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Nasal colonization of methicillin resistant *Staphylococcus aureus* (MRSA) does not predict subsequent infection in the intensive care unit

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ABSTRACT

Hospital acquired infections with *Staphylococcus aureus*; especially methicillin resistant *S. aureus* (MRSA) is a major cause of morbidity and mortality in the United States. The aim of this study was compare the rates of MRSA infections between MRSA colonized and not-colonized patients. A retrospective, electronic and paper chart review of all adult patients admitted to the intensive care unit (ICU) from 2007 to 2010 was screened for MRSA. Endpoints were pyogenic pneumonia, sepsis, endocarditis, skin and soft tissue infections, osteomyelitis and septic arthritis. Patients who were not screened for MRSA were excluded from the study. A total of 1203 patients were admitted and screened for MRSA colonization on admission to the ICU from 2007 to 2010. Two main groups were made for between colonized and not-colonized based on MRSA screening. Fifty-seven (57) positive colonized and 122 not-colonized patients' charts were randomly selected. The mean age of the study population was 61.7 ± 18.4 (range, 19–94); there were 80 (44.69%) males and 99 (55.31%) females. The occurrence of infection with MRSA with either lower respiratory tract infection or blood stream infection identified on the time of ICU admission was similar for patients with and without MRSA nasal colonization 3.51% vs. 2.46%; $p = 0.459$. There was no observed difference in the rates of MRSA infection between those who tested colonized and not-colonized.

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1. Introduction

Staphylococcus aureus is one of the leading causes of hospital-acquired infections (Richards et al., 1999a). It usually infects lower respiratory tract infections and surgical site (Richards et al., 1999b). It is the second leading cause of nosocomial, bacteremia, cardiovascular infections and pneumonia (Wisplinghoff et al., 2004), especially in individuals admitted to the intensive care unit (ICU). *S. aureus* infections are very difficult to treat due to rapidity of developing resistance to antimicrobial drugs. Resistance to penicillin and newer β-lactamase resistant antibiotics like methicillin and oxacillin was found soon after they were introduced in to clinical use in 1940s and 1960s respectively (Lowy, 2003); hence the term methicillin resistant *S. aureus* (MRSA). Centers for Disease Control and Prevention's (CDC's) data on National Nosocomial Infections Surveillance network have shown that MRSA represent >50% of *S. aureus* strains causing nosocomial infections patients admitted to intensive care units (National Nosocomial Infection Surveillance (NNIS) System, 2003). This resistance pattern has spread as use of penicillin increased, first between hospitals and then into the community. Hospitalizations that resulted in infections attributable to MRSA steadily increased between 2000 and 2005, nearly doubling in many areas in the United States (Zilberberg et al., 2008). Similarly, MRSA has become a common infection in the intensive care unit setting. At this time MRSA accounts for more than 60% of *S. aureus* infections that occur in ICU (National Nosocomial Infections Surveillance Calfee et al., 2008; (NNIS) System, 2004).

A national survey of nasal colonization with *S. aureus* conducted from 2001 to 2004 shows that colonization with *S. aureus* decreased in 2003–2004 to 28.6% from a previous level of 32.4% in 2001–2002 (Chambers, 2001). However prevalence of MRSA colonization rose from 0.8% to 1.5% during this same time period (Gorwitz et al., 2008). One reason for this observation may be increased antimicrobial use, such as fluoroquinolones, on suppression of methicillin sensitive *S. aureus* (MSSA) more than MRSA, subsequently promoting colonization of MRSA (Gorwitz et al., 2008). MRSA is now considered to be endemic or even epidemic in major hospitals in the United States as well as long-term facilities (Chambers, 2001). There is an increase risk for health care-associated MRSA infection among MRSA-colonized patients estimated to be almost 10 times that for patients who are not-colonized (Davis et al., 2004). This relationship has been established in surgical patients and studies have shown that *S. aureus* carriers have 2–10 fold increased risk of developing an *S. aureus* surgical site infection, mostly from the patient's endogenous flora (Davis et al., 2004; Kluytmans et al., 1995).

To decrease the incidence of health care associated MRSA infections, Society for Healthcare Epidemiology of America (SHEA) recommends active surveillance cultures at the time of hospital admission along with contact precautions for patients at high risk for MRSA carriage (Mangram et al., 1999; Muto et al., 2003). Risk factors vary by geographical location and demographic characteristics of the patient population but Hidron et al. (2005) identified independent risk factors for nasal colonization which include; hospitalization within the past 12 months, the presence of a skin or soft-tissue infection at admission, antimicrobial use within the 3 months before admission, and HIV-seropositive status (Hidron et al., 2005).

Cultural strategies for curtailing the spread of MRSA have centered on the prevention of cross-transmission, hand hygiene practices, cleaning and disinfection of the environment as well as timely identification of patients colonized with MRSA (Diekema and Climo, 2008). Nasal swabbing of all patients admitted to the hospital to detect asymptomatic patient harboring MRSA, a process called active surveillance culturing (ASC) has been tested with mixed result. ASC intend to identify MRSA carriers promptly so that contact precautions can be instituted in a timely manner to decrease the frequency of cross-transmission events to other patients. Many hospitals in United States now screen patients upon ICU admission for MRSA, using nasal swabs for MRSA detection by using polymerase chain reaction; some states have passed legislation mandating all patients at risk for MRSA be screened on admission, even-though Centers for Disease Control (CDC) guidelines and recent infection control position statement recommend against routine use of ASC to control MRSA (Weber et al., 2007). The aim of this study was to compare the rates of MRSA infections between MRSA colonized and not-colonized patients with the hypothesis that; nasopharyngeal colonization with MRSA does not predict subsequent MRSA related infections in the ICU and that similar rate of MRSA related infections between MRSA positive and MRSA negative patients.

2. Materials and methods

Approval of Institutional review board (IRB) was obtained from Saint Peters University Hospital (SPUH). A retrospective, electronic and paper chart review of all adult patients admitted to the intensive care unit (ICU) from 2007 –2010 was screened for MRSA. Data was also obtained from infection prevention and control office database of SPUH that implements and records all data regarding MRSA screening. Endpoints of this study were pyogenic pneumonia, sepsis, endocarditis, skin and soft tissue infections, osteomyelitis and septic arthritis. For each patient colonized with MRSA, two randomly selected not-colonized patients were matched as control. Demographics, etiology and place of residence prior to hospitalization were obtained. Patients in both groups with observed for subsequent MRSA related infections during their ICU stay as well as re-hospitalization during the study period. Patients who were not screened for MRSA on admission to ICU were excluded from the study.

Modified National Healthcare Safety Network (NHSH) definitions were used to define MRSA infections acquired in the ICU (Horan et al., 2008). Only lower respiratory tract infections (LRTIs) and bloodstream infections (BSIs) were evaluated, because they account for the majority of ICU acquired MRSA infection (National Nosocomial Infections Surveillance Horan et al., 2008; (NNIS) System, 2004). LRTIs were defined as a positive quantitative respiratory culture (>10^4 colony-forming units per mL for bronchoalveolar lavage and >10^5 colony-forming units per mL for tracheal aspirate or sputum, all respiratory cultures were performed quantitatively. BSIs were

Table 1 – Sex and age distribution of population.

	MRSA colonized		P-values	MRSA not-colonized		P-values	Total
	(n)	(%)		(n)	(%)		
Sex							
Male	22	38.59	$p < 0.01$	58	47.54	$p < 0.01$	80
Female	35	61.40	$p < 0.01$	64	52.46	$p < 0.01$	99
Total	57			122			179
Age							
18–30	0	–		4	3.28	$p < 0.05$	
31–45	4	7.02	$p < 0.05$	18	14.75	$p < 0.05$	
46–60	5	8.77	$p < 0.05$	18	14.75	$p < 0.05$	
61–75	13	22.81	$p < 0.05$	32	26.23	$p < 0.05$	
>75	35	61.40	$p < 0.05$	50	40.98	$p < 0.05$	
Total	57			122			

defined as the growth of MRSA from one or more blood cultures and a positive blood culture that was not related to an infection at another site. ICU acquired MRSA infection was defined as the development of MRSA infection more than 48 h after ICU admission and less than 48 h after ICU discharge (Schramm et al., 2006).

2.1. *Screening of MRSA patients at Saint Peters University Hospital (SPUH)*

SPUH uses amplification methods for rapid MRSA detection. The protocol for MRSA screening employed at SPUH is as follows:

a) Both nares of all patients admitted to intensive care unit are swab then, culturette sent to the laboratory for Polymerase chain reaction (PCR) analysis $\sum$.
b) If a positive MRSA history status was known on admission, the patient was place in private room; contact and resistant organism precaution will be initiated.
c) When patients are identified as PCR screen positive, the laboratory notifies the patient care unit and physician, contact precaution is therefore initiated.
d) On each return admission, previous positive patients are placed in isolation until negative status has been determined.

2.2. *Statistical analysis*

Chi-square and Fisher's exact tests was performed for all variables. For all analyses a two-tailed p value of <0.05 or <0.01 was considered statistically significant.

3. Results

A total of 1203 patients were admitted and screened for MRSA colonization on admission to the ICU from 2007 – 2010. Of these 179 patients chart were randomly selected for review, information regarding demographics, age, sex, place of residence, result of MRSA nasal swab and probable MRSA associated infection were obtained. Table 1 shows age and sex distribution of study population. The mean age of the study population was 61.7 ± 18.4 (range, 19–94); there were 80 (44.69%) males and 99 (55.31%) females.

As shown in Table 2, two main groups were made colonized and not colonized based on MRSA screening. Using MRSA nasal swab polymerase chain reaction (PCR) as screening tool. Fifty-seven (57) colonized and 122 not-colonized patients' charts were randomly selected for analysis. Among those colonized 2 (3.51%) evidence of lower respiratory tract infection, there was no positive blood culture for MRSA in this group. For the not-colonized group a total of 3 positive cultures –1 blood and 2 sputum (2.46%) were also obtained. The occurrence of infection with MRSA with either lower respiratory tract infections (LRTIs) or blood stream (BSIs) infections identified on the time of ICU admission was similar for patients with and without MRSA nasal colonization 3.51% vs. 2.46%; $p = 0.459$.

Table 3 shows place of patients' residence prior to ICU admission. Majority of patient's prior residence with and without MRSA colonization was their homes (67.18%). The likelihood of MRSA colonization was similar in both patients presenting from nursing home (14.03% vs 14.75%; $p = 0.326$); however patients who presented from rehabilitation center were more likely to be MRSA colonized (24.56% vs 12.29%; $p = 0.265$).

As shown in Table 4, sensitivity of admission MRSA nasal swab to predict only lower respiratory tract infections (LRTIs) was similar to either lower respiratory tract infections (LRTIs) or blood stream infections (BSIs) (3.51% vs 3.51%; $p = 0.473$).

Table 2 – Result of MRSA screen at the time of ICU admission.

MRSA infection	MRSA screen			
	Colonized		Not colonized	
	(No.)	%	(No.)	%
Positive	2(SC)	3.508	3(1 BC 2 SC)	2.46
Negative	55	96.49	119	97.54
Total	57		122	

Legend: SC-sputum culture; BC- blood culture; ICU- intensive care unit.

Table 3 – Place of residence prior to ICU admission.

Place of residence	MRSA screen			
	Positive		Negative	
	(No.)	%	(No.)	%
Home	35	61.40	89	72.95
Nursing home	8	14.03	18	14.75
Rehabilitation center	14	24.56	15	12.29
Total	57		122	

The positive predictive value for the admission nasal was highest for prediction for lower respiratory tract infections (LRTIs) 50.00% and lowest for blood stream infections (BSIs). Negative predictive value the admission nasal swab for only lower respiratory tract and both lower respiratory tract infections and blood stream infections was similar 68.39% vs 68.39%; $p = 0.754$. Disease prevalence was calculated to be 32.02% (95% CI: 25.24–39.42) ($p > 0.01$). The number of subsequent infections between those who are MRSA colonized (2 sputum cultures) versus MRSA not-colonized (1 blood culture and 1 sputum culture) patients was similar. No clinical disease attributed to MRSA was documented in both groups.

4. Discussion

Several investigations have attempted to define the benefits of routine MRSA surveillance as a strategy to prevent MRSA infections among hospitalized patients. The findings have been mixed, and the benefits of routine MRSA screening at the time of hospital or ICU admission are still debated (Chaberny et al., 2008; Diekema and Climo, 2008; Harbarth et al., 2008). Another potential role for MRSA screening in the ICU is as a guide for antimicrobial therapy of suspected infections. Previous studies have demonstrated MRSA colonization is a risk factor for subsequent infection with MRSA (Ellis et al., 2004; Wertheim et al., 2004). Unfortunately the accuracy of MRSA screening as a predictor for subsequent ICU acquired infections requiring empirical antimicrobial coverage for MRSA is unknown. This study have showed that MRSA nasal colonization has a very low sensitivity (3.51%) and a poor predictor of subsequent MRSA associated infection requiring antibiotics at the time of ICU admission. The identification of MRSA colonization would have improved if a more extensive surveillance that include swabs obtained from rectum, stool, gastric aspirate and groin was done. We believe this is likely the explanation for the poor performance of nasal swabs alone in predicting subsequent MRSA infections.

Most studies of MRSA colonization among hospitalized patients have focused on identifying MRSA colonization as predictor of infection for the entire population cohort being examined (Davis et al., 2004; Safdar and Bradley, 2008; Sakaki et al., 2009). Croft et al. (2009) demonstrated that MRSA colonization was a predictor of subsequent MRSA infection among trauma patient. Chen et al. (2009) examined nasal carriage of *S. aureus* in healthy children presenting with skin and soft tissue infection. Safdar and Bradley (2008) performed a systematic review to provide an overall estimate of the risk of MRSA infection after colonization with MRSA compared to methicillin-susceptible *S. aureus* (MSSA). The authors demonstrated that MRSA colonization was associated with four-fold increase in the risk of infection compared to MSSA colonization. Their analyses were four studies that evaluated the role of MRSA colonization as a determinant of subsequently occurrence of MRSA infections in the ICU setting (Fishbain et al., 2003; Squier et al., 2002).

Several studies have attempted to look at the benefits of MRSA screening as a tool to predict subsequent infections and as a strategy to prevent infections. However, the results have shown mixed results and the benefits of screening at the time of hospitalization or ICU admission is debatable (Kelly et al., 2009; Sarikonda et al., 2010). The main point of contention includes the efficacy of active surveillance culturing (ASC) and judicious use of heath care resources as reported by Huskins et al. (2011) in a cluster randomized control trial involving over 900 patients admitted to 18 ICU, the use of ASC in addition to universal glove precautions pending ASC results, did not reduce transmission of MRSA compared with existing practice. The authors hypothesized that additional interventions such as antiseptic bathing and improved environmental decontamination may be needed (Huskins et al., 2011). Another study conducted by the United States Veterans Affairs in a system-wide quality improvement initiative that looked at MRSA surveillance, contact precautions for colonized and infected patients, hand hygiene along with institutional culture change that sampled almost 2 million patients in 150 hospitals (Jain et al., 2011). The program was initially associated with a reduction in the rate of MRSA infection in intensive care units by 62% and general units by 45%. However, it was not possible to determine whether ASC was causally related to the observed drop in rates since this

Table 4 – Sensitivity, specificity, and positive and negative predictive values of nasal MRSA colonization for prediction of MRSA associated LRTI and BSI.

	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Positive predictive value, % (95% CI)	Negative predictive value, % (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
MRSA nasal swabs						
LRTI	3.51 (0.53–12.13)	98.35 (94.14–99.75)	50.00 (8.30–91.70)	68.39 (60.92–75.22)	2.12 (0.31–14.69)	0.98 (0.93–1.04)
BSI	0.00 (0.00–6.33)	99.17 (95.43–99.86)	0.00 (0.00–83.45)	67.61 (60.16–74.46)	0.00	1.01 (0.99–1.03)
Either LRTI or BSI	3.51 (0.53–12.13)	97.54 (92.97–99.46)	40.00 (6.49–84.60)	68.39 (60–92–75.22)	1.43 (0.25–8.31)	0.99 (0.93–1.05)

SC-sputum culture; BC-blood culture; ICU-intensive care unit; CI-confidence interval; LRTI-lower respiratory tract infection; BSI-blood stream infection.

study did not include control. Mathematical model thereafter demonstrated marginal to MRSA reduction (Gurieva et al., 2012). Our result did not show any difference in the rates of MRSA associated infection between those who tested colonized and not-colonized patients. This is consistent with other studies which showed poor correlation between colonized positivity and subsequent MRSA related infections (Croft et al., 2009).

5. Conclusion

The benefit of screening is still been debated. This study showed no difference in the rates of MRSA infection between those who tested colonized and not-colonized. However, data from nasal colonization can be use to augment infection control practices that aims to reduce MRSA burden in ICU setting. We recommend clinicians should not use the results of nasal swab colonization data alone to determine the need for empiric antibiotics.

5.1. *Limitations*

Study was done in a single ICU setting and the findings may not be applicable to other ICUs. Additionally this was a retrospective study that has limited the availability of accurate data due to documentation problems. We did not obtain colonization samples from sites other than the nares in our study. Finally the study was done in an ICU where an active infection-control program is in place aimed at preventing the transmission of MRSA, which may have influenced the results of this study by limiting the overall occurrence of MRSA colonization and infections. Hence larger, multicentered prospective studies are required to evaluate the usefulness and accuracy of MRSA screening in predicting subsequent infections.

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