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## Major Article

## Six-year multicenter study on short-term peripheral venous catheters-related bloodstream infection rates in 204 intensive care units of 57 hospitals in 19 cities of India: International Nosocomial Infection Control Consortium (INICC) findings

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For a list of all the members of the International Nosocomial Infection Control Consortium (INICC) and all the co-authors of this study, see the [Appendix](#).

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#### Key Words:

Hospital infection  
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 Surveillance

**Background:** Short-term peripheral venous catheters-related bloodstream infections (PVCr-BSIs) rates have not been systematically studied in developing countries, and data on their incidence by number of device-days are not available.

**Methods:** Prospective, surveillance study on PVCr-BSI conducted from September 1, 2013 to May 31, 2019 in 204 intensive care units (ICUs), members of the International Nosocomial Infection Control Consortium (INICC), from 57 hospitals in 19 cities of India. We applied US INICC definition criteria and reported methods using the INICC Surveillance Online System.

**Results:** We followed 7,513 ICU patients for 296,893 bed-days and 295,795 short term peripheral venous catheter (PVC)-days. We identified 863 PVCr-BSIs, amounting to a rate of 2.91/1,000 PVC-days.

Mortality in patients with PVC but without PVCr-BSI was 4.14%, and 11.59% in patients with PVCr-BSI. The length of stay in patients with PVC but without PVCr-BSI was 4.13 days, and 5.9 days in patients with PVCr-BSI. The micro-organism profile showed 68% of gram negative bacteria: *Escherichia coli* (23%), *Klebsiella* spp (15%), *Pseudomonas aeruginosa* (5%), and others. The predominant gram-positive bacteria were *Staphylococcus aureus* (10%).

**Conclusions:** PVCr-BSI rates found in our ICUs were much higher than rates published from industrialized countries. Infection prevention programs must be implemented to reduce the incidence of PVCr-BSIs.

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Short-term peripheral venous catheters (PVCs) therapy is among the most habitual invasive procedure performed in health care settings worldwide.<sup>1–3</sup> As stated in a recent systematic review, short-term PVCs are widely used, amount to 200 millions of them being inserted in the United States each year,<sup>3</sup> and according to different point-prevalence studies, they accounted to 80%, 90%, and 95% of all intravascular devices placed in hospitalized patients in France, in Scotland, and Spain, respectively.<sup>3</sup>

It has been stated in the 2016 Infusion Nurses Society standards of practice<sup>4</sup> and the 2017 International Nosocomial Infection Control Consortium (INICC) Bundle for the prevention of central and peripheral lines-related BSIs that there is no time limit recommended for PVC removal.<sup>5</sup>

Such high prevalence of short-term PVCs inserted regularly has been reported to result in considerable morbidity, excess length of stay (LOS) and hospital costs, prolonged antibiotics treatments, and BSIs.<sup>6</sup>

In addition, it has been reported that the overall PVC failure rate ranges from 35% to 50%,<sup>1,2,7</sup> with such failures being responsible for causing PVC-related adverse events, such as phlebitis, occlusion/

mechanical failure, infiltration, dislodgment, and bloodstream infections (BSIs).<sup>1,2,7–12</sup>

Since short-term PVCs have been rarely associated with BSIs, as stated in the 2011 CDC guidelines for the prevention of intravascular catheter-related BSIs,<sup>3,13,14</sup> most studies have therefore been focused on central line-associated BSIs (CLABSIs), rather than PVC-related bloodstream infections (PVCr-BSIs), which to date have not been thoroughly analyzed.<sup>6</sup>

PVCr-BSIs are confirmed by the presence of positive blood cultures related by clinical data to short-term PVCs.<sup>1</sup> In health care settings from industrialized countries, the incidence of PVCr-BSIs in ICU patients have been reported to be 0.5 per 1,000 short-term PVCs-days in ICUs from Australia, Italy and the United States,<sup>14</sup> and 0.67 PVCr-BSIs per 1,000 short-term PVCs-days in pediatric and neonatal ICUs from Australia.<sup>15</sup> As for the incidence of PVCr-BSI in resource-limited countries, there is a gap in the literature, as comprehensive data remain not available.

This prospective surveillance, which was conducted during 6 years, between September 1, 2013 and May 31, 2019 in 204 ICUs in 57 hospitals that participate in INICC,<sup>9–11,16</sup> is the first comprehensive



one conducted in India to analyze the incidence rate, bacterial resistance, LOS, and mortality attributable to PVCr-BSI.

## METHODS

### Background on INICC

INICC is comprised of a group of hospitals, in 210 cities, in 54 countries, and in 6 World Health Organization (WHO) regions: Africa, the Americas, Eastern Mediterranean, Europe, South East Asia, and Western Pacific.

INICC has become the oldest and largest source of aggregate standardized international data on the epidemiology of health care-associated infections (HAIs) worldwide.<sup>9,17</sup>

INICC is focused on the surveillance and prevention of HAIs in adult, pediatric and neonatal ICUs, step down units, inpatient wards, and of surgical site infections in surgical procedures hospital-wide.

### Study design

This prospective, cohort surveillance study was conducted by means of an online platform called INICC Surveillance Online System (ISOS). Through ISOS, validation of each PVCr-BSI was checked by infection preventionists and the recorded signs and symptoms of infection and the results of cultures, laboratory and radiographic studies, as well as other tests, are scrutinized to assure that the last US CDC-NHSN criteria for PVCr-BSIs were met, in accordance with the definition presented below.<sup>17,18</sup>

### INICC methods

The ISOS includes the implementation of CDC/NHSN's methodology, but adds the collection of other data essential to increase infection preventionists' sensitivity of to detect PVCr-BSIs, and avoid underreporting.<sup>17</sup> According to standard CDC/NHSN methods, numerators are the number of health care-acquired infections related to a specific, and denominators are device-days collected from all patients, as pooled data; that is, without determining the number of device-days related to a particular patient, and without collecting features or characteristics per specific patient.

This aspect differs from the ISOS, because the design of the cohort study through the ISOS also includes the infection preventionists' collecting of specific data per patient from *all* patients, both those with and those without PVCr-BSI, such as invasive devices utilization, age, gender, date of admission, date of discharge, LOS, microorganism profile of HAIs, bacterial resistance, and mortality, among several others.

### Outcome surveillance data collection and validation

This study presents the results of Outcome Surveillance of PVCr-BSIs in the ICU through the use of the ISOS, which follows the INICC protocol and allows the classification of prospective, active, and cohort data into specific module protocols.

The site-specific criteria include reporting instructions and provide full explanations integral to their adequate application. Infection preventionists collected daily data on PVCr-BSIs, and denominator data, such as specific device-days in the ICUs, patient-days, microorganism profile, and bacterial resistance.

Validation is an essential feature of the ISOS to maximize the sensitivity and accuracy of surveillance data. Each PVCr-BSI reported by an infection preventionist is validated (ie, scrutinized to be certain that all criteria are satisfied to justify its recording as a PVCr-BSI). The validation process also includes data reported for putatively uninfected patients to permit detection of unreported but true PVCr-BSIs. To do that, the ISOS shows an online message to the infection

preventionists asking them to check the criteria for that putative PVCr-BSI.<sup>17</sup>

### Training

The INICC team trained and provided infection preventionists with manuals, training tools, and tutorial movies, which described in detail how to perform surveillance and upload surveillance data through the ISOS.

In addition, investigators attended webinars, and had continuous access to a support team at the INICC headquarters in Buenos Aires, Argentina. The INICC support team evaluates on a routine basis that infection preventionists perform surveillance correctly through the ISOS online platform, and sends emails and shows online messages to infection preventionists asking them to check and review surveillance data and specific criteria.

### Definitions

**BSI:** We used US CDC/NHSN's definitions for BSI from its publication in 2013 and their amendments until its latest publication in 2019.<sup>19–22</sup>

**PVCr-BSI:** US CDC/NHSN's definitions do not include the surveillance definition of PVCr-BSI.<sup>19–22</sup> We applied the CDC/NHSN's definition for patients that met all the criteria for BSI, but never used central lines (CL), nor peripherally inserted central catheters, and that only used short-term PVCs, before and or after the acquisition of a BSI.

### Calculation

Data uploaded to ISOS were used to calculate PVCr-BSI rates per 1,000 device-days, mortality, and LOS, according to the following formulas: device-days consisted of the total number of PVC-days.

Crude excess mortality of PVCr-BSI equaled crude mortality of ICU patients with PVCr-BSI minus crude mortality of patients without PVCr-BSI.

Crude excess LOS of PVCr-BSI equaled crude LOS of ICU patients with PVCr-BSI minus crude LOS of patients without PVCr-BSI.

Device utilization ratio (DUR) equaled the total number of PVCr-days divided by the total number of bed days.

To calculate extra LOS and extra mortality, all CLABSI were excluded, and only patients with short-term PVCs, both with or without BSIs, were included.

### Follow-up of patients

To estimate PVCr-BSI rate and excess mortality attributable to PVCr-BSI, all patients were followed over 15 days, after step-down from the ICU.

### Statistical analysis

ISOS version 2.0 (Buenos Aires, Argentina), was used to calculate PVCr-BSI rates, DURs, LOS, and mortality. EpiInfo version 6.04b (CDC, Atlanta, GA), SPSS 16.0 (SPSS Inc. an IBM company, Chicago, IL). 95% confidence intervals and *P* values were determined for all outcomes.

### Setting

The study was conducted in 204 ICUs from 57 hospitals in 19 cities of India, through the implementation of the ISOS, as described above.

All the cohort of patients admitted to the ICUs during the study period was enrolled in the study with hospitals' Research Ethics Committees approval.

**Table 1**  
Type of ICU and hospitals' ownership

ICUs, type	No. of ICUs (%)
Cardiothoracic	11 (5.39)
Coronary	18 (8.82)
Medical	41 (20.10)
Medical-surgical	66 (32.35)
Neuro surgical	16 (7.84)
Neurologic	6 (2.94)
Oncology	2 (0.98)
Pediatric	9 (4.41)
Respiratory	4 (1.96)
Surgical	20 (9.8)
Trauma	5 (2.45)
Other	6 (2.94)
Total ICUs, n (%)	204 (100)
Hospitals	
Academic teaching, n (%)	8 (14)
Public, n (%)	6 (11)
Private community, n (%)	43 (75)
Total Hospitals, n (%)	57 (110)

ICU, intensive care unit.

In accordance with the INICC's Charter, the identity of all INICC hospitals and cities is kept confidential.<sup>17</sup>

## RESULTS

During the study period of 6 years, from September 1, 2013 to May 31, 2019, the mean length of participation of the ICUs was 20 months (SD: 27.3), range from 1 to 149 months.

Table 1 shows type of ICUs and type of hospitals' ownership.

Table 2 shows PVCr-BSI rates and DURs by type of ICU.

Table 3 provides data on crude ICU mortality and crude LOS in patients with and without PVCr-BSI.

Table 4 provides data on bacterial resistance of pathogens isolated from patients with PVCr-BSI in adult and pediatric ICUs.

Figure 1 shows microorganism profile of PVCr-BSIs.

**Table 2**

Pooled means, 95% confidence intervals of the distribution of short-term peripheral venous catheter-related bloodstream infections rates by type of location, in adult and pediatric intensive care units

Type of ICU	ICU, n	Patients, n	PVCr-BSIs, n	PVC days, n	Pooled PVCr-BSI rate	DU ratio, mean	95% CI for DU mean
Cardiothoracic	11	385	1	1,747	0.57	1.085	0.966 1.204
Coronary	18	1,875	19	7,225	2.63	1.082	1.059 1.105
Medical	41	14,088	81	59,116	1.37	0.967	0.959 0.976
Medical-surgical	66	41,709	686	164,719	4.16	1.012	1.006 1.017
Neuro surgical	16	2,818	2	12,123	0.16	0.994	0.972 1.017
Neurologic	6	446	14	2,009	6.97	1.142	1.109 1.175
Oncology	2	4	0	31	0.00	1.500	–0.091 3.091
Other	6	270	3	1,020	2.94	0.993	0.965 1.021
Pediatric	9	2,950	49	16,556	2.96	1.282	1.261 1.303
Respiratory	4	9	0	34	0.00	0.859	0.608 1.110
Surgical	20	4,781	2	23,346	0.09	0.982	0.966 0.997
Trauma	5	2,178	6	7,869	0.76	0.980	0.966 0.994
Pooled (adult and pediatric ICUs)	204	71,513	863	295,795	2.92	1.01	1.01 1.02

CI, confidence interval; DU, device utilization; ICU, intensive care unit; PVC, peripheral venous catheter; PVCr-BSI, short-term peripheral venous catheter-related bloodstream infections.

**Table 3**

Pooled means of the distribution of crude mortality and length of stay of intensive care unit patients with short-term peripheral venous catheter-related bloodstream infections in adult and pediatric intensive care units combined

	No. of deaths	No. of patients	Pooled crude mortality, % (mean; SD; 95% CI)	LOS, total days	Pooled mean LOS, days, (SD; 95% CI)
Adult and pediatric patients, without PVCr-BSI	2,926	70,650	4.14% (0.04; 0.20; 0.03–0.05)	291,800	4.13 (3.97; 4.12–4.13)
Adult and pediatric patients, with PVCr-BSI	100	863	11.59% (0.12; 0.05–0.18)	5,093	5.9 (5.54; 5.75–6.05)

CI, confidence interval; LOS, length of stay; PVCr-BSI, short-term peripheral venous catheter-related bloodstream infections.

**Table 4**

Antimicrobial resistance rates in the intensive care units of the International Nosocomial Infection Control Consortium

Pathogen, antimicrobial	PVCr-BSI	
	No. of pathogenic isolated tested at INICC ICUs, pooled (n)	Resistance percentage (%)
<i>Pseudomonas aeruginosa</i>		
FQs	11	27.3
PIP or TZP	11	27.3
AMK	11	27.3
IPM or MEM	9	33.3
FEP	9	44.4
<i>Klebsiella pneumoniae</i>		
CRO or CAZ	29	79.31
IPM, MEM or ETP	19	68.42
<i>Acinetobacter baumannii</i>		
IPM or MEM	5	80.0
<i>Escherichia coli</i>		
CRO or CAZ	39	66.7
IPM, MEM or ETP	20	25.0
FQs	59	61.0
<i>Staphylococcus aureus</i>		
OXA	14	50.0
<i>Enterococcus faecalis</i>		
VAN	2	0.0

AMK, amikacin; CAZ, ceftazidime; CRO, ceftriaxone; ETP, ertapenem; FQs, fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin, or ofloxacin); IPM, imipenem; MEM, meropenem; OXA, oxacillin; PIP, piperacillin; PVC, peripheral venous catheter; PVCr-BSI, PVC-related bloodstream infections; TZP, piperacillin-tazobactam; VAN, vancomycin.

## DISCUSSION

To date, there are no previous representative studies of PVCr-BSI rates at national level in India, neither in Asia, nor in resource-limited countries worldwide in the 6 WHO regions.

In a recent prospective study conducted in Southern Odisha, India, with insufficient sample size, which included just 87 patients, the PVCr-BSI rate was 40.6/1,000 PVC-days.<sup>23</sup> This study was conducted



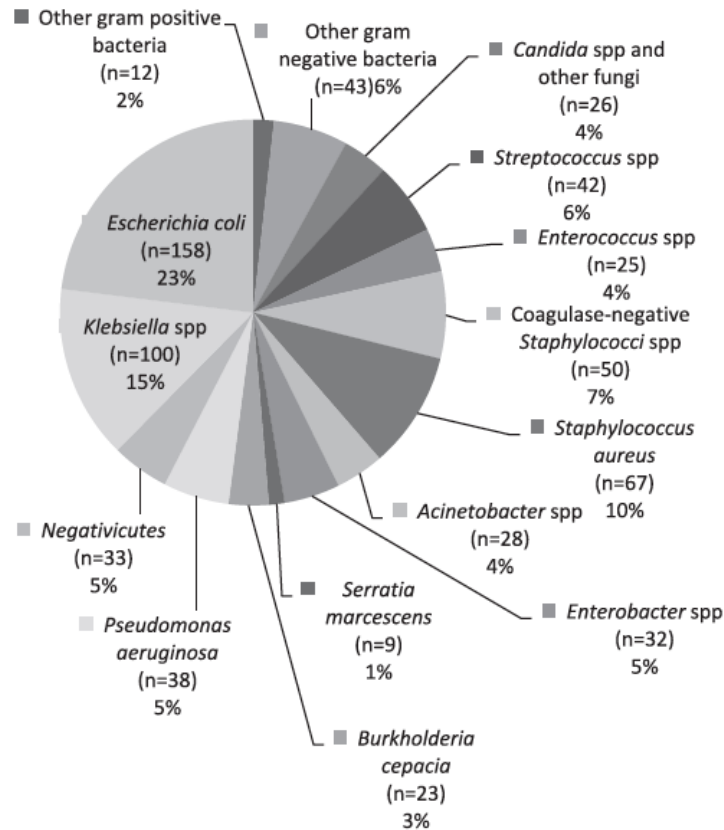


Fig 1. Microorganism profile of short-term peripheral venous catheter-associated bloodstream infections.

\*Other gram negative bacteria: It includes the following microorganisms that individually accounted for <1%: *Citrobacter* spp, *Megamonas*, *Providencia* sp, *Salmonella* spp, *Stenotrophomonas* spp, *Zymophilus*, *Achromobacter* spp, *Elizabethkingia meningoseptica*, *Haemophilus influenzae*, *Aeromonas* spp, and *Sphingomonas*.

\*\*Other gram positive bacteria: It includes the following microorganisms that individually accounted for <1%: coagulase-negative *Staphylococci* spp, *Listeria monocytogenes*, Methicillin resistant *Staphylococcus aureus*, *Rothia* sp, *Micrococcus* spp, *Staphylococcus epidermidis*.

\*\*\*Other: It includes *Candida* spp. and other 2 fungi that accounted for <1%: *Cryptococcus laurentii*; *Gardnerella vaginalis*.

at 1 hospital during 1 year, which is not enough to reach any kind of conclusions regarding rates.<sup>23</sup>

Our study, conducted during 6 years, in 204 ICUs, in 57 hospitals, in 19 cities in India with 7,513 patients, is the first comprehensive one to calculate PVCr-BSI rates per 1,000 device-days.<sup>8</sup> Our PVCr-BSI rate was 2.92 per 1,000 PVC-days. As far as we are concerned, the incidence of PVCr-BSI has been determined by number of PVC-days in only 2 studies from industrialized countries: back in 2006, in a systematic review with data from only 3 industrialized countries (the United States, Australia, and Italy), the rate was 0.5 PVCr-BSI per 1,000 PVC-days<sup>14</sup>; and in a recent study conducted in pediatric and neonatal ICUs from Australia, the rate was 0.67 PVCr-BSI per 1,000 PVC-days.<sup>15</sup>

In a systematic review published in 2019 by Alliance for Vascular Access Teaching and Research group the selected studies did not report PVC-days as denominators of PVCr-BSIs rates, and for that reason such data are not comparable with our present study.<sup>24</sup> The cited review published by AVATAR included studies whose PVCr-BSI rates were presented as follows<sup>24</sup>: Australia (0.39 PVCr-BSI per 10,000 occupied bed-days)<sup>25</sup>; Germany (3.04 PVCr-BSI per 1,000 patient days)<sup>26</sup>; Spain (1.17 PVCr-BSI per 10,000 patient days,<sup>27</sup> and 0.05 PVCr/1,000 patient days<sup>28</sup>; and the United States (0.0150 PVCr-BSI per 100 patient days,<sup>29</sup> and 0.57 PVCr-BSI per 1,000 patient days).<sup>30</sup>

Most studies have reported on the adverse consequences of BSIs in ICUs, and the comparison of infection risk using CL vs short-term PVCs, with CLs being much more prone to higher BSIs rates than with short-term PVCs.<sup>31-33</sup>

In 2014, INICC published data of CLABSI in India, prospectively collected during 10 years, from 2004 to 2013, from 236,700 ICU patients for 970,713 bed-days. Pooled rates for adult and pediatric ICUs were 5.1 CLABSIs per 1,000 central line-days.<sup>34</sup> The comparison of INICC previous data collected in India and published in 2014 of CLABSI with this study's INICC present data also collected and published in India by INICC on PVCr-BSI shows the pooled rate of CLABSI is 1.75 times higher than the PVCr-BSI rate. However, since around 80%-90% of the vascular catheters used worldwide are short-term PVCs, the raw number of BSIs due to PVC is around 6 times higher than due to CL.<sup>34</sup>

In our ICUs, the pooled mean of the distribution of crude mortality amounted to 11.59% of PVCr-BSIs cases, compared with 4.14% mortality of with PVC patients that were not infected. Similarly, in recent studies from Spain and Japan, mortality attributable to PVCr-BSI was 13.2% and 12.9%, respectively.<sup>27,35</sup>

The excess LOS of patients with PVCr-BSI in our study was 39% higher than in patients without PVCr-BSI; in the previously cited study from Japan, patients who had acquired PVCr-BSI required a longer duration of antibiotic treatment (33.5 vs 15.8 days;  $P=.004$ ) than patients without PVCr-BSI.<sup>35</sup>

The microorganism profile of PVCr-BSI found in our ICUs showed a predominance of gram negative bacteria (68%): *Escherichia coli* (23%), *Klebsiella* spp (15%), *Pseudomonas aeruginosa* (5%), *Enterobacter* spp. (5%), *Negativicutes* (5%), and others including *Serratia marcescens* and *Burkholderia cepacia* (15%). Within the 39% of gram positive bacteria found, the predominant one was *Staphylococcus aureus* (10%).

This highly contrasts with those findings from industrialized countries, in which gram positive pathogens were the predominant cause of PVCBSI.<sup>36</sup> In a recent study conducted in Japan the causative pathogens were Gram-positive in 58% of cases and Gram-negative in 35.8%, but ours concerning *Candida* spp. in 6.2% of cases.<sup>35</sup>

The predominance of gram positive pathogens causing PVCBSI in industrialized countries has been found in a wide range of studies, in which *S. aureus* PVCBSI has been identified in industrialized countries as a serious condition that could influence prognosis.<sup>27,35,37</sup> There are not available data showing microorganisms profile for PVCBSI from representative studies from other resource-limited countries.

The most prevalent pathogens found (*E. coli*, *Klebsiella* spp, and *S. aureus*), presented considerable resistance rates. Resistance of *P. aeruginosa* to fluoroquinolones (ciprofloxacin, levofloxacin, moxifloxacin, or ofloxacin), piperacillin, piperacillin-tazobactam, and amikacin was 27.3%, to imipenem (IPM) or meropenem (MEM) was 33.3%; of *Klebsiella pneumoniae* to ceftriaxone or ceftazidime was 79.31%, IPM or MEM or ertapenem was 68.42%; of *Acinetobacter baumannii* to IPM or MEM was 80.0%; of *E. coli* to CRO or CAZ was 66.7%, to IPM or MEM or ertapenem was 25.0%, to FQs was 61.0%.

Regarding gram-positive bacteria, in our study, resistance of *S. aureus* to oxacillin in 50% of cases which is similar to a 49% resistance reported in another study in India.<sup>23</sup> *Enterococcus faecalis* was 100% sensitive to vancomycin, which is also similar to the findings of the cited study conducted in India, in which vancomycin was 100% sensitive to the following gram-positive bacteria: *S. aureus*, coagulase-negative Staphylococci, and *Enterococcus* spp.<sup>23</sup>

The implementation of PVC insertion and maintenance bundles to decrease PVCBSI rates is common in industrialized countries.<sup>24,27</sup> To reduce the hospitalized patients' risk of infection, PVCBSI surveillance by number of device-days is essential, because it effectively characterizes the threatening situation created by PVCBSIs. This must be followed by the implementation of multifaceted and surveillance programs aimed at PVCBSI prevention and control.

Likewise, it is important to address the burden of antimicrobial resistance and report susceptibility to antimicrobials of PVCBSI-associated pathogens, to take effective measures to prevent resistant strains from being transmitted.<sup>24,27</sup>

In this particular study, INICC focused just on the ICU setting; that is, health care settings with the highest health care-acquired rates, in which patients' safety is most seriously threatened, due to their critical condition and exposure to invasive devices.<sup>38</sup> Through the last 17 years, INICC has undertaken a global effort in the 6 WHO regions: Africa, the Americas, Eastern Mediterranean, Europe, South East Asia, and Western Pacific to respond to the burden of HAIs, and has achieved extremely successful results, by increasing hand hygiene compliance, improving compliance with infection control bundles and interventions as described in several INICC publications.<sup>39–45</sup>

The primary application of these data is to serve as a guide for the implementation of prevention strategies and other quality improvement efforts for the reduction of PVCBSI rates and their related adverse events to the minimum possible level.

#### Study limitations

The purpose of this report is to obtain updated data on PVCBSI, device utilization (DU), bacterial resistance, LOS, and mortality of patients with and without PVCBSI in adult and pediatric ICUs, but it does not provide insights regarding the impact of INICC interventions, such as the implementation of INICC Multidimensional Approach and ISOS.<sup>17,46</sup> The impact of the adoption of such resources is to be published in prospective, interventional studies at hospitals that have participated in INICC during a considerable amount of years.<sup>41,44,45,47–64</sup>

Second, our study was limited by the fact that benchmarking with CDC-NSHN, or other institutions, was not possible because PVCBSI

rates are not reported to such institutions, or are not determined by PVC-days.<sup>65,66</sup>

Third, due to the low economic resources of our ICUs, probably cultures taken were less than ideal, which likely influenced the rates of PVCBSI, and the number of patients to whom blood cultures should have been taken, but were not, is unknown as these data were not registered.

Finally, we do not present data on trends over time for this 6-year study.

#### CONCLUSIONS

This study presents the only available comprehensive data from a developing country showing PVCBSIs per 1,000 PVC-days, and benchmarking of our findings was limited to the results of 2 studies from industrialized countries: a systematic review with data from the United States, Australia, and Italy published in 2006,<sup>14</sup> and a prospective study from Australia.<sup>15</sup>

Our PVCBSI rates were far much higher than the data available from industrialized countries, thereby it is evident that PVCBSIs in ICUs from resource-limited countries are a challenge for patient safety. PVCBSI systematic surveillance and prevention programs, including antibiotic resistance reports, should be widely implemented to allow a reduction in the incidence of PVCBSI and its adverse-related events worldwide.

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