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REVIEW

Methicillin-resistant *Staphylococcus aureus* multiple sites surveillance: a systemic review of the literature

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Purpose: The objective of this study was to evaluate the optimal number of sampling sites for detection of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization.

Methods: We performed a Medline search from January 1966 to February 2014 for articles that reported the prevalence of MRSA at different body sites. Studies were characterized by study design, country and period of the study, number of patients and/or isolates of MRSA, specimen type, sites of MRSA isolation, study population sampled, diagnostic testing method, and percentage of the MRSA isolates at each site in relation to the total number of sites.

Results: We reviewed 3,211 abstracts and 177 manuscripts, of which 17 met the criteria for analysis (n=52,642 patients). MRSA colonization prevalence varied from 8% to 99% at different body sites. The nasal cavity as a single site had MRSA detection sensitivity of 68% (34%–91%). The throat and nares gave the highest detection rates as single sites. A combination of two swabs improved MRSA detection rates with the best combination being groin/throat (89.6%; 62.5%–100%). A combination of three swab sites improved MRSA detection rate to 94.2% (81%–100%) with the best combination being groin/nose/throat. Certain combinations were associated with low detection rates. MRSA detection rates also varied with different culture methods.

Conclusion: A combination of three swabs from different body sites resulted in the highest detection rate for MRSA colonization. The use of three swab sites would likely improve the recognition and treatment of MRSA colonization, which may in turn reduce infection and transmission of MRSA to other patients.

Keywords: Staphylococcus colonization, swab sites, MRSA detection

Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) has become a major cause of hospital-associated infection since it was first discovered in Britain in the 1960s soon after the beta-lactam methicillin was introduced for clinical use against *Staphylococci*.[1] The emergence of MRSA infection has had a negative impact on hospital costs, resulting in longer hospital stays as well as morbidity and mortality.[2,3]

MRSA colonization is a major risk factor for subsequent MRSA infection.[4,5] In the USA and Singapore, studies found that 8.5% and 15% of MRSA-colonized patients, respectively, developed MRSA infection over subsequent years.[4,5] The presence of MRSA at multiple sites strongly predicts development of MRSA infection.[6,7] Colonized patients are an important reservoir of MRSA in hospitals, and diagnostic clinical samples can miss ~35%–84% of these colonized patients.[8,9]

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There is no general consensus on effective control measures and the optimum anatomical swabbing sites, which are least costly, for use as an infection control measure for MRSA.[9] Studies have been devised to determine the optimal site or combination of sites for detection of MRSA colonization. Issues of detection method, cost, efficiency, accuracy, and study design have been considered. Different countries have different policies on the number of sites for screening of MRSA colonization for optimum results. In the USA, nasal swabbing as the single site is recommended while in the UK, at least two sites are recommended.[9–11]

Bacteremia surveillance has been used as a passive method for measuring effectiveness of MRSA control methods, but this has a disadvantage of requiring long follow-up to determine whether infection control interventions have had an effect in a hospital.[12] There is a need to evaluate other surveillance measures to achieve optimum control of MRSA.[13] Our study is aimed at establishing the significance of MRSA isolation from different sites suspected of colonization as a surveillance measure.

Methods

Selection of articles for inclusion

Candidate articles were selected for the reference document, first on the basis of title, and then on reading the abstract. All candidate articles were retrieved before final selection. The articles qualified for selection for review if they met the following criteria: 1) original research written in English and published in a peer-reviewed journal; 2) explicit information on MRSA colonization sites; and 3) any article published after 1966 providing data on culture isolates of MRSA at both nasal and extra-nasal and results were available.

Focus of the study

The focus of this study was, primarily, to analyze MRSA colonization sites or multiple MRSA colonization sites as a method of MRSA detection.

Literature search

The study was based on an updated literature search in Medline. The search terms were: "MRSA surveillance", "Methicillin-resistant *Staphylococcus aureus* surveillance", "MRSA", "colonization site", ("Screening" OR Swab OR surveillance AND MRSA). The database search was supplemented by a bibliographic search in previous reviews in the field. The authors read all the abstracts to retrieve relevant articles, minimizing the possibility of selective selection.

Data extraction

The data extracted from each of the included studies consisted of the first author; year of publication; study design; country and period of the study; number of patients and/or isolates of MRSA; and the type of the culture specimen for MRSA, the site of MRSA isolation, and the percentage sensitivity of the MRSA isolates at each site in relation to the total sites.

Results

We reviewed 3,211 abstracts and 177 manuscripts, and 160 were excluded either due to the fact that the swabbing data were only from nasal sites or that the study population were mostly children. Seventeen full articles met the criteria for analysis as they had data on screening of both nasal and extra-nasal sites of adults at admission (Table 1).[14–30] The studies included for analysis were conducted between 1996 and 2014 (n=52,642 patients). Seven of the studies were conducted in South America, six in Europe, four in Asia, and none in Africa. Seven studies had study population from general wards, six from intensive care unit (ICU), and three from both ICU and general wards, while one was conducted on ward and outpatients. Eleven studies were prospectively while six were retrospectively done. Out of the 17 studies, 16 of them used directly plated MRSA culture media and one used both directly plated MRSA culture media and broth-enriched culture media. MRSA isolates were confirmed by disc diffusion assay in 16 studies, and in one study MRSA isolates were confirmed by both disc diffusion and molecular assays. Four studies had low MRSA prevalence of less than 6% (1.3%–4.1%), while the prevalence of MRSA in nine studies were high at ≥6% (6%–25%), and four studies did not state the prevalence of MRSA.

Fifteen of the 17 studies had nasal MRSA detection of less than 90% as a single area of MRSA colonization and the MRSA detection ranged from 34% to 89.7%, and only two of the 15 studies had MRSA nasal sensitivity of ≥90% as a single area of MRSA colonization.[24,25] The single-site screening of nares showed low MRSA in endemic areas[15,19,25,27] due to a high proportion of MRSA detected by nasal screening of 75.1% with a range of (65%–90%) (Table 2). Nasal colonization showed MRSA detection sensitivity of less than 50% (34%–48%) in three studies.[16,21,29]

Seven studies showed less than 90% MRSA detection sensitivity when nasal MRSA colonization was combined with one extra-nasal site.[14,16,19,20,23,29,30] Four studies had nasal/throat; five studies nasal or throat/groin; three studies had nasal/rectum; and one study had nasal/skin or wound as

best two combinations for MRSA detection sensitivity. Four studies had nasal/throat/groin; three studies had nasal/throat/rectum; while each of the two single studies had nasal/axilla/rectum and nasal/wound/perineum, respectively, as three best combinations for MRSA detection sensitivity (Table 1). Detection of MRSA colonization was enhanced by using broth-enriched culture media and performing molecular assay, and this helped in rapid detection and identification of MRSA from mixed flora samples.[20,22]

Discussion

Colonized patients are important reservoir of MRSA in hospitals, and diagnostic clinical samples can miss ~35%–84% of these colonized patients.[8,9] The level of endemicity of MRSA determines the kind of screening program needed in order not to miss occult carriers of MRSA and, therefore, increase cross transmission of MRSA hospital infection.[19,25,26] The importance of doing the MRSA colonization screening has been marred with issues of cost-benefit analysis and the indication for it.[19,22,27] Various countries have different policies on the number of sites for screening of MRSA colonization with optimum results.

Prevalence of MRSA colonization is not the same on different sites of patients' body, such as the axilla, hairline, groin, nose, perineum, rectum, throat, skin breakdown areas, eyes, and vagina.[14–30] The throat and nares show higher colonization detection as single sites ranging from 50.5% to 89.7%.[14–20,22–28,30] The two studies that showed ≥90% nasal MRSA colonization sensitivity as single site still needed extra-nasal combination to have required Negative Predictive Value of MRSA detection.[24,25] Single-site screening such as the nasal cavity is optimal for endemic areas with low MRSA prevalence,[15,19,25,27] and this single site is likely to miss significant detection of MRSA colonization in high-risk population.[14–16,21,29] The nasal cavity as a single site for detection of MRSA colonization was not able to meet MRSA detection of ≥90% in 15 of the 17 studies under review.[14–23,26–30] The study by El-Bouri[14] found 50% of two swab combinations were better than single nasal swabbing and 25% were likely missed by using nasal swabbing alone. This was also found in studies by Mertz et al and Bignardi and Lowes.[31–34]

Combination swabs from two sites improved MRSA detection rate to 50% with best combination being that of nasal or throat/groin,[18,22,24,28] followed by nasal/rectum or perineum.[15,17,21]

A three-site combination improved detection rate to 99% with the best combination being that of nasal/throat/groin or perineum or rectum.[14,16,19,20,28,30] In another study, the three-site combination did not reach the ≥90% sensitivity,[23] though the overall MRSA colonization at any site was 12.2% (1.3%–24%), and this could be due to a variation in the MRSA detection method. Nasal colonization was 47.6% (22.2%–87%), nasal plus one extra-nasal combination was 89.6% (62.5%–100%), and nasal plus two extra-nasal sites combination was 94.2% (81%–100%), as shown in Table 2. Similar findings were reported in a systematic review conducted by McKinnell et al.[31]

Most of the studies under review for extra-nasal screening were done in developed countries of USA, Europe, and Asia even though many studies have indicated the prevalence of MRSA in countries of Africa. Apart from level of endemicity, cost-benefit analysis has been mainly put under consideration when it comes to either using nasal swabbing alone or combination of extra-nasal sites.[15,32,35] Another issue is to do with acceptability of the method of swabbing at certain sites, like throat and perineum, by the study population.[15,27,36–39] Some studies found that throat swabbing was better at MRSA detection than nasal swabbing.[14,16,27,36–39] Fifteen of the 17 studies (88%) reviewed favored inclusion of extra-nasal swabbing for the detection of MRSA colonization. Two studies under review showed that the method of MRSA detection has effect on the detection of MRSA at different sites.[20,22] Lauderdale et al[20] found that direct culture method missed ~50% detection rate of MRSA from nasal swabbing as compared to broth-enriched medium. Broth-enriched culture improved detection rate of MRSA by 24% in swabs from the throat, axilla, and perineum. These results concurred with those of Grmek-Kosnik et al and Nonhoff et al.[40,41] The variation in the detection rate at different sites could also be attributed to MRSA load and method of detection and decolonization procedures.[23,42] The association was not seen in the study by Baker et al,[23] where it was found that the strongest predictor of extra-nasal colonization was nasal colonization and not broth-enriched medium. Currie et al[15] found that the sensitivity of rectal swabs increased from 59% to 67% for MRSA-Select plates when mannitol-salt agar (MSA-OX) with 4 mg/L oxacillin culture was used, but there was no significant change in sensitivities of nasal and open-skin-site swabs with MSA-OX culture. Use of PCR methods did not show any significant difference in the detection of MRSA.[23] The anatomical sites to be swabbed also have an effect on the culture results due to the fact that participants may decline to give consent, due to psycho-social stigma associated with very private or anatomically sensitive areas of the body to be swabbed. The throat or posterior pharynx,

Table 1 Participants, bacteriological testing, and outcomes of MRSA testing for identification of sites of MRSA colonization

Author name, country	Period of study	Study design	MRSA detection method	Swabbing method and site	Study population and size
El-Bouri and El-Bouri,[14] Wales	January 2010–November 2012	Retrospective	Chromogenic MRSA medium/ Columbia blood agar	Only simultaneously swabbed patients of all anatomical sites were accepted	Adults at high risk for MRSA due to frequent re-admission or others (4,769)
Currie et al,[15] Canada	January 2004–June 2007	Descriptive analysis	MSA-OX, MSA-FOX, MRSA-Select	First set of screening swabs	All surgical and medical patient with HA-MRSA risk factors (23,365)
Jang et al,[16] Republic of Korea	March 2010–February 2011	Prospective observational	BBL™ CHROMagar™ MRSA medium	Swabbed at the time of admission, 48 hours after admission, and then weekly	Adult patients (282)
Yang et al,[17] USA	February 2005–October 2007	Prospectively	MSA-OX	Swabbing once at anatomic sites in MRSA infected patients	Adults with SSTIs (117)
Datta et al,[18] India	January 2009–June 2010	Active surveillance	Blood agar and Mac Conkey agar and disc diffusion test using 30 ug cefoxitin disc on Mueller Hinton agar	Single anatomic swabbing	Adults in ICU (400)
Girou et al,[19] France	1993–1996	Prospective	Chapman agar	Swab from nasal, perineum, and axilla at admission and once a week	High-risk patients from MICU (3,686)
Lauderdale et al,[20] Taiwan	August 2005–February 2006	Retrospective	Sheep blood agar (SBA) and CHROM agar MRSA and broth-enriched culture	Swab sample set of nose, throat or sputum, axilla, and perineum within 24 hours admission	Patients on admission to a medical and surgical ICU (650)
Eveillard et al,[21] France	July 2002–June 2003	Prospective	Mannitol salt agar (MSA-Ofloxacin)	Screen swab at different anatomic sites on admission and also clinical sample and TID calculated	1,250 from ICU and other wards
Hombach et al,[22] Switzerland	August 2007–August 2008	Prospective	BD GeneOhm™ MRSA Assay, the Xpert™ MRSA assay and broth-enriched culture	Swabs from different sites on admission from MRSA high-risk patients	425
Baker et al,[23] USA	October 2008–February 2009	Prospective	Chromogenic agar plate	Swabs from acute care patients within 36 hours of admission	150
Mermel et al,[24] USA	September 2007–March 2008	Retrospective	MRSA-selective chromogenic medium and sheep blood agar	Adults inpatients previously identified as MRSA positive during the year prior to enrollment	53
Fishbain et al,[25] USA	August–November 2000	Prospective surveillance	5% sheep agar and MRSA screen agar	Adults on admission, swabs within 48 hours from both nares and both axilla	535
Lucet et al,[26] France	July 1997–December 1997	Prospective multicenter	Various media according to center	Adults in ICU swabs within 24 hours admission from nose and skin (both axilla and groin)	2,347
Papia et al,[27] Canada	May 1996–May 1997	Case control	Mannitol agar	Swabs from adults in acute care ward from different sites	1,742
Lautenbach et al,[28] USA	January 2008–May 2008	Cross-section	ChromAgar	Swabs on admission by research nurse and self on admission from different sites	56
Senn et al,[29] USA	2006–2009	Retrospective	M-Staphylococcus and MRSA-select agar	Swabs from different anatomic sites on admission for culture and PCR on adults	12,456
Bitterman et al,[30] Israel	2003–2006	Retrospective	BBL CHROMagar MRSA	Swabs from sites from ICU and non-ICU patients from screening sample (SS) and clinical diagnostic sample (CDS)	Not stated

MRSA positive number (%)	MRSA site colonization			Best site combination	
	Nasal	Extra-nasal	Proportion to be missed if nasal alone	Two	Three
925/4,769 (19.4%)	467/925 (50.5%)	458/925 (49.5%)	365 (39.5%)	Throat/groin 74.5% (71.7–77.3) Nose/groin 72.1% (69.2–75)	Throat/nose/groin 92% (90.1–93.6) Nose/throat/perineum 91% (88.9–92.7)
627/2,3365 (2.7%)	419/627 (66.8%)	208/627 (33.1%)	160 (34%)	Nares/rectum 586/612 (96% 94–98)	
59/282 (21%)	20/59 (34%)	39/59 (66.1%)	66%	Nasal/throat 50/59 (84.7%)	Nasal/throat/rectum (94.9%)
	48/71 (67%)	23/71 (32.4%)	17/71 (24%)	Nasal/inguinal (96%)	
90/400 (22.5%)	70/90 (77.8%)	20/90 (22.2%)	11 (12.2%)	Nose/throat 86/90 (95.5%), Throat/groin 84/90 (93.3%), Nose/groin 82/90 (91.1%)	
150/3,686 (4.1%)	35/45 (78.5%)	16/45 (35.6%)	5/45 (11%)	Nasal/perineum (88.9%)	Nasal/throat/perineum (98%)
65/650 (10%) Direct culture (157/650 [24%] broth-enriched)	114/157 (72.6%)	43/157 (27.3%)	27 (17.2%)	Nasal/throat 134/157 (85.4%)	Nasal/throat/perineum 146/157 (93.2%)
123/1,250 (9.8%)	53/123 (43.1%)	70/123 (56.9%)	54.3%	Nose/rectum (91.9%)	Nose/axilla/rectum (100%)
29/425 (6.8%)	26/29 (89.7%)	22/29 (76%)	≤1	Nose/groin (100%)	
16/150 (10.7%)	9/16 (56.2%)	6/16 (37.5%)	3 (2%)	Nasal/oropharynx (62.5%)	Nasal/oropharynx/perineum (81%)
Not stated	48/53 (91%)	40/53 (75.5%)	Similar sensitivity but combined samples increasing negative predictive value	Nares/groin (98%)	
20/535 (3.7%)	18/20 (90%)	5/20 (25%)	Similar sensitivity but combined samples increasing negative predictive value	Nasal/axillary (100%)	
162/2,347 (6.9%)	126/162 (77.8%)	72/162 (44.4%)	19/162 (7.2%)	Nasal/skin 148/162 (92%)	
23/1,742 (1.3%)	15/23 (65.2%)	13/23 (56.5%)	6/23 (26.1%)	Nasal/wound (91.3%)	Nasal/wound/perineum (95.7%)
Not stated	46/55 (84%)	48/55 (87%)	3/55 (5.5%)	Nares/throat 50/55 (91%)	Nares/throat/groin (98%)
3,137/12,456 (25.2%)	1,509/3,137 (48%)	1,628/3,137 (51.9%)	1,320/3,137 (42.1%)	Groin/throat (89%)	Nose/groin/throat (96%)
359	243/359 (67.7%)	117/359 (32.3%)	80/359 (22.2%)	Nares/perineum (89.6%)	Nares/perineum/throat (93.6%)

Abbreviations: OX, Ofloxacin; FOX, cefoxitin; MRSA, methicillin-resistant *Staphylococcus aureus;* TID, theoretical isolation days; ICU, intensive care unit; HA, hospital associated; SSTI, skin and soft tissue infection; MICU, medical ICU; PCR, polymerase chain reaction.

Table 2 Comparison of the prevalence of MRSA isolates detection between single nasal screening and nasal plus single extra-nasal or nasal plus multiple extra-nasal screening

Stratification of studies by MRSA prevalence	MRSA prevalence (% [CI])	Proportion of MRSA detected by nasal screening (range)	Proportion of extra-nasal MRSA screening detected (range)	Proportion of MRSA to be missed without extra-nasal screening (range)	Proportion of nasal plus one site combination (range)	Proportion of nasal plus two extra-nasal sites combination (range)
Low MRSA prevalence studies (≤6%)	3% (1.3–4.1)	75.1% (65–90)	37.6% (25–56.5)	23.7% (11–34)	94% (88.9–100)	96.9% (95.7–98)
High MRSA prevalence studies (≥6%)	16.3% (6.8–25.2)	64.6% (43.1–89.7)	46.4% (22.2–76)	26.8% (0.3–66)	85.9% (62.5–100)	92.7% (81–100)
All studies	12.2% (1.3–24)	68.2% (34–91)	47.6% (22.2–87.0)	21.4% (0.3–66)	89.6% (62.5–100)	94.2% (81–100)

Abbreviations: MRSA, methicillin-resistant *Staphylococcus aureus*; CI, confidence interval.

perineum, and rectum are likely to limit the sites available for access due to increased number of participants declining to give consent to swabbing, thus leading to discrepancy of results.[22,23]

Conclusion

We concur with previous published findings based on localized research analysis. Our systemic review of 52,642 cases indicates that a combination of three swabs from different sites provided the highest detection rate of MRSA colonization. The use of three swab sites is likely to improve recognition and treatment of MRSA, which may in turn reduce infection and transmission to other patients in hospital despite associated incremental costs.

Recommendation

The prevalence of MRSA carriage plays an important role in strategies used to manage colonization. The decision on the optimal sampling sites for MRSA detection should be determined by the goal of the intervention. If the intention is eradication in low-prevalence, MRSA-colonized populations, prospective surveillance and infection control should be re-enforced. For reduction in high-prevalence settings, prospective surveillance should be considered with universal screening.

Disclosure

The authors report no conflicts of interest in this work.

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