstream infections in 728 intensive care units of 41 Asian, African, Eastern European, Latin American, and Middle Eastern countries over 24 years

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Abstract

Objective: To identify central-line (CL)-associated bloodstream infection (CLABSI) incidence and risk factors in low- and middle-income countries (LMICs).

Design: From July 1, 1998, to February 12, 2022, we conducted a multinational multicenter prospective cohort study using online standardized surveillance system and unified forms.

Setting: The study included 728 ICUs of 286 hospitals in 147 cities in 41 African, Asian, Eastern European, Latin American, and Middle Eastern countries.

Patients: In total, 278,241 patients followed during 1,815,043 patient days acquired 3,537 CLABSIs.

Methods: For the CLABSI rate, we used CL days as the denominator and the number of CLABSIs as the numerator. Using multiple logistic regression, outcomes are shown as adjusted odds ratios (aORs).

Results: The pooled CLABSI rate was 4.82 CLABSIs per 1,000 CL days, which is significantly higher than that reported by the Centers for Disease Control and Prevention National Healthcare Safety Network (CDC NHSN). We analyzed 11 variables, and the following variables were independently and significantly associated with CLABSI: length of stay (LOS), risk increasing 3% daily (aOR, 1.03; 95% CI, 1.03–1.04; $P < .0001$), number of CL days, risk increasing 4% per CL day (aOR, 1.04; 95% CI, 1.03–1.04; $P < .0001$), surgical hospitalization (aOR, 1.12; 95% CI, 1.03–1.21; $P < .0001$), tracheostomy use (aOR, 1.52; 95% CI, 1.23–1.88; $P < .0001$), hospitalization at a publicly owned facility (aOR, 3.04; 95% CI, 2.31–4.01; $P < .0001$) or at a teaching hospital (aOR, 2.91; 95% CI, 2.22–3.83; $P < .0001$), hospitalization in a middle-income country (aOR, 2.41; 95% CI, 2.09–2.77; $P < .0001$). The ICU type with highest risk was adult oncology (aOR, 4.35; 95% CI, 3.11–6.09; $P < .0001$), followed by pediatric oncology (aOR, 2.51; 95% CI, 1.57–3.99; $P < .0001$), and pediatric (aOR, 2.34; 95% CI, 1.81–3.01; $P < .0001$). The CL type with the highest risk was internal-jugular (aOR, 3.01; 95% CI, 2.71–3.33; $P < .0001$), followed by femoral (aOR, 2.29; 95% CI, 1.96–2.68; $P < .0001$). Peripherally inserted central catheter (PICC) was the CL with the lowest CLABSI risk (aOR, 1.48; 95% CI, 1.02–2.18; $P = .04$).

Conclusions: The following CLABSI risk factors are unlikely to change: country income level, facility ownership, hospitalization type, and ICU type. These findings suggest a focus on reducing LOS, CL days, and tracheostomy; using PICC instead of internal-jugular or femoral CL; and implementing evidence-based CLABSI prevention recommendations.

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As reported by the International Nosocomial Infection Control Consortium (INICC) in pooled studies, rates of central-line-associated bloodstream infection (CLABSI) have been significantly higher in low- and middle-income countries (LMICs) than in high-income countries.^{1–3} According to a review, they ranged from 1.6 to 44.6 CLABSIs per 1,000 central-line (CL) days in adult and pediatric intensive care units (ICUs) and from 2.6 to 60.0 CLABSIs per 1,000 CL days in neonatal NICUs (NICUs).³ CLABSI rates significantly increased in ICUs of LMICs during the COVID-19 pandemic.⁴

Multiple logistic regression identified the acquisition of a CLABSI as an independent risk factor associated with ICU all-cause mortality (adjusted odds ratio [aOR], 1.84; 95% confidence interval [CI], 1.73–1.95; $P < .0001$).⁵ This association was also demonstrated in 9 Asian countries (aOR, 2.36; 95% CI, 2.14–2.61; $P < .0001$)⁶ and 10 Middle Eastern countries (aOR, 1.49; 95% CI, 1.33–1.66; $P < .00001$).⁷

CLABSIs are associated with higher mortality by 12%–25%⁸ and extra costs.^{9–12} The INICC reported that mortality in ICU patients without any healthcare-associated infection (HAI) is 17.1%, with CLABSI the mortality rate is 48.2%, and mortality is 63.4% with a CLABSI plus catheter-associated urinary tract infection (CAUTI) plus ventilator-associated pneumonia (VAP).²

Previous studies have identified the following variables as CLABSI risk factors: body mass index >40 kg/m²,¹³ multiple CLs,^{13,14} multilumen catheters,¹³ femoral site,^{15,16} guidewire exchange,¹⁴ heavy microbial colonization at insertion site or catheter hub,¹³ indwelling time,¹³ prolonged hospitalization before catheterization,¹³ neutropenia,¹³ total parenteral nutrition,^{13,14} patient cared for by a floating nurse,¹⁷ transfusion of blood products,¹³ prematurity,¹³ reduced ICU nurse-to-patient ratio,¹³ substandard CL care,¹³ and few others.

However, no study has analyzed multiple countries or different types of vascular catheters simultaneously to identify CLABSI risk factors in ICUs. Also, no study has been conducted prospectively over 24 years. Furthermore, no study has analyzed all the following 11 variables simultaneously and their association with CLABSI: sex, age, length of stay (LOS), CL days before acquisition of CLABSI, CL device utilization (DU) ratio as a marker of severity of illness of patients, different types of vascular catheters, tracheostomy use, hospitalization type, ICU type, facility ownership, and World Bank country classifications by income level.

The objective of this study was to report CLABSI rates per country, per continent, per type of ICU, per facility ownership, per income level (according to the World Bank), and per year. We also analyzed whether these 11 variables were CLABSI risk factors, and we sought to identify the safest type of CL.

Methods

Study population and design

This multinational, multicenter, cohort, prospective study included patients admitted to 728 ICUs of 286 hospitals in 147 cities in 41 countries of Africa, Asia, Eastern Europe, Latin America, and the Middle East across 24 years, between July 1, 1998, and February 12, 2022.

INICC surveillance online system

According to standard Centers for Disease Control and Prevention National Healthcare Safety Network (CDC NHSN) 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 patients.¹⁸ INICC HAI surveillance is carried out using an online platform, the ISOS, which includes CDC NHSN criteria and methods.¹⁸ The ISOS also adds the collection of patient-specific data on all patients, with and without HAI.¹⁹ Data were collected for all patients admitted to the ICU, which allowed matching by various characteristics and facilitated the estimation of CLABSI risk factors.

Prospective cohort surveillance of healthcare-associated infections

The data were collected on each patient at the time of their ICU admission. From admission to discharge, infection prevention professionals (IPPs) went to the bedside of each patient daily. All patients admitted to an ICU were prospectively included in this investigation, and their data were collected using the INICC surveillance online system (ISOS). Each IPP used a tablet at the bedside of each hospitalized patient in the ICU, logged into the ISOS, and uploaded the patient data in real time.¹⁹ At the time the patient was admitted, this information included details about the setting, country, city, admission date, and ICU type, as well as patient data, sex, age, hospitalization type, and used of invasive devices. Each IPP uploaded information about invasive devices and positive cultures until patient discharge.¹⁹ In patients with signs or symptoms of infection, an infectious diseases specialist approached the patient to determine the presence of HAI.¹⁹

Each participating hospital had a microbiology laboratory that identified microorganism profiles and bacterial resistance. Furthermore, 35 patients with missing data regarding age and/or sex (0.01% of the sample) were excluded from this analysis. This study was approved by the institutional review boards of the hospitals involved. All patient and hospital identifiers were kept confidential.

Study definitions

Healthcare-associated infection

Healthcare-associated infection (HAI) definitions used during surveillance were those published by Centers for Disease Control and Prevention (CDC) in 1991²⁰ and all subsequent updates.¹⁸ Over the 24 years of this study, all IPPs of the participant hospitals have applied the current and updated CDC definition of HAI. That is, whenever the CDC updated their definition, IPPs began using the new updated definitions.^{18,20}

Central line

A central line (CL) was defined as an intravascular catheter that terminated at or close to the heart or in one of the great vessels and was used for infusion, withdrawal of blood, or hemodynamic monitoring. The following are considered great vessels: aorta, pulmonary artery, superior or inferior vena cava, brachiocephalic veins, internal jugular veins, subclavian veins, external iliac veins, common iliac veins, femoral veins, in neonates, the umbilical artery or vein.¹⁸

Primary bloodstream infection

Primary bloodstream infection was defined as a laboratory-confirmed bloodstream infection (LCBI) that was not secondary to an infection at another body site.¹⁸

Central-line-associated bloodstream infection

Central-line-associated bloodstream infection (CLABSI) was defined as an LCBI in which an eligible BSI organism was identified and an eligible CL was present on or the day before.¹⁸

Laboratory-confirmed bloodstream infection 1

This term was used in a patient of any age who had a recognized bacterial or fungal pathogen not included on the NHSN common commensal list. This pathogen was identified from 1 or more blood specimens obtained by a culture or identified to the genus or species level by non-culture-based microbiologic testing methods. In addition, organism(s) identified in the blood were not related to an infection at another site.¹⁸

Laboratory-confirmed bloodstream infection 2

This term was used in a patient of any age who had at least 1 of the following signs or symptoms: fever (>38.0°C), chills, or hypotension. Also, the organism(s) identified in the blood are not related to an infection at another site, and the same NHSN common commensal is identified by culture from 2 or more blood specimens collected on separate occasions.¹⁸

Common commensal

Common commensal organisms included but were not limited to diphtheroids (*Corynebacterium* spp not *C. diphtheria*), *Bacillus* spp (not *B. anthracis*), *Propionibacterium* spp, coagulase-negative staphylococci (including *Staphylococcus epidermidis*), viridans-group streptococci, *Aerococcus* spp, *Micrococcus* spp, and *Rhodococcus* spp.¹⁸

Central-line-device utilization ratio

The central-line-device utilization ratio (CL-DU) was calculated as a ratio of CL days to patient days for each location type. As such, the CL-DU of a location measures the use of invasive devices and constitutes an extrinsic CLABSI risk factor. The CL-DU ratio also serve as a marker for the severity of illness of patients which is an intrinsic HAI risk factor.¹⁸

World Bank country classification by income level

The World Bank assigns the world's economies to 4 income groups: low, lower-middle, upper-middle, and high. The classifications are based on gross national income (GNI) per capita in the current US dollars. Low-income countries are those with GNI < US\$1,045. Lower-middle income countries are those with GNI from US\$1,046 to US\$4,095. Upper-middle income countries are those with GNI from US\$4,096 to US\$12,695. High-income countries are those with GNI > US\$12,695.²¹ The inclusion of high-income countries allowed us to compare the risk factors for CLABSI among LMICs with those of high-income countries and identify if the income of the country is independently associated as a risk factor for CLABSI.

Facility or institution ownership type

Publicly owned facilities are 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 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 gains for the unit(s) that establish, control, or finance them. For-profit, privately owned facilities are legal entities set up for the purpose of producing goods and services and can generate a profit or other financial gains for their owners.²²

Statistical analyses

For risk factor analysis, we conducted a case-control study nested in a prospective cohort study. Patients with and without CLABSI

Table 1. Setting and Patient Characteristics^a

Variable	No. (%) ^b
Patient Characteristic	
Total patients	278,241
Total patients days	1,815,043
Average LOS, mean (SD)	6.52 (7.96)
Sex	
Male	169,134 (60.79)
Female	109,107 (39.21)
Age, mean (SD)	52.13 (23.97)
Survival status	
Alive	241,108 (86.65)
Death	37,133 (13.35)
Patients per hospitalization type	
Medical hospitalization	203,008 (72.96)
Surgical hospitalization	75,233 (27.04)
CLABSI, n	3,537
Invasive device utilization	
CL device utilization ratio	178,031.8
Mean (SD)	0.64 (1.64)
Total CL days	777,463
Mean (SD)	4.61 (9.97)
CL days per type of vascular catheter	
Subclavian	307,934 (39.61)
Jugular	215,941 (27.78)
Arterial	159,715 (20.54)
Femoral	51,053 (6.57)
Hemodialysis temporary	31,745 (4.08)
PICC ^c	11,075 (1.42)
Tracheostomy use	
Yes	2,374 (0.85)
No	275,867 (99.15)
Setting and facilities characteristics	
ICUs	728
Patients admitted per type of ICU	
Medical-Surgical ICU	168,690 (60.63)
Medical ICU	30,745 (11.05)
Coronary ICU	26,540 (9.54)
Pediatric ICU	15,476 (5.56)
Surgical ICU	14,839 (5.33)
Cardio-thoracic ICU	8,023 (2.88)
Neuro-Surgical ICU	5,278 (1.90)
Adult-Oncology ICU	3,107 (1.12)
Trauma ICU	2,701 (0.97)
Neurologic ICU	1,653 (0.59)
Pediatric-Oncology ICU	1,189 (0.43)
Hospitals, n	286
Patients admitted per facility ownership	

(Continued)

Table 1. (Continued)

Variable	No. (%) ^b
Publicly owned facilities	65,275 (23.46)
For-profit privately owned facilities	118,207 (42.48)
Teaching hospitals	82,631 (29.70)
Not-for-profit privately owned facilities	12,128 (4.36)
Cities	147
Countries	41
Countries, stratified per income level according to the World Bank	
Lower-middle-income country	10 (28.57)
Upper middle-income country	19 (54.29)
High-income country	6 (17.14)

Note. ICU, intensive care unit; CL, central-line; DU, device utilization; LOS, length of stay; CLABSI, central-line-associated bloodstream infection; SD, standard deviation.

^aData collected from July 1, 1998, to February 12, 2022, over 24 years.

^bData are no. (%) unless otherwise specified.

^cPeripherally inserted central catheter.

were compared using multiple logistic regression. Statistically significant variables were independently associated with an increased risk for CLABSI. We used the Wald test, and statistical significance was set at .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 analyzed following 11 variables and their association with CLABSI: (1) age; (2) male or female sex; (3) LOS before acquiring a CLABSI; (4) CL days before acquisition of CLABSI; (5) CL-DU ratio as a marker of severity of illness of patient; (6) different types and insertion sites of vascular catheters (ie, internal jugular, femoral, arterial, subclavian, temporary catheter for hemodialysis, peripherally inserted central catheter or PICC); (7) tracheostomy use; (8) medical or surgical hospitalization type; (9) ICU type (ie, medical-surgical, medical, pediatric, surgical, coronary, neurosurgical, cardio-thoracic, neurologic, trauma, oncology pediatric, or oncology adult); (10) facility ownership (publicly owned, not-for-profit privately owned, for-profit privately owned, and teaching hospital)²²; and (11) income level per country according to the World Bank (ie, low, lower-middle, upper-middle, or high).²¹ The evaluated outcome was the acquisition of CLABSI according to the CDC NHSN definitions.¹⁸

For analyses of CLABSI risk factors, we used data from 35 countries: Argentina, Bahrain, Brazil, Bulgaria, China, Colombia, Costa Rica, Cuba, Dominican Republic, Ecuador, Egypt, El Salvador, India, Jordan, Kosovo, Kuwait, Lebanon, Malaysia, Mexico, Mongolia, Morocco, Nepal, Pakistan, Panama, Peru, Philippines, Poland, Romania, Saudi Arabia, Slovakia, Sri Lanka, Thailand, Turkey, United Arab Emirates, and Vietnam. All of these countries collected all 11 independent variables of interest: sex, age, LOS, CL days, CL-DU ratio, different types and insertion sites of vascular catheters, tracheostomy use, hospitalization type, ICU type, facility ownership, and income level per country.

For estimation of CLABSI rates, we used data from all 41 countries including the 35 countries listed above and following 6 countries that collected only CL days and CLABSI events: Greece, Macedonia, Papua New Guinea, Russia, Serbia, Tunisia.

All statistical analyses were performed using R version 4.1.3 software (R Foundation for Statistical Computing, Vienna, Austria).

Table 2. Central-Line–Associated Bloodstream Infections Rates Stratified per Country and per Region

Country	Patients, No. (%)	Patient Days, No.	CL days, No.	CLABSI, No.	CLABSI Rate ^a	95% CI
1. Argentina	23,589 (7.29)	168,234	67,222	500	7.44	7.41–7.45
2. Bahrain	1,223 (0.38)	11,205	8,053	26	3.23	3.18–3.26
3. Brazil	16,894 (5.22)	150,181	136,354	309	2.27	2.25–2.27
4. Bulgaria	991 (0.31)	9,544	7,328	53	7.23	7.17–7.29
5. China	4,323 (1.34)	35,999	18,195	41	2.25	2.23–2.27
6. Colombia	17,159 (5.30)	127,842	92,587	457	4.94	4.92–4.95
7. Costa Rica	1,468 (0.45)	6,413	5,300	6	1.13	1.10–1.16
8. Cuba	1,029 (0.32)	6,617	4,543	7	1.54	1.50–1.57
9. Dominican Republic	1,417 (0.44)	10,569	4,503	70	15.55	15.43–15.66
10. Ecuador	943 (0.29)	16,826	9,003	33	3.67	3.62–3.70
11. Egypt	5,750 (0.18)	66,521	47,401	259	5.46	5.44–5.48
12. El Salvador	1,127 (0.35)	9,811	6,727	52	7.73	7.66–7.79
13. Greece	100 (0.03)	NA	1,743	12	6.88	6.76–7.00
14. India	151,485 (46.79)	1,963,884	782,167	2,788	3.56	3.56–3.56
15. Jordan	5,105 (1.58)	39,200	17,495	117	6.69	6.64–6.72
16. Kosovo	247 (0.08)	3,462	1,607	5	3.11	3.02–3.19
17. Kuwait	7,046 (2.18)	101,688	43,188	90	2.08	2.07–2.09
18. Lebanon	6,291 (1.94)	54,448	32,449	70	2.16	2.14–2.17
19. Macedonia	3,550 (0.11)	NA	37,216	16	0.43	0.42–0.43
20. Malaysia	5,747 (1.78)	43,913	36,452	168	4.61	4.58–4.63
21. Mexico	9,001 (2.78)	69,880	66,387	480	7.23	7.20–7.25
22. Mongolia	2,457 (0.76)	23,363	10,123	33	3.26	3.22–3.29
23. Morocco	3,582 (1.11)	25,061	5,684	82	14.43	14.32–14.52
24. Nepal	2,008 (0.62)	25,806	13,335	21	1.57	1.55–1.59
25. Pakistan	713 (0.22)	5,738	5,659	162	28.63	28.48–28.76
26. Panama	947 (0.29)	8,771	8,670	97	11.19	11.11–11.25
27. Papua New Guinea	17 (0.01)	106	8	1	125	117.37–132.99
28. Peru	2,033 (0.63)	12,752	10,043	51	5.08	5.03–5.12
29. Philippines	5,479 (1.69)	33,028	11,773	92	7.81	7.76–7.86
30. Poland	1,907 (0.59)	NA	30,160	113	3.75	3.72–3.76
31. Romania	976 (0.30)	8,465	4,346	463	106.53	106.23–106.84
32. Russia	97 (0.03)	1,116	412	7	16.99	16.59–17.39
33. Saudi Arabia	27,275 (8.42)	322,683	164,966	758	4.59	4.58–4.60
34. Serbia	186 (0.06)	1,862	580	17	29.31	28.87–29.75
35. Slovakia	937 (0.29)	NA	11,200	46	4.11	4.06–4.14
36. Sri Lanka	326 (0.10)	2,398	2,210	5	2.26	2.20–2.32
37. Thailand	648 (0.20)	2,774	670	0	0	NA
38. Tunisia	221 (0.07)	1,909	651	2	3.07	2.93–3.20
39. Turkey	13,171 (4.07)	258,098	138,289	1,390	10.05	10.03–10.07
40. United Arab Emirates	384 (0.12)	53,273	387	2	5.17	4.94–5.39
41. Vietnam	4,279 (1.32)	51,644	28,067	129	4.60	4.57–4.62
Region						
Pooled	331,796	...	1,870,943	728	4.82	4.64–4.93
Asia	177,155 (53.39)	2,186,255	906,449	3,434	3.79	3.78–3.79
Latin America	75,606 (22.79)	587,896	411,339	2,061	5.01	5.00–5.01

(Continued)

Table 2. (Continued)

Country	Patients, No. (%)	Patient Days, No.	CL days, No.	CLABSI, No.	CLABSI Rate ^a	95% CI
Middle East	70,047 (21.11)	934,086	458,563	2,795	6.10	6.08–6.10
Eastern Europe	8,988 (2.71)	NA	94,592	728	7.70	7.67–7.71

Note. CL, central line; DU, device utilization; CLABSI, central-line-associated bloodstream infection; CI, confidence interval.

^aRate of CLABSI per 1,000 CL days.



Fig. 1. Rate of CLABSI per 1,000 central line days, stratified by country.

Results

From July 1, 1998, to February 12, 2022, over 24 years, a multinational, multicenter, cohort, prospective surveillance study of CLABSIs was conducted in 728 ICUs of 286 hospitals in 147 cities in 41 countries from Africa, Asia, Eastern Europe, Latin America, and the Middle East, participating in INICC. Patients admitted to Asian facilities represent 53.39% of the sample, followed by patients in Latin America (22.79%), the Middle East (21.11%), and Eastern Europe (2.71%).

In this cohort study, the length of participation of hospitals varied from 1.1 to 226.07 months (mean, 38.47; SD, 42.62). Table 1 shows data pertaining to setting and patient characteristics. Table 2 and Fig. 1 show CLABSI rates per 1,000 CL days per country and per region. Table 3 shows CLABSI rates stratified by ICU type, income level according to the World Bank, and facility ownership. Fig. 2 shows CLABSI rates stratified by year.

Using multiple logistic regression, the following variables were identified as statistically significantly associated with CLABSI (Table 4): LOS, risk increasing 3% daily; number of CL days, risk

increasing 4% per CL day; surgical hospitalization; tracheostomy; hospitalization at a publicly owned facility or at a teaching hospital; and hospitalization in a middle-income country. The ICU type with highest risk was adult oncology, followed by pediatric oncology, pediatric, and medical. The CL types with the highest risk were internal-jugular and femoral. PICC had the lowest risk for CLABSI.

Discussion

Pooled rates of CLABSI in our study of 4.82 CLABSI per 1,000 CL days were similar to the pooled CLABSI rates reported by the INICC of 5.30 CLABSIs per 1,000 CL days.² Our present study, which shows CLABSI rates stratified per country and per region, contributes to the identification of countries and regions with higher and lower CLABSI rates (See Fig. 1). On the other hand, the pooled rate of CLABSI in our present study was significantly higher than that reported by the CDC NHSN of 0.8 CLABSIs per 1,000 CL days.¹⁸ In this study, we detected a trend of significant reduction in the CLABSI rate per year (See Fig. 2). This CLABSI reduction rate is probably associated with INICC infection

Table 3. Central-Line–Associated Bloodstream Infections Rates Stratified per ICU Type, According to World Bank Country Classifications by Income Level and Facility Ownership Type

Variable	Patients, No.	Patient Days, No.	CL Days, No.	CLABSI, No.	CLABSI Rate	95% CI
ICU type^a						
Pooled	282,793	1,845,988	1,241,905	3,685	2.97	2.96–2.97
Adult-oncology	3,472	16,872	9,464	72	7.61	7.55–7.66
Pediatric-oncology	1,509	9,342	5,493	27	4.92	4.85–4.97
Pediatric	15,751	121,343	57,935	307	5.30	5.28–5.31
Medical	31,440	221,455	112,847	391	3.46	3.45–3.47
Neurologic	1,667	11,423	4,532	15	3.31	3.25–3.36
Medical-surgical	170,950	1,118,379	743,216	2,360	3.18	3.17–3.17
Neuro-surgical	5,627	36,280	14,769	38	2.57	2.54–2.59
Cardio-thoracic	8,099	47,766	49,217	109	2.21	2.20–2.22
Surgical	14,924	98,097	72,544	150	2.07	2.05–2.07
Trauma	2,707	12,979	5,780	10	1.73	1.69–1.76
Coronary	26,647	152,052	166,108	206	1.24	1.23–1.24
Lower-middle income						
Pooled	151,858	874,822	650,949	1,700	2.61	2.60–2.61
Publicly owned facilities	1,507	85,692	65,101	272	4.18	4.16–4.19
For-profit privately owned facilities	13,999	425,814	236,278	754	3.19	3.18–3.19
Teaching hospitals	51,704	303,826	322,562	622	1.93	1.92–1.93
Not-for-profit privately owned facilities	10,860	247,750	174,000	857	4.93	4.91–4.93
Upper-middle income						
Pooled	96,388	662,350	423,291	1,582	3.74	3.73–3.74
Publicly owned facilities	21,425	152,818	114,948	402	3.50	3.48–3.50
For-profit privately owned facilities	41,998	252,252	126,853	314	2.48	2.46–2.48
Teaching hospitals	31,589	247,750	174,000	857	4.93	4.91–4.93
Not-for-profit privately owned facilities	1,376	9,530	7,490	9	1.20	1.17–1.22
High income						
Pooled	34,547	308,816	167,665	403	2.40	2.39–2.41
Publicly owned facilities	30,706	274,659	137,478	351	2.55	2.54–2.56
Teaching hospitals	1,253	11,615	16,040	34	2.12	2.09–2.14
For-profit privately owned facilities	2,588	22,542	14,147	18	1.27	1.25–1.29

Note.

ICU, intensive care unit; CI, confidence interval.

^aICUs are listed in order of the highest to lowest central-line–associated bloodstream infection (CLABSI) rate.

prevention interventions implemented during the last 24 years at these hospitals, which have been participating in this network of hospitals that voluntarily use the ISOS and the INICC multidimensional approach.^{23–29} On the other hand, CLABSI rates increased twice: once in 2014 due to the addition of several new hospitals to the INICC network that had significantly higher CLABSI rates, and again in 2020 due to the COVID-19 pandemic (See Fig. 2).

The LOS was linked to a 3% daily increase in the CLABSI risk. Jeon et al³⁰ conducted a study to examine the role played by LOS as a CLABSI risk factor. They conducted logistic regression and observed a nonlinear increase in the hazard of BSI with increasing LOS. The association between a longer LOS and an increased risk of CLABSI can largely be explained by the increased LOS among those who have underlying morbidity and require invasive procedures.³⁰

We detected an incremental risk of acquiring CLABSI of 4% per CL day. Rey et al³¹ also found an association of CL days as a CLABSI risk factor.³¹

In this study, the CL type with the highest risk of CLABSI was internal jugular, followed by femoral. In contrast, Lorente et al¹⁵ found that the femoral site had higher risk for CLABSI than the jugular site. In another study, the femoral site is safer than the jugular site in patients with tracheostomy. These findings suggest that the use of tracheostomy in addition to the jugular site leads to a higher risk than the femoral site.³²

In this study, PICC was the CL with the lowest risk of CLABSI. Chopra et al³³ conducted a meta-analysis analyzing the risk of CLABSI associated with PICC compared with central venous catheters (CVCs). In their study, PICCs were associated with a lower risk of CLABSI than were CVCs (RR, 0.62; 95% CI, 0.40–

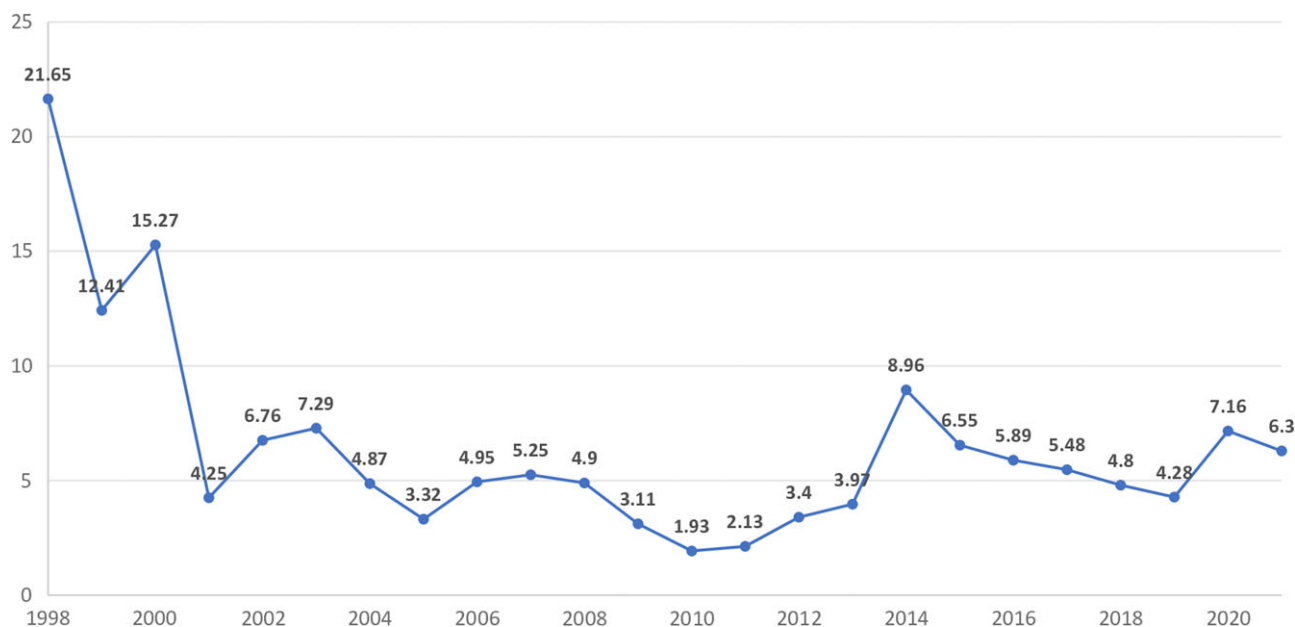


Fig. 2. CLABSI rate per 1,000 CL-days, per year.

0.94).³³ Also, Hon *et al*³⁴ conducted a meta-analysis analyzing rate of CLABSI between tunneled CVCs versus PICCs in adult home parenteral nutrition. In their study, PICC use was associated with a significantly lower rate of CLABSI (RR, 0.40; 95% CI, 0.19–0.83).³⁴

In our study, patients admitted to adult oncology and pediatric oncology ICUs had the highest risk of CLABSI. The CL–DU ratio, as a marker of severity of illness of patients, was highest at those types of ICUs,¹⁸ which could explain why these ICUs were associated with the highest risk of CLABSI.

We also noted that publicly owned facilities and teaching hospitals had a significantly higher risk of CLABSI than for-profit privately owned facilities. This finding is consistent with a previous study conducted in NICUs, in which the CLABSI rate per 1,000 CL days at university hospitals was 14.3 (95% CI, 12.9–15.7), the CLABSI rate at publicly owned facilities was 14.6; 95% CI, 11.0–19.1, and the CLABSI rate at for-profit, privately owned facilities was 10.8 (95% CI, 8.5–13.5).³⁵

Additionally, middle-income countries had a significantly higher risk of CLABSI than high-income countries. This finding could be explained by the likelihood of lower-quality programs in LMICs compared with high-income countries.³ In a previous study conducted in NICUs, analyzing the impact of the income level of the country and CLABSI, the CLABSI rate per 1,000 CL days in low-income countries was 37.0 (95% CI, 16.0–71.8) and the CLABSI rate in upper–middle-income countries was 17.6 (95% CI, 15.3–20.2).³⁵ In another study conducted in PICUs, the CLABSI rate in LMICs was 12.4 (95% CI, 10.5–14.3) and the CLABSI rate in upper–middle-income countries was 7.0 (95% CI, 6.3–7.9).³⁶ In both studies, the higher the income level of the country, the lower the CLABSI rate.

We did not detect an association between sex and CLABSI. This finding is consistent with other studies that also did not detect such association.³⁷

We did not detect an association between age and CLABSI, which is inconsistent with the study of Hsu *et al*,³⁸ who identified age >65 years as a CLABSI risk factor. We most likely did not find such an association because we controlled for 11 independent variables that were more significantly associated with CLABSI risk than age.

Some of the CLABSI risk factors identified in our study are unlikely to change, such as the income level of the country, facility ownership, hospitalization type, and ICU type. However, some of the risk factors for CLABSI we identified can be modified: CL days, LOS, use of tracheostomy and use of internal jugular or femoral lines.

Based on our findings, we should focus on strategies to reduce CL use, reduce LOS, prefer PICC instead of internal jugular or femoral insertion, and implement an evidence-based set of CLABSI prevention recommendations, such as those recently published by the Society for Healthcare Epidemiology of America (SHEA), Association for Professionals in Infection Control and Epidemiology (APIC), and the Infectious Diseases Society of America (IDSA).¹³ Also, the very high rate of CLABSI prevalent in LMICs^{1–4} can be reduced by utilizing a strategy of monitoring compliance with recommendations and providing performance feedback to healthcare personnel, as has been demonstrated in several LMICs.^{23–29}

Our study had several limitations. First, because this study was part of a surveillance system in which hospitals voluntarily participated for free; thus, these findings are not representative of all hospitals in LMICs. Second, changes in personal or professional practices may have influenced risk over time. Third, changes to CLABSI definitions made by the CDC that we adopted immediately may have influenced outcomes. Fourth, the unequal contribution of data by the participating hospitals may have affected these findings. Fifth, more clinical and epidemiological data as well as water quality could be useful to characterize the situation.

Table 4. Multiple Logistic Regression Analysis of Risk Factors for Central-Line–Associated Bloodstream Infections

Variable	aOR	95% CI	P Value
(1) Age	1.00	0.99–1.00	<.0001
(2) Sex, male	1.05	0.98–1.13	.17
(3) Length of stay	1.03	1.03–1.04	<.0001
(4) CL days	1.04	1.03–1.04	<.0001
(5) CL-DU ratio	0.91	0.89–0.93	<.0001
(6) Surgical hospitalization	1.12	1.03–1.21	<.0001
(7) Vascular catheter/insertion site			
Internal jugular	3.01	2.71–3.33	<.0001
Femoral	2.29	1.96–2.68	<.0001
Subclavian	2.13	1.92–2.36	<.0001
Arterial	1.89	1.69–2.13	<.0001
Hemodialysis temporary	1.84	1.41–2.39	<.0001
PICC ^a	1.48	1.02–2.18	.04
(8) Tracheostomy use	1.52	1.23–1.88	<.0001
(9) ICU type			
Adult-oncology ICU	4.35	3.11–6.09	<.0001
Pediatric-oncology ICU	2.51	1.57–3.99	<.0001
Pediatric ICU	2.34	1.81–3.01	<.0001
Medical ICU	2.04	1.61–2.59	<.0001
Medical-surgical ICU	1.93	1.56–2.39	<.0001
Surgical ICU	1.43	1.09–1.87	.01
Coronary ICU	0.86	0.65–1.14	.29
Neurosurgical ICU	0.99	0.67–1.14	.98
Neurologic ICU	1.64	0.91–2.96	.11
Trauma ICU	0.85	0.43–1.71	.66
(10) Facility ownership			
Publicly owned facilities	3.04	2.31–4.01	<.0001
Teaching hospitals	2.91	2.22–3.83	<.0001
For-profit privately owned facilities	2.01	1.52–2.63	<.0001
(11) Income level classification according with World Bank			
Upper–middle-income country	2.41	2.09–2.77	<.0001
Lower–middle-income country	2.23	1.93–2.58	<.0001

Note. CI, confidence interval; CL, central line; DU, device utilization; ICU, intensive care unit; LOS, length of stay; CLABSI, central-line–associated bloodstream infection; aOR, adjusted odds ratio.
^aPeripherally inserted central catheter.

Finally, the IPPs of the participating hospitals did not collect information on disease severity scores; instead, we used the CL-DU ratio to assess the severity of illness, and we adjusted the analysis to account for this independent variable.

Conclusion

The importance and relevance of this study lie in the fact that (1) it is a prospective cohort study using a standardized form with a denominators and numerators validation system, (2) always using the updated criteria and CLABSI definitions of the CDC NHSN, (3) with a duration longer than any study about risk factors for CLABSI never published before, (4) with the participation of a number of ICUs and countries, collecting data on patients,

patient-days, and CLABSIs that were never collected before for an analysis of risk factors for CLABSI, and (5) with multiple logistic regression analysis adjusting for risk factors for 11 variables that have never been analyzed simultaneously before. Undoubtedly, this scientific work provides evidence about the independent variables that are risk factors for CLABSI and can serve as a guide for practice at the hospital level and also be incorporated into recommendations, whether regional, national, or international.

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potential competing interests, such as employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

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