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Major Article

Multinational prospective cohort study of incidence and risk factors for central line-associated bloodstream infections in ICUs of 8 Latin American countries

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Background: Our objective was to identify central line (CL)-associated bloodstream infections (CLABSI) rates and risk factors in Latin-America.

Methods: From January 1, 2014 to February 10, 2022, we conducted a multinational multicenter prospective cohort study in 58 ICUs of 34 hospitals in 21 cities in 8 Latin American countries (Argentina, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, Mexico, Panama). We applied multiple-logistic regression. Outcomes are shown as adjusted-odds ratios (aOR).

Results: About 29,385 patients were hospitalized during 92,956 days, acquired 400 CLABSIs, and pooled CLABSI rate was 4.30 CLABSIs per 1,000 CL-days. We analyzed following 10 variables: Gender, age, length of stay (LOS) before CLABSI acquisition, CL-days before CLABSI acquisition, CL-device utilization (DU) ratio, CL-type, tracheostomy use, hospitalization type, intensive care unit (ICU) type, and facility ownership, Following variables were independently associated with CLABSI:

LOS before CLABSI acquisition, rising risk 3% daily (aOR=1.03;95%CI=1.02-1.04; $P < .0001$); number of CL-days before CLABSI acquisition, rising risk 4% per CL-day (aOR=1.04;95%CI=1.03-1.05; $P < .0001$); publicly-owned facility (aOR=2.33;95%CI=1.79-3.02; $P < .0001$). ICU with highest risk was medical-surgical (aOR=2.61;95%CI=1.41-4.81; $P < .0001$). CL with the highest risk were femoral (aOR=2.71;95%CI=1.61-4.55; $P < .0001$), and internal-jugular (aOR=2.62;95%CI=1.82-3.79; $P < .0001$). PICC (aOR=1.25;95%CI=0.63-2.51; $P = .52$) was not associated with CLABSI risk.

Conclusions: Based on these findings it is suggested to focus on reducing LOS, CL-days, using PICC instead of femoral or internal-jugular; and implementing evidence-based CLABSI prevention recommendations.

Latin American countries have significantly higher rates of central-line associated bloodstream infections (CLABSI) than high-income countries, according to research by the International Nosocomial Infection Control Consortium (INICC). This is demonstrated in reports for each individual Latin American country,[1-10] international reports that include Latin American countries,[11,12] and reviews of the literature that include Latin American countries.[13-16]

According to a 2009 study, the CLABSI rate ranged from 1.6 to 44.6 CLABSIs per 1,000 central line (CL)-days in adult ICUs and from 2.6 to 60.0 CLABSIs per 1,000 CL-days in neonatal intensive care units in low and middle income countries (LMIC), including Latin America.[13]

CLABSIs are linked to 12%-25% greater mortality[17] and higher costs.[18] Intensive care unit (ICU) patients without any health care-associated infections (HAIs) had a mortality rate of 17.1%, CLABSI patients have a mortality rate of 48.2%, and CLABSI patients with CAUTI and VAP have a mortality rate of 63.4%, according to INICC.[11]

Studies have already identified the following factors as CLABSI risk factors (RFs): lower nurse-to-patient ratio in the ICU,[19] float nurse providing care for the patient,[20] total parenteral nutrition,[19,21] extended stay in the hospital before catheterization,[19] indwelling time,[19] heavy microbial colonization at insertion site or catheter hub,[19] multiple CLs,[19,21] multilumen catheters,[19] femoral site,[22,23] guidewire exchange[21] and a couple of other variables.

However, no study has simultaneously looked at multiple countries (Argentina, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, Mexico, Panama) or different kinds of CLs to figure out CLABSI RFs in ICUs. Furthermore, no prospective research has been done over 9 years. No study has simultaneously looked into the associations between the following 10 variables and CLABSI: gender, age, length of stay (LOS) prior to CLABSI acquisition, CL-days prior to CLABSI acquisition, the ratio of CL-device utilization (DU) as a measure of patients' illness severity, the types of CL, the use of tracheostomy, the type of hospitalization, the type of ICU, and the ownership of the facility. The objectives of this study are to identify CLABSI rates and the CLABSI RFs among the aforementioned 10 variables and the safest type of CL.

METHODS

Study population and design

Between January 1, 2014 and February 10, 2022, a period of 8 years, this international, multicenter, cohort, prospective study was conducted with patients admitted to 58 ICUs of 34 hospitals in 21 cities in 8 Latin American countries (Argentina, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, Mexico, Panama).

Prospective cohort surveillance of health care associated infections

Data for each patient were collected at the time of ICU admission. Each patient's bedside received daily visits from infection prevention professional (IPP) from the time of admission until discharge. Data were gathered on all prospectively enrolled patients who were admitted to an ICU using the INICC Surveillance Online System (ISOS). An IPP visits each hospitalized patient in the ICU with a tablet, links to ISOS, and uploads the patient's data in real-time.[24]

The information is provided during the time of admission and includes details about the location, including the country, city, admission date, and ICU type, as well as details about the patient, including gender and age, the type of hospitalization, and the use of invasive devices. IPPs upload data about the patient's invasive devices and positive cultures up until the patient is discharged. When a patient displays symptoms or signs of infection, a specialist in infectious diseases evaluates the patient to check for HAI.[24] When IPPs upload the culture results to the ISOS, the ISOS right away notifies them and guides them to an online module where they can verify all the CDC NHSN HAI criteria to confirm the presence and kind of HAI.[24]

The participating hospitals' IRBs approved the study. Confidentiality is maintained for both patient and hospital identities.

INICC surveillance online system

The characteristics of any particular patient or the number of device-days linked with specific patients are not included in the standard CDC/NSHN methodology, which say that HAI denominators are device-days gathered from all patients as pooled data.[25] The ISOS, an online platform used for INICC HAI surveillance, uses the CDC NHSN criteria and standards.[25] Additionally, ISOS gathers data on each patient individually, including those with and without HAI.[24] The determination of CLABSI RFs is made possible by the capacity to compare data from all patients admitted to the ICU using multiple variables.

Study definitions

Health care associated infection

The CDC's definitions of HAI were utilized during surveillance and all of their updates going forward through 2022.[25] Throughout the entire 9-year study period, the IPPs of all participating hospitals used the most recent CDC definition of HAIs. That is, whenever the CDC amended its criteria, our IPPs began using the new, updated definitions.[25]

Central line

An intravascular-catheter that terminates at or close to the heart, or in one of the great vessels AND is 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/vein.[25]

Primary bloodstream infection

A laboratory-confirmed bloodstream infection (LCBI) that is not secondary to an infection at another body site.[25]

Central line-associated bloodstream infection

A LCBI where an eligible BSI organism is identified, and an eligible CL is present on the LCBI or the day before.[25]

Laboratory-confirmed bloodstream infection 1

Patient of any age has a recognized bacterial or fungal pathogen, not included on the NHSN common-commensal list: Identified from 1 or more blood specimens obtained by a culture OR Identified to the genus or species level by nonculture based microbiologic testing methods. *AND* Organism(s) identified in the blood are not related to an infection at another site.[25]

Laboratory-confirmed bloodstream infection 2

A patient of any age has at least *one* of the following signs or symptoms: fever (>38.0°C), chills, or hypotension. AND 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.[25]

Common commensal

Common Commensal organisms include, but are not limited to, *diphtheroids* (*Corynebacterium* spp. not *C. diphtheria*), *Bacillus* spp. (not *B. anthracis*), *Propionibacterium* spp., coagulase-negative *staphylococci* (including *S. epidermidis*), viridans group *streptococci, Aerococcus* spp. *Micrococcus* spp. and *Rhodococcus* spp.[25]

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 RF. CL/DU ratio also serve as a marker for the severity of illness of patients which is an intrinsic RF for HAI.[25]

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 gains 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 gains for their owners).[26]

Statistical analysis

Patients with and without CLABSI were compared using multiple logistic regression. Statistically significant variables were independently associated with an increased risk for CLABSI. 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 analyzed following ten independent variables and its association with the outcome (CLABSI): (1) age; (2) gender (female, male); (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) type and insertion site of CL (internal jugular, femoral, subclavian, PICC, temporary for hemodialysis); (7) tracheostomy use; (8) hospitalization type (medical, surgical); (9) ICU type (medical-surgical, medical, pediatric, surgical, coronary, neurosurgical, cardiothoracic, adult-oncology); and (10) facility ownership (publicly owned, not-for-profit privately owned, for-profit privately owned, and teaching hospitals).[26] The evaluated outcome was the acquisition of CLABSI according to CDC/NHSN definitions.[25]

For analysis of CLABSI RF we use data of following 8 countries (Argentina, Brazil, Colombia, Costa Rica, Dominican Republic, Ecuador, Mexico, Panama) that collected all required ten independent variables (gender, age, LOS before CLABSI acquisition, CL-days before CLABSI acquisition, CL/DU ratio, CL type, tracheostomy use, hospitalization type, and ICU type, facility ownership. All statistical analyses were performed using R software, version 4.1.3.

RESULTS

A multinational, multicenter, cohort, prospective surveillance research of CLABSIs was conducted over an 8-year period, from January 1, 2014, to February 10, 2022, in 58 ICUs of 34 hospitals located in 21 cities in 8 Latin American nations that are participating in INICC.

The hospitals' participation times in this cohort research ranged from 1.17 to 226.07 months (Mean, 35.44; SD, 42.67). The patient's characteristics and setting data are shown in Table 1. The stratified CLABSI rates is shown in Table 2 according to and per country. Pooled CLABSI rate was 4.30 CLABSIs per 1,000 CL-days (400 CLABSIs/92,956 CL-days).

Using multiple logistic regression, it was demonstrated that the following variables had a significant correlation with CLABSI: LOS before CLABSI acquisition, rising risk of 3% each day (aOR=1.03, 95%CI=1.02-1.04, $P < .0001$), number of CL-days before CLABSI acquisition, rising risk of 4% per CL-day (aOR=1.04, 95%CI=1.03-1.05, $P < .0001$), and hospitalized at a publicly-owned facility (aOR=2.33, 95%CI=1.79-3.02, $P < .0001$) when compared to teaching hospitals or for profit privately owned facilities hospitals. Medical-surgical ICU had the highest risk (aOR=2.61, 95%CI=1.41-4.81, $P < .0001$). CLs with the highest risk were femoral (aOR=2.71, 95%CI=161-4.55, $P < .0001$), and internal-jugular (aOR=2.62, 95%CI=1.82-3.79, $P < .0001$). PICC was not associated with risk for CLABSI (Table 3). Period from 2014 to 2016 (aOR=6.38, 95%CI=4.27-9.56, $P < .0001$) showed the highest risk followed from the period from 2017 to 2019 (aOR=2.16, 95%CI=1.59-2.93, $P < .0001$), both compared with the period from 2020 to 2022.

Age, gender, tracheostomy use, and type of hospitalization, were not associated with CLABSI risk in this study after controlling for all 10 confounders (Table 3).

Table 1
Setting and patient characteristics. Period 2014 to 2022

	Patients without CLABSI	Patients with CLABSI
Period	January 1, 2014 to February 10, 2022	January 1, 2014 to February 10, 2022
Years, n	9	9
ICUs, n	58	58
Hospitals, n	34	34
Cities, n	21	21
Countries, n	8	8
Total patients, n	28,985	400
Total patients-days, n	190,275	7,432
Average LOS, mean, SD	Mean = 6.56, SD = 7.30	Mean = 18.58, SD = 15.45
CLABSI, n	0	400
Survival status, n (%)		
Alive	25,306 (87.31%)	284 (71.00%)
Death	3,679 (12.69%)	116 (29.00%)
Number of patients admitted per facility ownership, n (%)		
For-profit privately owned facilities	15,202 (52.45%)	133 (33.25%)
Publicly owned facilities	9,320 (32.15%)	233 (58.25%)
Teaching hospitals	4,288 (14.79%)	41 (10.25%)
Not-for-profit privately owned facilities	175 (0.60%)	3 (0.75%)
Number of patients per Hospitalization type, n (%)		
Medical hospitalization	17,124 (59.08%)	230 (57.5%)
Surgical hospitalization	11,861 (40.92%)	170 (42.5%)
Number of patients admitted per type of ICU, n (%)		
Medical-Surgical ICU	17,731 (61.17%)	287 (71.75%)
Coronary ICU	3,140 (10.83%)	24 (6.00%)
Medical ICU	2,319 (8.00%)	25 (6.25%)
Surgical ICU	2,010 (6.93%)	10 (2.50%)
Pediatric ICU	1,832 (6.32%)	35 (8.75%)
Cardio-thoracic ICU	1,265 (4.36%)	14 (3.50%)
Neuro-Surgical ICU	303 (1.05%)	2 (0.50%)
Adult-Oncology ICU	158 (0.55%)	3 (0.75%)
Gender, n (%)		
Male	16,080 (55.48%)	238 (59.50%)
Female	12,905 (44.52%)	162 (40.50%)
Age, mean, SD	Mean = 52.24, SD = 24.33	Mean = 46.22, SD = 24.81
Device-days and device utilization ratio		
Total CL-days, n	88,032	4,924
CL-days per patient, n, mean, SD	Mean = 4.51, SD =7.92	Mean = 12.60, SD= 17.72
CL-utilization ratio, mean, SD	Mean = 0.61, SD = 1.76	Mean = 0.87, SD = 0.64
Number of CL-days per type of CL, n (%)		
Subclavian	51,789 (58.83%)	2,715 (55.14%)
Jugular	21,050 (23.91%)	1,310 (26.60%)
Femoral	6,442 (7.32%)	430 (8.73%)
Hemodialysis temporary	3,899 (4.43%)	203 (4.12%)
PICC	4,852 (5.51%)	266 (5.40%)
Tracheostomy use, n (%)		
Yes	684 (2.35%)	17 (4.25%)
No	28,404 (97.65%)	383 (95.75%)
Number of patients per time period		
Time period 1 (2014-2016)	20,010 (69.04%)	289 (72.25%)
Time period 2 (2017-2019)	7,999 (27.60%)	57 (14.25%)
Time period 3 (2020-2022)	976 (3.36%)	54 (13.50%)

CL, central line; CLABSI, central line associated bloodstream infection; *ICU*, intensive care unit; *LOS*, length of stay; *SD*, standard deviation.

DISCUSSION

Pooled CLABSI rates from our study showed a rate of 4.30 CLABSIs per 1,000 CL-days. The CLABSI rates of our study are lower than the pooled CLABSI rates reported by INICC, which are 5.30 CLABSIs per 1,000 CL-days and include 45 countries in Asia, Africa, Eastern Europe, Latin America, and the Middle East.[11] The pooled rate of CLABSI in our current study, on the other hand, is significantly higher than those in the CDC NHSN report, which are 0.8 CLABSI per 1,000 CL-days.[25]

When applied multiple logistic regression to identify risk factors for CLABSI, on the one hand, we found that the CLs with the highest risk of CLABSI were femoral, and internal jugular. On the other hand, PICC was not associated with risk for CLABSI. Coincidentally, Templeton et al[27] identified the femoral and internal jugular veins as those with the highest risk for CLABSI, and Alonso-Echanove et al[20] identified PICC with a lower risk of CLABSI.

We discovered a 4% daily increase in the risk of acquiring CLABSI associated with the duration of a CL. Costello et al, conducted a matched case control study at a pediatric ICU to identify CLABSI risk factors. One of the independent risk factors identified for CLABSI was central line days > or =7 (OR = 6.06 [1.65-21.83]).[28]

The risk of CLABSI increased by 3% every day in correlation with the LOS. García et al[29] conducted a study at a neonatal ICU to identify risk factors for CLABSI. Multivariate analysis showed that length of hospitalization >/=14 d (OR 4.6, 95% CI 1.8-11.4) was independent factors associated with CLABSI.

Patients admitted to medical/surgical intensive care units have the highest risk of CLABSI, according to the current study. These ICUs have a high CL/DU ratios, a measure of the severity of patients'

Table 2
Central line associated bloodstream infections rates stratified per country, per ICU type, per facility ownership, and per vascular catheter. Period 2014 to 2022

	Patients, n	Patient-days, n	CLABSI, n	CL-days, n	CLABSI rate[c]	95% CI
Country *						
1. Argentina	5,595	38,752	110	23,723	4.64	4.61-4.66
2. Brazil	8,695	60,992	48	52,186	0.92	0.91-0.93
3. Colombia	7,525	51,734	58	28,402	2.04	2.03-2.06
4. Costa Rica	531	2,306	1	1,674	0.60	0.56-0.64
5. Dominican Republic	1,330	7,453	40	3,432	11.66	11.54-11.77
6. Ecuador	611	3,950	10	3,168	3.16	3.10-3.22
7. Mexico	4,805	30,343	125	23,961	5.22	5.19-5.25
8. Panama	293	2,177	8	1,783	4.49	4.39-4.59
ICU type †						
1. Adult-oncology	161	552	3	374	8.02	7.74-8.31
2. Medical-surgical	18,018	123,408	287	86,658	3.31	3.30-3.32
3. Pediatric	1,867	17,153	35	11,554	3.03	2.99-3.06
4. Surgical	2,020	5,755	10	4,319	2.32	2.27-2.36
5. Neuro-surgical	305	2,866	2	1,891	1.06	1.01-1.11
6. Medical	2,344	17,223	25	12,180	2.05	2.03-2.08
7. Coronary	3,164	20,932	24	13,107	1.83	1.81-1.85
8. Cardio-thoracic	1,279	8,376	14	7,857	1.78	1.75-1.81
9. Trauma	154	729	0	103	0	NA
10. Pediatric-oncology	13	63	0	34	0	NA
11. Neurologic	60	650	0	252	0	NA

CI, confidence interval; *CL*, central line; *CLABSI*, central line associated bloodstream infection; *ICU*, intensive care unit;
*Countries are listed alphabetically.
†ICUs types are listed in order of the highest to lowest central line associated bloodstream infections rate.
[c]CLABSI per 1,000 central line-days.

illnesses, which may explain why these ICUs are linked to the highest risk of CLABSI.[25]

Additionally, this study found that publicly owned facilities have substantially greater risk for CLABSI than teaching hospitals or for-profit privately owned facilities. But, according to a prior NICU study, the CLABSI rate per 1,000 CL-days in teaching hospitals was 14.3, with a 95% confidence interval of 12.9-15.7, and at publicly owned facilities was 14.6; with a 95% confidence interval of 11.0-19.1.[30]

Table 3
Multiple logistic regression analysis of risk factors for central line associated bloodstream infections. Period 2014 to 2022

	aOR	95% CI	*P* value
Length of stay	1.03	1.02-1.04	<.0001
CL-days	1.04	1.03-1.05	<.0001
CL-utilization ratio	0.83	0.64-1.09	<.0001
Tracheostomy use	0.84	0.49-1.46	.52
Age	1.00	0.99-1.00	.03
Reference level: female gender			
Gender, male	1.12	1.00-1.39	.09
Reference level: Absence of CL			
Femoral	2.71	1.61-4.55	<.0001
Jugular	2.62	1.82-3.79	<.0001
Subclavian	2.35	1.69-3.28	<.0001
PICC	1.25	0.63-2.51	.52
Hemodialysis temporary	1.01	0.43-2.31	.98
Reference level: For-profit privately owned facilities			
Publicly owned facilities	2.33	1.79-3.02	<.0001
Teaching hospitals	0.89	0.61-1.32	.09
Reference level: Medical Hospitalization			
Surgical Hospitalization	1.01	0.81-1.27	.23
Reference level: Cardio-thoracic ICU			
Medical-Surgical ICU	2.61	1.41-4.81	<.0001
Medical ICU	1.59	0.75-3.35	.26
Pediatric ICU	1.55	0.72-3.36	.06
Surgical ICU	1.38	0.56-3.41	.66
Coronary ICU	1.33	0.64-2.73	.42
Neuro-Surgical ICU	0.42	0.07-2.51	.41
Reference level: Time period 3 (2020-2022)			
Time period 1 (2014-2016)	6.38	4.27-9.56	<.0001
Time period 2 (2017-2019)	2.16	1.59-2.93	<.0001

aOR, adjusted odds ratio; *CI*, confidence interval; *CL*, central line; CLABSI, central line associated bloodstream infection; ICU, intensive care unit; LOS, length of stay.

Tracheostomy use did not appear to increase the risk of CLABSI in our study. Al-Shukri et al, conducted a study to estimate CLABSI risk factors, and one of the identified risk factors for ICU-acquired CLABSIs was tracheostomy use (OR = 5.34, *P* = .004).[31]

There was no correlation between gender and CLABSI in the current investigation. This finding is not consistent with a study, that found an association among female gender and CLABSI risk,[31] and is also not consistent with a study that found that male gender was associated with higher risk of CLABSI.[32] As a conclusion, available data shows contradictory outcomes regarding the association of gender with risk for CLABSI.

Age and CLABSI were not found to be related in the current study, and it is inconsistent with the study of Hsu et al[33] because they identified that age >65 years as a CLABSI RF. We adjusted for 10 independent variables that are more closely linked with CLABSI risk than age, consequently, this could explain why we were unable to detect such a connection.

We identified that the ownership of the facility and the kind of ICU are 2 CLABSI RFs, but they are unlikely to change. However, some of the RFs for CLABSI that we identified, like CL-days before CLABSI acquisition, LOS before CLABSI acquisition, and the use of femoral or internal jugular lines, are modifiable. In light of our findings, it is suggested that we focus on ways to reduce the use of CL, shorten hospital stays prioritize PICC over femoral or internal jugular, and implement a set of evidence-based CLABSI prevention recommendations, such as those just recently issued by APIC/IDSA/SHEA/.[19]

The highly high prevalence of CLABSI that is typical in Latin America[1-16] may also be decreased by a system of monitoring compliance with recommendations and providing performance feedback to healthcare providers, as demonstrated in other LMICs.[34-40]

Our study has some limitations. First off, because it is a subset of a surveillance system in which institutions willingly engage for free, this study is not representative of all hospitals in Latin America. Second, the CLABSI rates in our study are probably lower than the CLABSI rates reported in other hospitals that are not participating in our study because the hospitals that take part in our surveillance system are probably the ones who have a higher-quality CLABSI surveillance and prevention program. Third, it's probable that changes in personal or professional behavior over time have had an impact on risk.

Fourth, the CLABSI definition changes made by the CDC that we swiftly accepted could have had an impact on the outcomes. Last but not least, we didn't include risk adjusted for severity of illness, we used the CL/DU ratio to measure the severity of patients' illnesses rather than the disease severity scores that were collected by the IPPs of the participating institutions, and we adjusted the analysis to take this independent variable into account.

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