



Research Article

# Impact of Povidone Application to nares in Addition to Chlorhexidine Bath in Critically Ill Patients on MRSA Nosocomial Bacteremia and CLABSI

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**Citation:** Nahra R, Darvish S, Gandhi S, Gould S, Floyd D, et al. (2023) Impact of Povidone Application to nares in Addition to Chlorhexidine Bath in Critically Ill Patients on MRSA Nosocomial Bacteremia and CLABSI. J Community Med Public Health 7: 370. DOI: <https://doi.org/10.29011/2577-2228.100370>

**Received Date:** 07 September, 2023; **Accepted Date:** 19 September, 2023; **Published Date:** 22 September, 2023

## Abstract

**Background:** Nosocomial MRSA bacteremia results in a significant increase in morbidity and mortality in hospitalized patients. We aimed to analyze the impact of applying 10% Povidone twice daily to both nares in addition to Chlorhexidine bathing on nosocomial MRSA bacteremia in critically ill patients. **Method:** Quality improvement Study was done with pre and post-design. The study period is from January 2018 until February 2020 and February 2021 and May 2021. The control period (From January 2018 to May 2019) consisted of CHG bathing alone, and in the intervention period, we added 10% Povidone iodine to the nares of critically ill patients. We analyzed Rates of nosocomial MRSA bacteremia and CLABSI and potential cost savings. **Results:** There were no significant differences in rates of MRSA bacteremia in critically ill patients. Nosocomial MRSA bacteremia was significantly lower during intervention period on Medical/surgical areas (MSA). CLABSI were significantly lower during intervention period in critically ill patients. There was no *Staphylococcus aureus* CLABSI in CCA during intervention period. The intervention also resulted in significant cost savings. **Conclusion:** The application of 10% Povidone iodine twice a day in addition to CHG bathing resulted in a significant decrease in CLABSI in Critically ill patients and a reduction in nosocomial MRSA in the non-intervention areas. The results of our study are confounded by the COVID pandemic. Further trials are needed to tease out individual patients benefit of the intervention.

**Keywords:** Nosocomial MRSA bacteremia; CLABSI; Povidone -iodine; MRSA; Decolonization; CHG

## Introduction

Methicillin-Resistant *Staphylococcus aureus* (MRSA) has been implicated in major nosocomial infections resulting in a significant increase in mortality, morbidity, length of stay, and direct healthcare cost [1-4]. Thus, much research has been devoted to minimizing the impact on hospitalized patients. Universal decolonization in the ICU setting is associated with reduced rates of MRSA clinical isolates and bloodstream infection from any pathogen in the critical space [5,6] and has also been shown to be more cost-effective than targeted decolonization or standard of care (consisting of screening and isolation) [7].

Traditionally, MRSA decolonization has been performed with Mupirocin in the nares and Chlorhexidine (CHG) wipes or bath [7]. Decolonization using Mupirocin and CHG was shown to have a significant impact on MRSA infections in some but not all studies [8,9]. Mupirocin's cost and potential for resistance make its widespread use more challenging.

Povidone-iodine (PI) for MRSA decolonization has been used as an alternative to Mupirocin. In a randomized control trial in a surgical cohort, swabbing the nares with PI was more successful in *Staphylococcus aureus* deep surgical site infection when compared to Mupirocin [10]. In a recent nursing home prospective cohort trial, 4 swabs of 5% PI, and 2 swabs of 10% PI performed equally well in decreasing MRSA colonization [11]. PI has been shown to successfully decolonize patients with MRSA before surgery [12,13].

We aimed to study the impact of universal decolonization of patients using 10% PI applied twice a day on each nostril, in addition to CHG bathing on rates of MRSA infections, and Central-line associated Bloodstream infections (CLABSI), in patients in the critical care areas and its potential "trickle down" effect on hospital-wide infections.

## Methods

### Study Design

The hospital where the study took place is a level 1 trauma, tertiary care center with 600 beds located in an urban area, on the east coast of the United States. The hospital services a very diverse population. We conducted a Quality Improvement (QI) project with a pre and post design using a time-based comparison of the effect of adding PI to nares to the usual practice of CHG bathing alone in adult critically ill patients. The QI was conducted in the Critical Care Area (CCA) defined as medical ICU, trauma ICU, cardiac ICU and neuro ICU. We excluded the neonatal ICU

(NICU) patients from the intervention. The institutional IRB deemed the study exempt of full IRB review.

### Intervention

During the control period, all patients received daily baths with CHG 2 % wipes. During the intervention period, in addition to the CHG bathing, every patient admitted to a Critical care area (CCA includes medical, surgical/trauma, neurological, and cardiological Critical care units) had each nostril swabbed with 10% PI twice a day starting on the morning of the second calendar day of admission to a CCA. This was continued until the patient's discharge from the CCA.

The intervention period is May 2019 -Feb 2020 and February 2021-May 2021 (total of 19 months). The hiatus in the project is a result of the COVID pandemic. The pandemic-imposed changes in established infection prevention practices in response to supply shortages and use of crisis standards of care. Uncertainties about future surges and the sporadic availability of PI, personal protective equipment and cleaning products played a role in our decision to halt the project for a few months. Once SARS-CoV-2 vaccines were available and the supply chain seemed to be improving, we resumed the intervention. The control period was constituted of 16 months (January 2018 to April 2019) immediately preceding the intervention and the period during which the intervention was halted (July 2020- January 2021) (total of 22 months).

### Education and Quality Assessment

Nursing education on the use of 10 % PI consisted of sharing information on multiple huddles during the day and night shifts as well as distribution of written instructions on how to use the PI. Nurses were also instructed on how to document the use of the PI in a flowchart in the Electronic Medical Records (EMR). The education was a combined effort between unit leaders, and nurse educators in the target units to ensure quality and compliance.

We tracked the utilization of 10 % PI weekly as part of our re supplying product to the different units. We also pulled from EMR utilization of PI. Monitoring of Environmental Services (EVS) and Hand hygiene procedures and the product did not change during the intervention period. The only exception was period March 2020- June 2020. That period reflects start of COVID-19 pandemic during which the hospital experienced unprecedented supply chain disruption that affected the cleaning products as well as type and quality of Alcohol-Based Hand Rub (ABHR) used by healthcare workers. No new interventions to address hand hygiene were efficiently implemented between January 2018 and May 2021.

### Definitions

Nosocomial or healthcare-associated MRSA bacteremia is defined by National Healthcare Safety Network (NHSN) as MRSA

bacteremia that developed on Day 4 of hospitalization [14]. This entity is usually reported as a Standardized Infection Ratio (SIR). In this QI we will report this variable as a rate. The denominator is patient days for the specific unit to which the nosocomial MRSA bacteremia is attributed to.

Central Line-Associated Bloodstream Infection (CLABSI) per NHSN is a bacteremia associated with a central or PICC line, not attributed to a secondary site or meeting criteria for commensal organism. For purpose of this QI, we are also reporting this variable as a rate. The denominator is line days.

Since nosocomial Methicillin-Sensitive *Staphylococcus aureus* (MSSA) and Gram-negative Rod (GNR) are not tracked by NHSN we used CLABSI involving MSSA and GNR as a surrogate for hospital-onset bacteremia [15]. Details of organisms associated with CLABSI during the study period and designated comparative period is shown in table 2. Note that we combined under Enterobacterales the following organisms *Escherichia coli*, *Klebsiella pneumonia*, *Proteus mirabilis*, *Morganella morganii*, *Serratia marcescens*.

### Outcome measure

#### Primary endpoint

- i. Incidence of nosocomial MRSA bacteremia in CCA, and medical-Surgical Area (MSA).

#### Secondary endpoints

- i. Incidence of CLABSI in CCA, MSA.

- ii. Discreet number of bacteremia and specific organism involved in CLABSI.
- iii. Cost of care was extrapolated from Agency for Healthcare Research and Quality (AHQR). The cost analysis was done using AHQR published data to avoid inflation of cost when analysis is done for events in critically ill patients.

### Statistical Analysis

We present the rates of infections as N/1,000-line days for CLABSI, and N/1,000 patient days for nosocomial MRSA in blood culture as Mean (95% CI). Trend in the use of PI was explored. We performed a Non-parametric Kernel regression analysis to determine whether universal decolonization (use of PI) was associated with nosocomial MRSA and CLABSI. Differences in the number of microorganisms associated with CLABSI before and after PI were also explored using Wilcoxon signed-rank test. All analyses were conducted in R version 4.2.2 and conclusion made at 5% significance level.

### Results

#### Rate of MRSA bacteremia

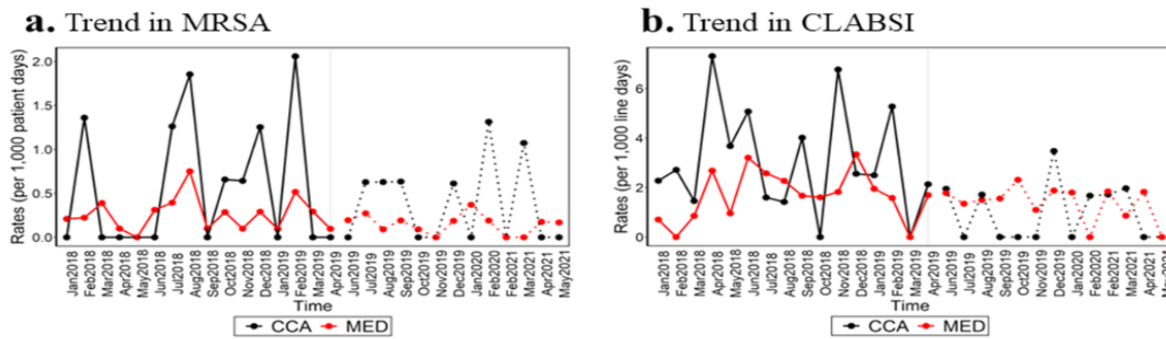
We present in Table 1 the rates of nosocomial MRSA in blood culture in the CCA, and MSA for both the intervention and control period. During intervention period nosocomial MRSA in blood culture was significantly lower for MSA, however though we had a decrease in total number of nosocomial MRSA in blood culture in CCA it did not reach statistical difference.

	MRSA			CLABSI		
	Before	After	P Value	Before	After	P Value
CCA	0.57 (0.10, 4.38)	0.38 (0.05, 3.97)	0.4	3.05 (1.08, 8.13)	0.96 (0.18, 4.80)	<b>0.0075</b>
MED SURG	0.26 (0.02, 3.68)	0.14 (0.02, 3.68)	<b>0.05</b>	1.68 (0.35, 5.69)	1.37 (0.22, 5.26)	0.34
<b>Total</b>	<b>0.41 (0.06, 4.04)</b>	<b>0.26 (0.03, 3.83)</b>	<b>0.22</b>	<b>2.37 (0.71, 6.91)</b>	<b>1.16 (0.19, 5.03)</b>	<b>0.06</b>

**Table 1: Rates of nosocomial MRSA bacteremia and CLABSI during the study period.** The MRSA column represent with nosocomial MRSA bacteremia single event per unit within 14 days divided by patient days for the assigned area analyzed. The CLABSI represents events of bacteremia associated with a central line divided by line days in the specific area.

**Incidence of CLABSI**

CLABSI in the CCA was significantly lower in the intervention period 1.05(±1.05) compared to the Control period 2.7(±2) CLABSI/1,000-line days. We also present in Figure 1 the trend of CLABSI rates over the study period. There was no difference in the CLABSI rates in the MSA. When looking closely at the microbiology results from the CLABSI, we see that there were no *Staphylococcus aureus* CLABSI in the intervention periods in the CCA.



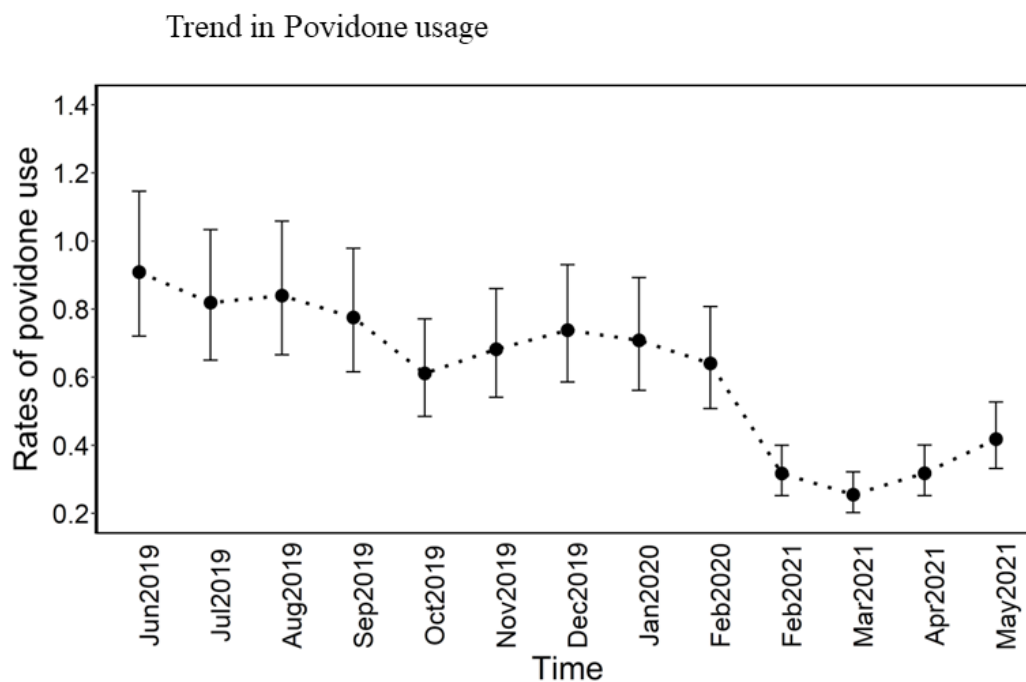
**Figure 1: CLABSI rates in Critical care Area January 2018-May 2021.** a: Temporal trends in the number of MRSA per 1000 patient-days before and after the intervention periods. b: Temporal trends in the number of CLABSI per 1000 line-days before and after the intervention periods. a & b are the raw counts divided by the patient days or line days for each month.

Using CLABSI as a surrogate for bacteremia we saw the intervention significantly dropped the count of bacteremia across the board for CCA (p value=0.0195 (Table 2) and the combined CCA+MSA (p value=0.0313). Though there was less incident of bacteremia in the non-intervention area (MSA) it did not reach statistical significance.

	Med Surg before PI	Med Surg after PI	P value	CCA before PI	CCA after PI	P value
<i>Candida species</i>	4	2		4	3	
<i>Pseudomonas species</i>	2	3		1	2	
<i>Acinetobacter baumannii</i>	3	0		3	0	
Enterobacterales ( <i>E. coli</i> , <i>Klebsiella</i> , <i>proteus</i> , <i>morganella</i> , <i>Serratia marscense</i> )	6	6		4	1	
<i>Stenotrophomonas</i>	1	1		0	0	
<i>Bacteroides</i>	0	0		2	0	
<i>Fusobacterium</i>	0	0		1	0	
<i>Staphylococcus aureus</i>	9	5		5	0	
Staph coag negative	2	3		2	1	
<i>Enterococcus</i>	4	1		3	0	
Total bacteremia count	31	21	0.16	25	7	<b>0.0195</b>

**Table 2: Microbiology results for CLABSI Jan 2018-May 2021.** This table shows the individual CLABSI and attributed micro organisms before and after the intervention was initiated in the CCA.

We analyzed the usage of PI during the study period. While the use of PI was consistent between June 2019 and Feb 2020, there was a significant drop in the usage after February 2020 (Figure 2).



**Figure 2: Povidone usage in CCA:** Temporal trends in the usage of Povidone adjusted for length of stay for each month.

### Cost analysis

Though the PI swabs were provided free of charge we estimated the cost of the intervention based on the usage of swabs during the intervention period. The action of swabbing patient nostrils twice a day is not strenuous on the nursing staff and therefore no cost was associated with it. Therefore, the estimated cost of intervention is based on the actual cost of the swabs. The estimated total cost for supplies (based on the 2022 market price) is 53,500 US dollars. A review of the medical literature for bacteremia shows an estimated cost per episode ranging between 32K to 36K US\$ [16]. The decrease in Nosocomial MRSA bacteremia event by 20 incidents resulted in an estimated average cost saving of US\$ 34, 000 (range between US\$ 640,000 to US\$720,000). This is a conservative estimate assuming none of the Nosocomial MRSA bacteremia is associated with VAP, as cost of pneumonia is higher than septicemia alone even when adjusted for length of stay [21]. Cost of CLABSI based on AHQR in 2017 is estimated to be US\$48,000 with a range of US\$ 27,000-69,000 [19]. During intervention period we had 21 less incident of CLABSI through the institution. Thus, the savings from applying PI would range from US\$ 619,000 to US\$ 703,000 for CLABSI alone.

The overall cost saving factoring in product cost, savings on CLABSI and Nosocomial MRSA bacteremia was of US \$2,005,850. Though the reduction in CLABSI reached statistical significance, the decrease in Nosocomial MRSA bacteremia event did not reach statistical significance in CCA.

### Discussion

In this project, we showed that applying PI swabs to nares in addition to application of CHG to skin decreased significantly the incidence of CLABSI infection in critically ill patients. We also show that this intervention resulted in substantial cost savings. Interestingly despite no significant decrease of Nosocomial MRSA bacteremia during intervention period, we had no *Staphylococcus aureus* CLABSI in the intervention period. Our results are concordant with results from other studies [8].

Our study, unfortunately, occurred at the time of the first COVID surge. COVID pandemic resulted in significant strain on our nursing staff; as it has been established by few studies quality measures, such as healthcare-associated infections, are highly affected by nursing staff experience and ratio [17,18]. Nursing Staff shortages resulted from illness, the pursuit of traveling opportunities and new-to-practice nurses entering the workforce can be challenging. Along with increased patient acuity, supply chain challenges had negatively impacted quality of care delivered [19-21]. In our institution, analysis of EMR showed that our usage of PI swabs to the nares was significantly decreased after February 2020 (Figure 2). Unfortunately, we could not control and factor in our statistical analysis the impact of COVID on quality of care delivered. We do recognize it is not an issue unique to our institutions [21-23]. With particular focus on hospital-acquired infections (HAI), the NHSN report published in 2022 shows a significant increase in all HAI tracked by NHSN in 2020 compared to 2019 [28]. For instance, 2020 CLABSI SIR started with a 12% decrease compared to the same period in 2019, however as COVID settled a significant increase was seen. In the state where the QI was done the 2020 third quarter (Q3) CLABSI Standardized Infection Ratio (SIR) of 0.86 was 59% higher than the SIR from 2019-Q3 of 0.54. CLABSI and MRSA lab ID are considered quality metrics. It is worth mentioning that Patients with COVID-19 infection are noted to be at an increased incidence of *Staphylococcus aureus* infection [24,25]. Despite a nationwide increase of MRSA bacteremia, we think the simple intervention of adding application of PI swabs to nares while maintaining a well-established practice of using CHG wipes for critically ill patients allowed us to keep the number of infections below pre pandemic levels in the CCA though it did not reach statistical significance. We did not have a similar increase in MRSA bacteremia (99% increase) similar to other local institutions.

PI swabs application in addition to CHG resulted in a significant decrease in CLABSI from all causes and no *Staphylococcus aureus* CLABSI. With CLABSI being used as a surrogate for healthcare-associated bacteremia<sup>15</sup> we feel the intervention had, a beneficial effect on overall healthcare associated bacteremia in the CCA we did not evaluate if that translated in improved patient outcome [26] as the study was not designed to assess individual patients. After the QI was concluded we were able to query electronic medical record for documentation of PI swabs usage. An additional drawback was our inability to assess real time PI swab use or intervene if PI swabs were not use for each patient, we extrapolated compliance based on distribution to units and did education if usage went down.

Moreover, the project was a Quality improvement project and did not have the rigor of randomized control trials. Our approach,

as any QI, has the benefit of mimicking real-life situation [27]. As described above the cost of the intervention would have been based on the cost of PI swabs to nares, which would have been of 53500 US \$ for the duration of the QI. The QI was not designed to address impact of the intervention on mortality and morbidity of individual patients. Given the structure of QI projects, we pulled the nosocomial MRSA bacteremia from NHSN which allows for duplicate events if the inpatient location of the patient is different when the blood is obtained. This downside of the study might inflate our nosocomial MRSA bacteremia rates. Therefore, a more structured study design such as a randomized controlled trial appropriately powered might be able to answer questions regarding the patient population where the intervention would have the highest impact.

## Conclusion

Application of PI swabs twice a day in addition to CHG bathing resulted in significant decrease in catheter associated blood stream infection in critically ill patients. The impact of the intervention on nosocomial MRSA bacteremia needs to be further evaluated in a randomized trial.

## Conflict of Interest

Medline<sup>®</sup> provided the Povidone Iodine and sponsored the QI. The company did not work on the data presented. None of the authors report conflict of interest.

## Funding

\*The QI project was financially supported by Medline<sup>®</sup>. Medline<sup>®</sup> had no involvement on study design and on analysis of the results.

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**Citation:** Nahra R, Darvish S, Gandhi S, Gould S, Floyd D, et al. (2023) Impact of Povidone Application to nares in Addition to Chlorhexidine Bath in Critically Ill Patients on MRSA Nosocomial Bacteremia and CLABSI. *J Community Med Public Health* 7: 370. DOI: <https://doi.org/10.29011/2577-2228.100370>

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