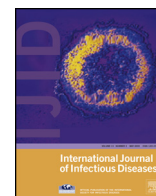


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Impact of an International Nosocomial Infection Control Consortium multidimensional approach on central line-associated bloodstream infection rates in adult intensive care units in eight cities in India



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SUMMARY

Objective: To evaluate the impact of the International Nosocomial Infection Control Consortium (INICC) multidimensional infection control approach on central line-associated bloodstream infection (CLABSI) rates in eight cities of India.

Methods: This was a prospective, before-and-after cohort study of 35 650 patients hospitalized in 16 adult intensive care units of 11 hospitals. During the baseline period, outcome surveillance of CLABSI was performed, applying the definitions of the CDC/NHSN (US Centers for Disease Control and Prevention/National Healthcare Safety Network). During the intervention, the INICC approach was implemented, which included a bundle of interventions, education, outcome surveillance, process surveillance, feedback on CLABSI rates and consequences, and performance feedback. Random effects Poisson regression was used for clustering of CLABSI rates across time periods.

Results: During the baseline period, 9472 central line (CL)-days and 61 CLABSIs were recorded; during the intervention period, 80 898 CL-days and 404 CLABSIs were recorded. The baseline rate was 6.4 CLABSIs per 1000 CL-days, which was reduced to 3.9 CLABSIs per 1000 CL-days in the second year and maintained for 36 months of follow-up, accounting for a 53% CLABSI rate reduction (incidence rate ratio 0.47, 95% confidence interval 0.31–0.70; $p = 0.0001$).

Conclusions: Implementing the six components of the INICC approach simultaneously was associated with a significant reduction in the CLABSI rate in India, which remained stable during 36 months of follow-up.

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1. Introduction

Central line-associated bloodstream infections (CLABSIs) are responsible for increased lengths of hospital stay and increased attributable mortality in high-income countries¹ and in limited-resource countries,² including India.³ CLABSIs are also responsible for increased health care costs, as reported in studies from high-income countries¹ and from some limited-resource countries in Latin America;^{2,4} however, no data on costs of CLABSIs are available from India.

The incidence of CLABSI is many times underestimated in limited-resource countries, as basic infection control programs are not systematically implemented.⁵ Device-associated healthcare-acquired infection (DA-HAI) rates in the intensive care units (ICUs) of limited-resource countries are three to five times higher than in high-income countries, as reported by the International Nosocomial Infection Control Consortium (INICC) in pooled studies,⁵ and particularly in India.³

In developing countries, the socioeconomic level of the country has an impact on DA-HAI rates in the pediatric⁶ and neonatal⁷ ICU settings. However, far too little attention has been paid to this, as only two studies addressing this issue have been published. The results of one of the studies showed that lower-middle-income countries had higher CLABSI rates than upper-middle-income countries in pediatric ICUs (12.2 vs. 5.5 per 1000 central line (CL)-days).⁶ Similarly, in the other study, CLABSI rates were significantly higher in neonatal ICU patients from low-income countries than in those from lower-middle-income countries or upper-middle-income countries (37.0 vs. 11.9 ($p < 0.02$), and vs. 17.6 ($p < 0.05$) CLABSIs per 1000 catheter-days, respectively).⁷ Unfortunately, no studies from developing countries that have analyzed this issue in adult ICUs (AICUs) are available.

In developed countries, it has been demonstrated that surveillance is fundamental to the prevention of CLABSIs, which can be reduced by more than 30%.⁸ Implementing infection control bundles, including the five interventions (1) hand hygiene, (2) skin antisepsis with chlorhexidine, (3) maximal barriers, (4) insertion into the subclavian vein, and (5) timely CL removal, has been associated with a reduction in the incidence density of CLABSI in developed countries.⁹

The present study was designed to determine the effect of a multidimensional program for CLABSI prevention in 16 AICUs of 11 hospitals, in eight cities of India. Our program was implemented from September 2004 to February 2012 and included six simultaneous interventions: (1) practice bundle, (2) education, (3) outcome surveillance, (4) process surveillance, (5) feedback of CLABSI rates, and (6) performance feedback on infection control practices. The design of the INICC multidimensional approach follows the basic recommendations published in the guidelines of the Society for Health Care Epidemiology of

America (SHEA) and the Infectious Diseases Society of America (IDSA) in 2008.¹⁰

So far there has been no systematic research on the effect of such an approach in India, the second most populous country in the world, with a population of around 1 300 000 000 people. This provided sufficient ethical and theoretical justification for conducting this particular study, and through its publication, increase and spread awareness of this public health burden in India.¹¹

2. Methods

2.1. Background on INICC

Founded in Argentina in 1998, the INICC was the first multinational research network established to control and reduce HAIs at the international level through the analysis of data collected on a voluntary basis by a pool of hospitals worldwide.¹² The goals of the INICC include the development of a dynamic global hospital network that applies systematic surveillance of HAIs with standardized definitions and methodologies, the promotion of evidence-based infection control practices, and the performance of applied infection control research to reduce rates of HAIs, the associated mortality, excess lengths of hospital stay, costs, and bacterial resistance.¹³

2.2. Setting and study design

The study was conducted in 16 AICUs in 11 hospitals, all members of the INICC, in eight cities of India. Each hospital had been actively participating in the INICC surveillance program for a minimum of 6 months, with an infection control team (ICT) comprised of infection control professionals (ICPs) and a medical doctor with a formal education and background in internal medicine, critical care, infectious diseases, and/or hospital epidemiology.

This prospective, before-and-after study was performed over two time-periods: the baseline period and the intervention period. The institutional review board at each hospital approved the study protocol (Figure 1).

2.3. Baseline period

The baseline period included only the performance of outcome surveillance and process surveillance. The length of the baseline period was 3 months for the following three reasons: (1) This is the time needed to conduct the following activities at INICC headquarters in Argentina on a monthly basis: receiving those case report forms (CRF) completed at all participating ICUs from India; conducting a validation process of filled CRFs; sending

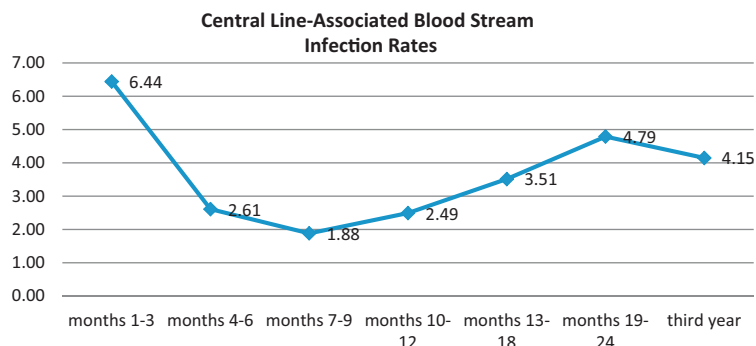


Figure 1. Central line-associated blood stream infection rates by period.

queries to participating ICUs; receiving and analyzing replies to queries; uploading and analyzing CRF data; producing monthly reports containing charts and tables with the results of outcome and process surveillance; sending monthly reports to each ICU; presenting the monthly report to health care workers (HCWs) at the participating ICUs at monthly infection control meetings, with the aim of providing feedback on CLABSI rates and their consequences and performance feedback to increase awareness about CLABSIs and to improve compliance with infection control practices.¹¹ (2) The sample size of patients and number of months of data collection during the baseline period are sufficient for comparison with the sample size of patients and number of months of data collection during the intervention period. From a statistical perspective, the issue is addressed by considering the changes in rates over time. The relatively short baseline period may have had an impact on the standard errors of our estimates. However, we found that this did not bias the results, because there were no systematic differences between the two groups. (3) Our priority was to start the intervention as early as possible in order to achieve the desired results—reducing the CLABSI and mortality rates as soon as possible.

2.4. Intervention period

The intervention period was initiated after 3 months of participation in the INICC program. This was a cohort study, and for that reason, each ICU joined the INICC program at a different time. Thus, by the day we analyzed the impact of the INICC intervention, the ICUs had undergone different lengths of intervention. The average length of the intervention period was 17.54 months (standard deviation 8.9 months, range 5–36 months).

2.5. INICC multidimensional infection control approach

The INICC multidimensional infection control approach included the following items: (1) bundle of infection control interventions, (2) education, (3) outcome surveillance, (4) process surveillance, (5) feedback of CLABSI rates, and (6) performance feedback of infection control practices.

2.5.1. Components of the central line-care bundle for CLABSI

Components of the CL-care bundle for CLABSI were as follows:¹⁰

1. Perform hand hygiene before CL insertion or manipulation;¹⁴
2. Use sterile gauze or a transparent sterile dressing to cover the insertion site;¹⁰
3. Maintain a good condition of the sterile dressing. Change the gauze every 48 h and the transparent dressing every 7 days;¹⁰
4. Remove the CL as early as possible, when not necessary;¹⁰
5. Change the administration set every 96 h; unless used for fat, nutrition, or blood precuts, and in these cases change every 24 h;¹⁰
6. Use a chlorhexidine-based antiseptic for skin preparation;¹⁰
7. Preferably use the subclavian vein;¹⁰
8. Use an all-inclusive catheter cart or kit;¹⁵
9. Use maximal sterile barrier precautions during CL insertion;¹⁰
10. Avoid using several times those vials meant to be used only once;¹⁰
11. Disinfect line hubs, needleless connectors, and infection ports before accessing the CL.¹⁰

Other effective interventions were discussed but not applied because of budget limitations, namely the following five practices were partially applied or not applied:

1. Use of a split septum instead of mechanical valves or a three-way stopcock;¹⁰

2. Use of a chlorhexidine impregnated sponge at the insertion site;¹⁰
3. Daily bath with chlorhexidine;¹⁰
4. Use of antimicrobial impregnated catheters;¹⁰
5. Use of closed collapsible flexible containers instead of open semi-rigid vented or glass vented IV containers.¹⁶

2.5.2. Education

Monthly sessions of education for CLABSI prevention were provided by the ICP to the HCWs in charge of the insertion, care, and maintenance of CLs, based on SHEA and IDSA guidelines.^{10,11}

2.5.3. INICC surveillance methods

The INICC surveillance program included two components: outcome surveillance (DA-HAI rates and their adverse effects, including mortality rates) and process surveillance (adherence to hand hygiene (HH) and other basic preventive infection control practices).¹³

Investigators were required to complete outcome and process surveillance forms in their ICUs, which were then sent for monthly analysis to the INICC headquarters office in Buenos Aires.

2.5.4. Outcome surveillance

Outcome surveillance included rates of CLABSI per 1000 CL-days, use of invasive devices (CL, mechanical ventilator, and urinary catheter), severity of illness score, underlying diseases, use of antibiotics, culture taken, microorganism profile, bacterial resistance, length of stay, and mortality in the ICU.¹³

CLABSI definitions and surveillance methods were in accordance with the definitions for HAI developed by the US Centers for Disease Control and Prevention (CDC) for the National Healthcare Safety Network (NHSN) program.¹⁷ Additionally, INICC methods were adapted to the limited-resource setting of developing countries, due to their different socioeconomic status.¹³ The ASIS (Average Severity of Illness Score) was used instead of the APACHE II score (Acute Physiology and Chronic Health Evaluation) due to budget limitations of participating ICUs in this limited-resource country. Thus, we used the ASIS score, as historically used by the CDC National Nosocomial Infections Surveillance.¹⁸

2.5.5. Definitions

When CLABSI was suspected, the CL was removed aseptically and the distal 5 cm of the catheter cut off and cultured using the standardized semi-quantitative method.^{17,18} Concomitant blood cultures were drawn percutaneously in most cases. At each hospital, standard laboratory methods were used to identify microorganisms, and standardized susceptibility testing was performed.^{17,18} A laboratory confirmed CLABSI was defined in the following case: A patient with a CL from whom a recognized pathogen is isolated from one or more percutaneous blood cultures after 48 h of catheterization; the pathogen cultured from the blood is not related to an infection at another site; and the patient has one or more of the following signs or symptoms: fever ($\geq 38^\circ\text{C}$), chills, or hypotension. In the case of skin commensals being isolated (diphtheroids, *Bacillus spp*, *Propionibacterium spp*, coagulase-negative staphylococci, and micrococci), the organism had to have been recovered from two or more separate blood cultures.^{17–19}

2.5.6. Process surveillance

Process surveillance was designed to assess compliance with easily measurable key infection control practices, such as surveillance of compliance rates for HH practices and specific measures for the prevention of CLABSI.¹³

Due to budget limitations, only five out of 11 components of the bundle were monitored:

1. The hand hygiene (HH) compliance rate was based on the frequency with which HH was performed as indicated in HCW infection control training. Observing ICPs were trained to record HH opportunities and compliance on a form, during randomly selected observation periods of 30 min to 1 h, 3 times a week. In particular, the INICC direct observation comprised the “Five Moments for Hand Hygiene” as recommended by the World Health Organization (WHO). The ‘Five Moments’ included the monitoring of the following moments: (1) before patient contact, (2) before an aseptic task, (3) after body fluid exposure risk, (4) after patient contact, and (5) after contact with patient surroundings.²⁰ Although HCWs knew that hand hygiene practices were regularly monitored, they were not informed of the schedule for HH observations.
2. Data on compliance with CL care measures were recorded 5 days a week on a form that evaluated if infection control procedures were correctly carried out by the HCW. The ICP observing the activity in the AICU completed a standardized form that contained the following data: total number of inserted CLs for each patient for the whole ICU; total number of dressings placed to protect the puncture site, in order to evaluate the number of patients with a sterile dressing.¹³
3. The ICP completed a standardized form that contained the total number of dressings in correct condition and an evaluation of whether the dressing was clean, dry, and correctly adhered to the puncture site, so as to evaluate the number of dressings in the correct condition.¹³
4. The ICP also completed a standardized form that contained the total number of cases in which the dates in the administration set were written, with the aim of measuring the number of patients with the number of days of the administration set in place, and evaluating if the set was replaced by or before 96 h.¹³
5. Finally, the ICP completed a standardized form including the date of insertion and removal of each CL, to evaluate the number of days the CL was inserted and the earliest possible removal of the CL when not necessary.

2.5.7. Feedback on DA-HAI rates

Every month, the INICC research team at INICC headquarters in Buenos Aires, prepared and sent to each ICT a final report of the results of outcome surveillance data sent by the investigators at each hospital, i.e., monthly DA-HAI rates, length of stay, bacterial profile and resistance, and mortality.¹³

Feedback on DA-HAI rates was provided to HCWs working in the AICU by communicating the patient outcomes. The resulting rates were reviewed by the ICT at monthly meetings, where charts were analyzed. Statistical graphs and visuals were displayed in prominent locations inside the ICU to provide an overview of DA-HAI rates. This infection control tool is important to increase awareness of patient outcomes in the ICU and to enable ICT and ICU staff to focus on the necessary issues and apply specific strategies to improve high DA-HAI rates.

2.5.8. Performance feedback

Upon processing the hospital process surveillance data on a monthly basis, the INICC research team at INICC headquarters in Buenos Aires prepares and sends to each ICT a final report of the results of process surveillance rates, including compliance with HH and care of CLs.¹³

Performance feedback is provided to HCWs working in the AICU by communicating the assessment of practices routinely performed by them. The resulting rates are reviewed by the ICT at monthly meetings, where charts are analyzed; statistical graphs and visuals are posted inside the ICU to provide an overview of rates measuring compliance with infection control practices. This infection control tool is key to enabling the ICT and ICU staff to

focus on the strategies necessary to improve low compliance rates.

2.6. Statistical methods

Patient characteristics during the baseline and intervention periods in each ICU were compared using Fisher’s exact test for dichotomous variables and an unmatched Student’s *t*-test for continuous variables. 95% Confidence intervals (CI) were calculated using VStat (Castiglia). Relative risk (RR) ratios with 95% confidence intervals (CI) were calculated for comparisons of rates of CLABSI using Epi Info v. 6. *p*-Values of < 0.05 by two-sided tests were considered significant.

We conducted two types of analysis to evaluate the impact of our intervention on CLABSI rates. First, we performed an analysis to compare the data of the first 3 months (baseline period) with the remaining pooled months (intervention period), using the RR, 95% CI, and *p*-value. Second, in order to analyze a progressive CLABSI rate reduction, we used Poisson regression. We divided the data into the first 3 months (baseline period), followed by a 9-month period (intervention period), and two annual follow-up periods for the second and third years. We compared the CLABSI rates for each follow-up period with the baseline CLABSI rate. For this comparison, we used the baseline data only of those hospitals that contributed to the follow-up during that period (i.e. excluding from the baseline those hospitals with long lengths of follow-up that only contributed a shorter length of surveillance). We used random effects Poisson regression to account for clustering of CLABSI rates within hospitals across time periods. These models were estimated using Stata 11.0. For this analysis we used the incidence rate ratio (IRR), 95% CI, and *p*-value.

3. Results

During the whole study, a total of 35 650 patients were hospitalized in 16 AICUs during 173 056 days, amounting to 90 370 CL-days. Participating hospitals were classified according to the type of hospital and type of AICU. The first ICUs to participate were enrolled in September 2004, and the most updated data included our analysis dates from February 2012 (Table 1).

Patient characteristics, such as thoracic surgery, immune compromise, mechanical ventilator use, and ASIS, were similar in the two periods (Table 2). However, the mean age of patients was higher during the intervention period (Table 2).

In relation to compliance rates, during the baseline period, HH compliance improved significantly and the CL use ratio was reduced. Compliance with other measures, such as date on

Table 1

Characteristics of the participating ICUs and hospitals (from September 2004 to January 2011)

Data	AICUs, <i>n</i>	AICU patients, <i>n</i>
Type of ICU, <i>n</i> (%)		
Cardiac surgical	1 (6%)	3024
Cardiac medical	1 (6%)	2348
Surgical	3 (19%)	5053
Medical	4 (25%)	5230
Adult step-down	1 (6%)	1353
Medical surgical	6 (38%)	17 743
All AICUs	16 (100%)	35 650
Type of hospital, <i>n</i> (%)		
Private community	9 (82%)	28 682
Academic teaching	1 (9%)	2348
Public	1 (9%)	4620
All hospitals	11	35 650

ICU, intensive care unit; AICU, adult ICU.

Table 2
Characteristics of patients, hand hygiene compliance, central line care compliance, central line use, and CLABSI rates in phase 1 (baseline period) and phase 2 (intervention period)

Patient characteristics	Phase 1—baseline	Phase 2—intervention	RR	95% CI	p-Value
Study period by hospital in months, mean ± SD (range)	3	17.54 ± 8.9 (5–36)	-	-	-
Number of patients	3747	31 903	-	-	-
Bed-days, ^a n	17 395	155 661	-	-	-
Number of CL days, ^b n	9472	80 898	-	-	-
CL duration, mean ± SD	2.53 ± 4.4	2.54 ± 5.8	-	-	0.9
Number of MV days, ^b n	4088	35 636	-	-	-
MV use, ^c mean	0.24	0.23	0.97	0.94–1.0	0.13
Age, years, mean ± SD	55.0 ± 18.0	56.3 ± 18.0	-	-	0.0001
ASIS score, mean ± SD	2.62 ± 1.14	2.6 ± 1.1	-	-	0.7
Male	2590 (69%)	20 602 (65%)	0.94	0.9–0.97	0.0013
Female	1156 (31%)	11 259 (35%)	-	-	-
Thoracic surgery, n (%)	11 (1%)	91 (1%)	0.97	0.52–1.82	0.94
Immune compromise, n (%)	11 (1%)	142 (1%)	1.52	0.82–2.81	0.18
Hand hygiene compliance, n (%)	73% (1467/2013)	84% (17 914/21 327)	1.15	1.1–1.22	0.0001
Compliance with date on administration set % (n/n)	97% (4405/4532)	96% (39 581/41 247)	0.99	0.96–1.02	0.42
Compliance with placed dressing % (n/n)	99% (4493/4532)	98% (40 248/41 247)	0.98	0.95–1.02	0.313
Compliance with correct condition of dressing % (n/n)	94.4% (4277/4532)	92% (37 904/41 247)	0.97	0.94–1.01	0.1
CL use, ^c mean	0.54	0.52	0.95	0.93–0.97	0.0001
No. of CLABSI, n	61	404	-	-	-
CLABSI rate per 1000 CL-days (95% CI)	6.4 (4.9–8.3)	3.9 (3.5–4.3)	0.61	0.46–0.81	0.0007

ASIS, Average Severity of Illness Score; CI, confidence interval; CL, central line; CLABSI, central line-associated bloodstream infection; MV, mechanical ventilation; RR, relative risk; SD, standard deviation.

^a Bed-days: the total number of days that patients are in the ICU during the selected time-period.

^b CL-days: the total number of days of exposure to a central line for all of the patients in the selected population during the selected time-period; MV-days: the total number of days of mechanical ventilation for all of the patients in the selected population during the selected time-period.

^c CL and MV use ratios were calculated by dividing the total number of CL-days or MV-days by the total number of bed-days.

Table 3
CLABSI stratified by length of participation of each ICU in the INICC; Poisson regression analysis

Time since joining INICC	Number of ICUs	CL-days, n	CLABSI, n	Crude LCBI rate/1000 CL-days	IRR accounting for clustering by ICU	p-Value
1–3 months (baseline)	16	9472	61	6.44 (95% CI 4.9–8.3)	1.0	-
4–6 months	16	8814	23	2.61 (95% CI 1.7–3.9)	0.42 (95% CI 0.26–0.68)	0.0001
7–9 months	14	12 210	23	1.88 (95% CI 1.2–2.8)	0.31 (95% CI 0.19–0.51)	0.0001
10–12 months	13	8429	21	2.49 (95% CI 1.5–3.8)	0.30 (95% CI 0.18–0.50)	0.0001
13–18 months	15	18 220	64	3.51 (95% CI 2.7–4.5)	0.41 (95% CI 0.28–0.59)	0.0001
19–24 months	12	14 412	69	4.79 (95% CI 3.7–6.1)	0.48 (95% CI 0.34–0.70)	0.0001
Third year	9	18 813	78	4.15 (95% CI 3.3–5.2)	0.47 (95% CI 0.31–0.70)	0.0001

CI, confidence interval; CL, central line; CLABSI, central line-associated bloodstream infection; ICU, intensive care unit; INICC, international nosocomial infection control consortium; LCBI, laboratory-confirmed bloodstream infection; IRR, incidence rate ratio.

administration set, placed dressing and correct condition of dressing, were high and similar in the two periods (Table 2).

During the baseline period, we recorded 9472 CL-days, for a CL use mean of 0.54. There were 61 CLABSIs, for an overall baseline rate of 6.4 CLABSIs per 1000 CL-days (Table 2). Merging all data from the intervention period, during the implementation of the multidimensional infection control program, we recorded 80 898

CL-days, for a CL use mean of 0.52. There were 404 CLABSIs for an incidence density of 3.9 per 1000 CL-days. These results showed an overall reduction in the CLABSI rate from baseline of 39% (from 6.4 to 3.9 CLABSIs per 1000 CL-days; RR 0.61, 95% CI 0.5–0.8; $p = 0.0001$) (Table 2).

On the other hand, using Poisson regression, we found a progressive CLABSI reduction. The baseline CLABSI rate (during first 3 months of the study) was 6.4 CLABSIs per 1000 CL-days, which reduced progressively during the intervention period to 4.1 CLABSIs per 1000 CL-days in the third year, amounting to a 53% CLABSI rate reduction (IRR 0.47, 95% CI 0.31–0.70; $p = 0.0001$) (Table 3).

The microorganism profile is shown in Table 4. The predominant microorganism in both phases was *Klebsiella spp.*

4. Discussion

This study set out with the aim of assessing the effect of a multidimensional infection control approach in the ICU setting in India, a limited-resource country. If compared with rates in developed countries, the baseline rate of CLABSI found in this study (9.0 per 1000 CL-days) is around eight-fold higher than in the USA (1.1 per 1000 CL-days; as determined by the CDC/NSHN²¹) and higher than the CLABSI rate determined by KISS (1.4 per 1000 CL-days).²²

Table 4
Microorganism related to CLABSI in AICUs in phase 1 (baseline period) and phase 2 (intervention period)

Microorganisms isolated	Baseline, % (n)	Intervention, % (n)
<i>Klebsiella spp</i>	32% (11)	25% (72)
<i>Acinetobacter spp</i>	18% (6)	10% (30)
<i>Candida spp</i>	12% (4)	15% (42)
<i>Staphylococcus aureus</i>	12% (4)	2% (7)
<i>Enterococcus spp</i>	6% (2)	4% (11)
<i>Pseudomonas spp</i>	6% (2)	16% (45)
<i>Escherichia coli</i>	3% (1)	7% (19)
<i>Enterobacter spp</i>	0% (0)	7% (20)
<i>Flavobacterium spp</i>	0% (0)	5% (15)
Coagulase-negative staphylococci	6% (2)	4% (11)
<i>Stenotrophomonas spp</i>	0% (0)	2% (6)
Other microorganisms	6% (2)	3% (9)
Total	100% (34)	100% (287)

AICU, adult intensive care unit; CLABSI, central line-associated bloodstream infection.

In comparison with pooled CLABSI rates from other developing countries, our CLABSI baseline rate is similar to those reported in the third and fourth international INICC reports published in 2010 (7.6 CLABSIs per 1000 CL-days)²³ and 2012 (6.8 CLABSIs per 1000 CL-days).²⁴

Within the scope of other studies addressing the burden of CLABSIs in India, the CLABSI rate of our study is similar to the rate found in another study conducted in India, showing 7.92 CLABSIs per 1000 CL-days.³

In previous studies performed by INICC member hospitals, it was shown that the implementation of a six-component multidimensional approach for CLABSI resulted in significant reductions in the rates of CLABSI in Argentina (46.63 vs. 11.10 CLABSIs per 1000 CL-days),²⁵ Mexico (46.3 vs. 19.5 CLABSIs per 1000 CL-days),²⁶ in AICUs (14.5 vs. 9.7 CLABSIs per 1000 CL-days),²⁷ and in pediatric ICUs (10.7 vs. 5.2 CLABSIs per 1000 CL-days).²⁸

In our study, patient characteristics, such as thoracic surgery, immune compromise, mechanical ventilator use, and the ASIS severity of illness score, showed similar patient intrinsic risk in both study periods. By contrast, the mean age of patients was higher during the intervention period, meaning that the patient intrinsic risks were higher in the intervention period. During the implementation of the INICC multidimensional approach, we found an improvement in process surveillance rates, with higher HH compliance, and the CL use ratio was reduced. Compliance with other measures, such as the date on the administration set, placed dressing and correct condition of dressing, were high and similar in both phases. During the study period, the high CLABSI rate at baseline was reduced from 9.0 to 4.1 per 1000 CL-days, showing a 53% CLABSI rate reduction and evidencing the effectiveness of the applied multidimensional approach.

Comparing our study with an earlier bundle study,⁹ we found some differences. First, the previously published bundle included five elements, whereas we included 11. Second, compliance was not measured for any of the bundle components, whereas we checked compliance with five bundle components. Third, characteristics of patients during the baseline and intervention periods were not collected or analyzed so as to check and compare individual features, whereas we did, and found that our patients were statistically similar in the two periods. Fourth, the follow-up period was 18 months, whereas we included a 36-month follow-up period. Fifth, the intervention included only a bundle and a check list, whereas our study included the above-mentioned six simultaneous interventions. Finally, microorganisms responsible for the CLABSIs were not provided, whereas in our study we included the CLABSI microorganism profile for both the baseline and intervention periods. The most important differences were measurements of the population features and compliance with bundle elements, which allowed us to analyze the real impact of our intervention by excluding confounders associated with patient characteristics and infection control practices.

Regarding the microorganism profile, we identified a predominance of *Klebsiella spp* during both periods; this is similar to other studies conducted in limited-resource countries.²³

This study had limitations. The main limitation of this study is that our findings cannot be generalized to all ICU patients in India. However, in this study it was proved that a multidimensional approach is fundamental to reduce the incidence of CLABSIs in the ICU setting. Second, the use of a 3-month baseline period, which is short, may have led to an overestimation of the effect of the intervention. Nevertheless, the sample size was sufficient during the baseline period and the confidence intervals for the baseline rate were narrow. Third, there may be significant variation in the level of quality control in the laboratories that support each individual hospital and we could not quantify in detail all the interventions included in our multidimensional approach, such as

education. Fourth, there might have been some ‘Hawthorne effect’ upon our study results; however, after years of continuous study intervention with regular monitoring, the potential effect is certainly diluted, as behavior is gradually internalized as a permanent social norm. In addition, due to the fact that our study design applies observational methods on HCW practice behaviors, evidence may be less solid or have less corroborative value than in other study designs. Finally, because of budget limitations, we were not able to quantify compliance with some of the components of our bundle. Thus we could not evaluate their individual implications or other contextual factors related to the ICU or hospitals individually. Nevertheless, our main goal was to reduce the high baseline CLABSI rates found in ICUs and the individual evaluation would have required more allocation of time, contributing to unnecessary harm for ICU patients.

In conclusion, this is the first multicenter study to report a substantial reduction in CLABSI rates in the ICU setting in India. Although some patient intrinsic risks were higher during the intervention period, the implementation of our multidimensional approach resulted in significant reductions in the CLABSI incidence rate. These systematically collected data serve as guidance for strategies to improve patient care practices, as demonstrated in several studies conducted in limited-resource countries.^{26,27} These preventive strategies, proven effective in the INICC ICUs of India, can promote a wider acceptance of infection control programs in hospitals, leading to significant CLABSI reductions worldwide.

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Ethics: Every hospital’s institutional review board agreed to the study protocol, and patient confidentiality was protected by codifying the recorded information, making it only identifiable to the infection control team.

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