Central line colonization, central line infection, Central line-associated and Catheter-related bloodstream infections in Greek pediatric intensive care patients: a prospective one year study

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ABSTRACT

Central line colonization, central line infection, Central line-associated and Catheter-related bloodstream infections in Greek pediatric intensive care patients: a prospective one year study

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The purpose of this study (prospective one year study of all patients requiring a central line) is to present central line colonization, central line infection, central line-associated and catheter-related bloodstream infection rates, risk factors, and the outcomes in a multidisciplinary Greek pediatric intensive care unit.

81 patients required 136 episodes of catheterization with duration of 9 (5.25-14.75) days. Device utilization ratio was 0.8. Eleven patients developed 17 episodes of central line-associated blood-stream infection (CLABSI) in 1629 catheter days, given a CLABSI rate of 10.43:1000. 3 catheter tip cultures revealed the same microorganism as the bloodstream infection (BSI), specified a cathe-ter-related (CRBSI) rate of 1.84:1000. Catheter tip infection occurred at a rate of 3.69:1000, where-as catheter colonization at 8.59:1000. Gram-positive microorganisms predominated in CLABSIs (52.94%), whilst Gram-negative pathogens predominated in colonization (64.28%), infection (66.66%), and CRBSI (66.66%), Acinetobacter baumanii being the principal pathogen. CLABSI patients had longer duration (days) of catheterization (17 vs 9, P=0.014), mechanical ventilation (17 vs 8, P=0.014), and unit stay (17 vs 10, P=0.037), without an impact on mortality. CLABSIs occurred more often in patients with Hickman catheters (P=0.003), co morbidities

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(P=0.000), multiple catheterizations (P=0.003), complications (P=0.008) and corticosteroid use (P=0.044). Hickman catheters [odds ratio (OR) 8.381; 95% confidence intervals (CI): 1.1-66.1, P=0.044] and co morbidities [OR: 5.904; 95% CI: 1.2-28.9, P=0.029)] were independent predictors of CLABSIs.

CLABSI rate in our study is higher than the international standards. Preventive measures, such as improvements in central line insertion and maintenance bundles of care, are necessary, to lower this baseline rate in future comparisons.

INTRODUCTION

Primary Bloodstream Infections (BSIs) are the main Health Care Associated Infections (HAIs) in the USA and the second HAIs in European Pediatric Intensive Care Unit (PICU) patients, with substantial effect on cost and outcome[1,2]. Attributable cost for each BSI ranged from $36,000 to $50,000 per episode, with attributable mortality rates of 12 to 25%[3,4]. Despite the consensus that these infections independently increase length of stay and hospital costs, their effect on mortality, in studies that controlled for severity of illness, is controversial[4].

The current surveillance definition of BSIs is Central Line-Associated Blood Stream Infections (CLABSIs) and most of them are related to Central Venous Catheter (CVC) use[5]. CLABSIs are considered preventable HAIs and a big campaign has started worldwide to lower their rates as much as possible, after implementation of bundles of care for catheter insertion and maintenance[6,7] .Mean pooled CLABSI rate for USA pediatric patients have declined from 7.6:1000 catheter days (1992-2004) to 5.2:1000 (2004-2006) and to 3.0-2.3:1000 recently (2006-2009) [3,4,8]. Higher values, ranging from 6.8-13.8:1000 are reported in older USA and other European and international studies, with the highest values coming from developing countries[9-12].

Studies focusing specifically on pediatric BSIs have found that arterial catheterization, extracorporeal life support, and presence of co morbidities and/or a genetic abnormality are independent infection risk factors, after controlling for potential confounders such as age and severity of illness[3]. Non elective admission for medical management, transportation outside PICU to the radiology or operating room suites, duration of catheterization, lower body weight and receipt of parenteral nutrition, blood transfusion and hydrocortisone were independently associated with CLABSIs as well, as the presence and/or the need for

multiple central lines and the performance of guide wire exchange on the line[3,10,12-15].

The aim of the current prospective cohort study is to present the infectious complications after CVC use in pediatric intensive care patients of a single center, to investigate infection risk factors, and to explore their effect on the outcome. Moreover, baseline CLABSI rate under current local infection control policies is expected to serve as a benchmark for future comparisons, after improvements in insertion and maintenance bundles of care, according to guidelines.

MATERIALS AND METHODS

Setting

A multidisciplinary 8-bed PICU of a tertiary mixed adult/pediatric 1000-bed hospital of Northern Greece which provides admission to infants with age of >40 days to children up to 14 years, in all diagnostic categories, except postoperative congenital heart diseases patients. Full, 24hrs/7days coverage of a Pediatric Intensivist is provided and the nurse to patient ratio ranges between 1:2 in morning shifts to 1:3–1:4 in afternoon and night shifts, according to bed occupancy, which is around 90%.

Patients/ Catheters

All consecutive PICU admissions, from 1/1/2011 to 31/12/2011, that required a CVC, were prospectively studied. In order to estimate the true incidence of CLABSIs, all type of CVCs were included; e.g. simple (not tunneled, not antiseptic/antimicrobial) temporary polyurethane catheters, and permanent Hickman catheters. Patients with readmissions, as well as patients needed more than one CVC during their stay were also included. Insertion of temporary CVCs were done under anatomical land mark points and maximum sterile barriers, by the attending physician or supervised trainees, using the Seldinger technique. Skin antisepsis was done with povidone iodine 10% and/or chlorexidine gluconate 0.5%-isopropyl alcohol 60%, due to lack of the recommended 2% clorexidine gluconate in Greece. No guide wire exchange was performed. Hickman catheters were inserted in the operation room. Catheter maintenance was done according to local protocols, plus chlorexidine gluconate-impregnated sponges (CHLX-IS) over insertion site (Biopatch; Antimicrobial Dressing; Johnson&Johnson Wound Management, Ethicon, Inc., Somerville, NJ). Due to the observational character of the study which did not require any deviation from routine medical care, institutional review board approval was waived. Informed consent was obtained only for the placement of the permanent catheters.

Study protocol

Data collected included demographics, critical illness severity (Pediatric Risk of Mortality, PRISM III-24), the presence of co morbidities and readmissions, treatment characteristics,

the type, site, size and length of CVC, the location of insertion, the presence and/or the need for multiple CVCs, and users experience[16]. Mechanical complications during insertion and maintenance, catheter duration and total catheter days, catheter colonization, the associated infections and their epidemiology, duration of mechanical ventilation (MV) and length of stay in the PICU (LOS), the outcome of the infections and the outcome of the patients were also recorded. The catheters stayed as long as needed if they were functioning without evidence of local or systemic complications. Surveillance (via CVC) blood cultures were taken twice per week, whether in case of clinical signs of sepsis 2 sets of blood cultures (peripheral and via CVC) were taken simultaneously. All catheters were removed aseptically and the distal 5 cm of the catheter tip was cultured by the semi quantitateve Maki's method.

Definitions

We used the 2008 criteria for CLABSI as a primary BSI in a patient that had a CVC within the 48 hours period before the development of the BSI and is not bloodstream related to an infection at another site, plus clinical sepsis criteria in patients $\leq$ 1 year, e.g., [fever>38^{o}C or hypothermia<37^{o}C (rectal), apnea or bradycardia] and blood culture not done or no organisms detected in blood, and no apparent infection at another site, and physician institutes treatment for sepsis.[5] Catheter colonization was defined as a positive semi quantitative tip culture with>15 colony-forming units/catheter tip without clinical sepsis; catheter infection as the previous criterion plus clinical sepsis, and catheter related blood stream infection (CRBSI) as a positive BSI with the same microorganism as catheter tip[4]. Device Utilization Ratio (DUR) was set as the proportion of total patient days in which central lines are used, e.g. central line days/patient days[6] .

Statistical analysis

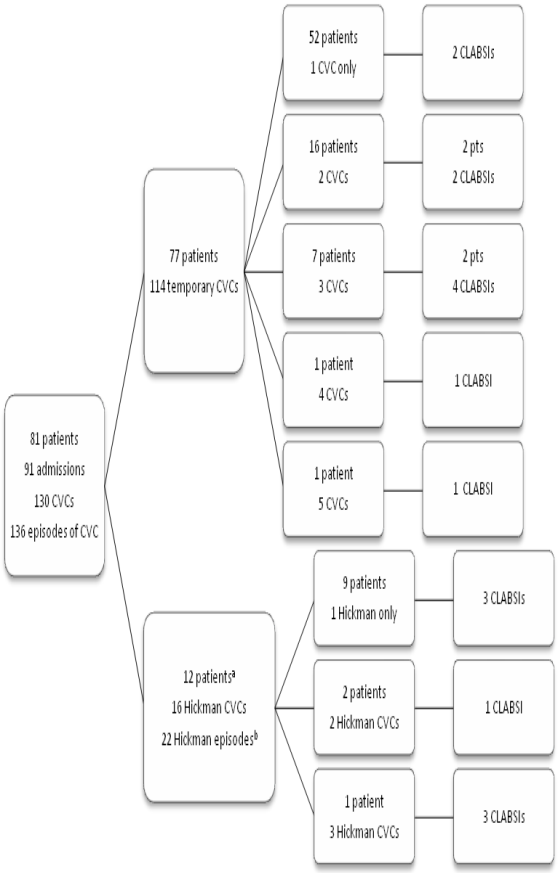
Categorical variables were expressed as counts (percentages) and continuous variables as means ± standard deviation (SD) or median with interquartile range (IQR), according to their distribution. Differences in patients with and without CLABSIs were sought with the use of Student's t-test for independent samples, Mann-Whitney *U* test and Chi-square test, as appropriate. Factors found to be statistically significant in the univariate analysis were examined in multivariate analysis as well, using Cox regression model. Statistical significance was set at $P<0.05$. Data were analyzed using SPSS 17 for windows (SPSS, Chicago, IL).

RESULTS

Among 136 patients admitted in 2011, 81 patients presented with 91 admissions, required a CVC. One hundred and thirty CVCs were inerted; 114 temporary and 16 Hickman ca-

theters, which, due to readmissions of patients having their Hickman in situ, resulted in 136 episodes of catheterization, as shown on the flow chart, in Figure 1.

Figure 1. Flow chart of patients requiring a CVC during the study period.



CVC: central venous catheter; CLABSI: central line-associated blood stream infection; [a]4 Patients were admitted with Hickman CVCs whereas 8 patients have had a temporary CVC first; [b]due to readmissions having their Hickman in situ, permanent CVCs resulted in 22 episodes of catheterization.

There were 66 emergency medical (72.52%), 14 elective postoperative (15.38%) and 11 (12.08%) trauma admissions. Demographic data and patient characteristics, on the whole cohort of our patients, as well as the differences between the patients who developed or not CLABSI, are shown in Table 1. Age, sex, severity of the disease, readmission, location of insertion and user experience didn't seem to play a role on the development of CLABSIs. On the contrary, patients with co morbidities and patients needed multiple catheterizaations were more likely to develop CLABSI. Among treatment characteristics, only the use of corticosteroids was an infection risk factor.

Catheter and outcome characteristics are also exposed in Table 1. Hickman catheters were more likely to develop CLABSIs (32.80%) contrary to femoral, which demonstrated lower infection rate (7.30%). Catheter size and number of lumens didn't seem to play a role on CLABSI occurrence. However, the presence of mechanical complications during insertion and maintenance was related to CLABSI development. Duration of catheterization was longer in patients with CLABSIs, mainly due to increased catheters days in patients with Hickman catheters. Catheterization time was similar in patients with temporary CVCs, with and without CLABSI. Patients with CLABSIs spend more days ventilated and stayed in the unit longer, a fact that affected neither the outcome of the

infection itself, nor the outcome of the patient. DUR was 0.8.

Table 1. Patient and catheter characteristics according to the development of central line-associated bloodstream infection.

Characteristics	Total n = 136	CLABSI n = 17	No CLABSI n = 119	p value
Age, median (IQR), mo	24 (12 – 69)	60 (12 – 120)	24 (12 – 60)	0.114[d]
Infants, 1-12 mo, n (%)	43 (31.6)	5 (29.4)	38 (31.9)	0.834[e]
Sex male, n (%)	58 (42.6)	5 (29.4)	53 (44.5)	0.238[e]
PRISM III-24, median (IQR)	6 (3 – 10)	3 (0.0 – 9.7)	6.50 (4 – 10)	0.066[d]
Readmissions[a], n (%)	14 (15.4)	2 (11.8)	12 (10.1)	0.117[e]
Co morbidities, n (%)	55 (40.4)	15 (88.2)	40 (33.6)	0.000[e]
Multiple CVC, n (%)	84 (61.8)	16 (94.1)	68 (57.1)	0.003[e]
Insertion in PICU[b], n (%)	105 (92.1)	10 (100.0)	95 (91.3)	0.332[e]
Consultant[b], n (%)	72 (63.2)	9 (90.0)	63 (60.6)	0.176[e]
Corticosteroids[c], n (%)	65 (47.8)	12 (70.6)	53 (44.5)	0.044[e]
Immunodeficiency, n (%)	13 (9.6)	3 (17.6)	10 (8.4)	0.225[e]
Shock, n (%)	25 (18.4)	5 (29.4)	20 (16.8)	0.209[e]
Inotropes, n (%)	24 (17.6)	2 (11.8)	22 (18.5)	0.496[e]
Parenteral nutrition, n (%)	25 (18.4)	3 (17.6)	22 (18.5)	0.933[e]
Arterial line, n (%)	127 (93.4)	15 (88.2)	112 (94.1)	0.361[e]
Mechanical ventilation, n (%)	134 (98.5)	17 (100.0)	117 (98.5)	0.590[e]
CVC site, n (%)				0.011[e]
Femoral	96 (70.6)	7 (41.2)	89 (74.8)	0.004[e]
Subclavian	15 (11.0)	3 (17.6)	12 (10.1)	0.35[e]
Jugular	3 (2.2)	0 (0.0)	3 (2.5)	_
Hickman	22 (16.2)	7 (41.2)	15 (12.6)	0.003[e]
Number of lumens, n (%)				0.057[e]
One	11 (8.1)	3 (17.6)	8 (6.7)	_
Two	83 (60.7)	5 (29.4)	78 (64.7)	_
Three	42 (30.4)	8 (47.1)	34 (27.7)	_
CVC size, temporary CVCs[b], n (%)				0.16[e]
4 Fr	69 (60.7)	3 (30.0)	66 (63.7)	_
5.5 Fr	35 (30.4)	5 (50.0)	30 (28.4)	_
7-8 Fr	10 (8.9)	2 (20.0)	8 (7.9)	_
Mechanical complications, n (%)	30 (22.1)	8 (47.1)	22 (18.5)	0.008[e]
Total CVCs, median (IQR), days	9 (5.2 – 14.7)	17 (6.5 – 35.5)	9 (5 – 13)	0.014[d]
Hickman CVCs, mean ± SD, days	25.81 ± 20.53	41.00 ± 25.04	18.73 ± 13.94	0.014[f]
Temporary CVCs, mean ± SD, days	9.30 ± 5.47	10.90 ± 6.27	9.15 ± 5.38	0.337[f]
MV, median (IQR), days	9 (5 – 15)	17 (6.0 – 30.0)	8 (5.0 – 13.0)	0.014[d]
LOS, median (IQR), days	10 (7.0 – 16.7)	17 (7.5 – 35.5)	10 (6.0 – 15.0)	0.037[d]
Death, episodes of catheterization, n (%)	16 (11.7)	2 (11.8)	14 (11.8)	1[e]
Death, admissions[a], n (%)	16/91 (17.6)	2/11 (18.2)	14/80 (17.5)	0.956[e]

CLABSI: central line-associated bloodstream infection; IQR: interquartile range; PRISM: pediatric risk of mortality; CVC: central venous catheter; PICU: pediatric intensive care unit; SD: standard deviation; MV: mechanical ventilation; LOS: length of stay; [a]91 admissions; [b]114 temporary CVC only; [c]methylprednizolone 4mg//kg/day and/or dexamethazone 0.6mg/kg/day, for > 7 days; [d]Mann-Whitney U test; [e]χ^2 test; [f]t-test for independent samples.

Epidemiology and incidence of CVC colonization and infections is demonstrated in Table 2. Eleven patients developed 17 episodes of CLABSIs in 1629 catheter days, given a CLABSI rate of 10.43:1000. Among them, 3 only catheter tip cultures revealed the same microorganism as the BSI, specified a CRBSI rate of 1.84:1000. Catheter tip infection occurred in 6 (4.61%) catheters given a rate of 3.69:1000, whereas catheter colonization occurred in 14 (10.76%) catheter tips setting a rate of 8.59:1000. Gram-positive microorganisms were the key pathogens in CLABSIs (52.94%) whereas Gram-negative pathogens predominated in catheter colonization (64.28%), catheter tip infection (66.66%), and CRBSI (66.66%) and *Acinetobacter baumanii* being the predominant pathogen (28.57%, 33.33% and 33.33% respectively).

Risk factors for CLABSI development are summarized in Table 1. Among them, two only were confirmed as independent predictors of CLABSIs in multivariate analysis. Patients with co morbidities were almost 6 times more likely to develop CLABSI (95% CI: 1.2-28.9,

P=0.029) and patients with Hickman catheters were 8 times more liable to CLABSI compared to patients with temporary CVCs (95% CI:1.1-66.1, *P*=0.044) (Table 3).

Table 2. Epidemiology and incidence of central venous catheter colonization and infections in 136 episodes of catheterization and 1629 catheter days.

Organisms	CVC colonization n = 14	CVC infection n = 6	CLABSI n = 17	CRBSI n = 3
Gram-negative organisms, n (%)	9 (64.3)	4 (66.7)	7 (41.2)	2 (66.7)
Acinetobacter baumanii	4 (28.6)	2 (33.3)	3 (17.6)	1 (33.3)
Pseudomonas aeruginosa	3 (21.4)	1 (16.7)	1 (5.9)	0 (0.00)
Klebsiella spp.	0 (0.00)	0 (0.00)	1 (5.9)	1 (33.3)
Enterobacter spp.	2 (14.3)	1 (16.7)	2 (11.8)	0 (0.00)
Gram-positive organisms, n (%)	4 (28.6)	1 (16.7)	9 (52.9)	1 (33.3)
Coagulase-negative staphylococci	3 (21.4)	1 (16.7)	7 (41.2)	1 (33.3)
Enterococcus spp.	0 (0.0)	0 (0.0)	2 (11.8)	0 (0.0)
Micrococcus spp.	1 (7.1)	0 (0.0)	0 (0.0)	0 (0.0)
Fungal, n (%)	1 (7.1)	1 (16.7)	1 (5.9)	0 (0.0)
Candida parapsilosis	1 (7.1)	1 (16.7)	1 (5.9)	0 (0.0)
Incidence, per 100 catheters	10.76	4.61	13.07	2.30
Incidence, per 1000 catheter-days	8.59	3.69	10.43	1.84

CVC: central venous catheter; CLABSI: central line-associated bloodstream infection; CRBSI: central line-related bloodstream infection.

Table 3. Independent risk factors for central line-associated blood stream infections.

Risk Factors	B	SE	Wald χ^2	d(f)	Sig	Exp (B)	95% CI
Co morbidities	1.77	0.81	4.79	1	0.02	5.9	1.2-28.94
Multiple CVCs	0.98	1.1	0.8	1	0.37	2.68	0.3-23.3
Hickman CVC	2.12	1.05	4.06	1	0.04	8.38	1.06-66.14
Complications	0.14	0.62	0.05	1	0.82	1.15	0.33-3.93
Corticosteroids	0.4	0.59	0.45	1	0.50	1.49	0.46-4.78
Femoral CVC	-0.22	0.82	0.07	1	0.78	0.80	0.16-4.0

Cox regression analysis; B: regression coefficient; SE: standard error; d(f): degree of freedom; Sig: significance level; Exp (B): the predicted change in the hazard for a unit increase in the predictor; CI: confidence interval; CVC: central venous catheter.

DISCUSSION

We found a CLABSI rate of 10.43:1000, much higher than the recent USA rate for pediatric patients which is around 3:1000, but quite close to older USA and other European and international studies.[3,6-14] Differences in patient populations and variability in critical care practices and local infection control, could explain, at least partly, this high rate. USA PICUS have more than 50% of postoperative cardiothoracic patients who are quite stable, with less illness severity and shorter length of stay, opposite to our population with low postoperative, high medical emergency and a reasonable fraction of trauma patients.[8,16] O'Grady et al. reported that trauma patients documented the highest CLABSI rate, and non elective admission for medical management was found as independent predictor of CLABSIs in the study of Costello *et al*. supporting our speculation.[4,14] The necessity for greater CVC use for patient treatment and monitoring, as indicated by the higher DUR ratio of 0.80, compared to the average 0.50 of USA studies, might have also played a role.[17] Moreover, duration of catheterization, a fact that is not always mentioned, was quite long,

and CLABSIs were mainly developed after 10 days of catheterization with temporary and 40 days of catheterization with Hickman catheters. Duration of catheterization is reported as independent infection risk factor in some pertinent studies, a fact that was partly confirmed by our results, showing longer duration of catheterization only in patients with Hickman catheters who developed CLABSI.[10,13-15.]

Most CVCs were inserted in the femoral vein (70.60%), yet their contribution to CLABSIs was rather low (7.29%), contrary to Hickman catheters which showed the highest infection rate (43.75%) and were found as independent predictors of CLABSIs increasing more than 8 times the infection risk. This finding hasn't been published previously, probably due to differences in study protocol. Hickman catheters are not usually included in relevant studies; if they were included an analogous conclusion could have been drowned.

Multiple catheterizations, presence of complications and corticosteroid use that were found as CLABSI risk factors in the univariate analysis, are reported as independent risk factors in the literature; though this finding was not established in our patients, probably due to small study size.[3,12,14] On the opposite, factors that were identified as independent predictors elsewhere (e.g., parenteral nutrition, arterial line) weren't confirmed by our study, possibly due to differences in local practice (e.g., lower frequency of parenteral nutrition, better care of arterial lines).[3,10,12,15] Apart from Hickman catheters, only the presence of co morbidities was found as independent predictor of CLABSI in our population, increasing six times the likelihood of CLABSI, in accordance to published data.[3,14,15]

Patients with CLABSIs spend more days ventilated (17 vs. 8, P=0.014), and stayed in the unit longer (17 vs. 10, P=0.037), a fact that apparently increased their PICU cost, as reported to pertinent studies. However, the presence of CLABSI, under the conditions of our study, was not associated with the mortality rate which was identical in patients with and without CLABSI (11.76% vs. 11.76%, P =1), in agreement to the majority of published data. [3,4,6,7]

We choose to use CHLX-IS in catheter maintenance, based on published benefits, and to counteract the lack of 2% chlorexidine on skin antisepsis. Catheter colonization (10.76%) in the present study is comparable to colonization in infants and children with CVCs and CHLX-IS use (14.8%), while colonization rate (8.59:1000) is close to values of 7.8-8.6: :1000 that reported in the biggest study of CHLX-IS use in adults.[4,6,7]

Gram-positive pathogens predominated in CLABSIs (52.94%), followed by Gram-negative (41.17%) and fungal infections (5.88%), according to related studies.[3,4,6,7] Interestingly,

no case of *Staphylococcus Aureus* was recorded, contrary to reported values of around 10.00%. Our results follow the international CLABSI pattern which shows that nearly 60.00% of infections are caused by Gram-positive bacteria. However, we demonstrated less Gram-positive and more Gram-negative infections. This prevalence of Gram-negative pathogens is apparent as well in catheter colonization (64.28%), catheter infection (66.66%) and CRBSI (66.66%), *Acinetobacter baumanii* being the predominant pathogen (28.57%, 33.33% and 33.33% respectively). Our latter data follow the national adult ICU profile of central line colonization and infection where *A.baumanii* presented in 37.10% episodes of colonization, 36.40% of infections, and 57.1% of CRBSI, and are probably related to local preponderance of Gram-negative microorganisms.[18]

The major limitation of our study is that it is a relatively small one centre study, which poses barriers in the generalization of our results. Though, there are strong points as well. Firstly, the international definitions we used enabled us to compare our data to international standards and allow us to set a benchmarking for future comparisons. Secondly, we applied an illness severity score validated for Greek PICU patients, a fact that is not always found in relevant studies, that makes comparisons between groups more reliable.[19] Moreover, we included all kind of CVCs, temporary and permanent to have a realistic CLABSI view. Furthermore, we studied details on catheter colonization, infection and CRBSI rate, to have a deeper insight on CVCs infections and not just the surveillance observation that CLABSI rate offer. Such a strict protocol is harder to be followed, and the information derived, despite the small study size is, we consider, valuable.

CONCLUSION

We set the baseline CLABSI rate and saw the differences in rate, causative microorganisms and risk factors as indicative infection control measures to be taken by our unit. Keeping our findings into account, better results are expected in the future post intervention period, after improvements in catheter insertion and maintenance bundles of care, according to guidelines.

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