Prevalence of Nasal Carriage of Methicillin-Resistant *Staphylococcus aureus* among Health Care Workers in a Tertiary Care Hospital, Jazan Province, Kingdom of Saudi Arabia

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Abstract: Background: Globally, methicillin resistant *Staphylococcus aureus* (MRSA) is one of the leading bacteria causing nosocomial infections. Hence, we conducted a study on the colonization of MRSA among health care workers (HCWs) from a south coastal region of Saudi Arabia. Materials and Methods: A total of 174 nasal swab samples were collected from HCWs (physicians, nurses, lab specialists and workers) from different departments of a tertiary care hospital, Jazan Province, Saudi Arabia. MRSA strains were identified using an automated VITEK 2 microbial identification system (bioMérieux, Marcy l'Etoile, France). Results: Our results reveal that 27% of HCWs were colonized with *S. aureus,* and among them, 12.1% were MRSA, and 14.9% were methicillin sensitive *Staphylococcus aureus* (MSSA) strains. MRSA carriage among HCWs was 2.9% in doctors, 7.5% in nurses and 0.6% in laboratory staff. The MRSA carriage rate in HCWs, according to their working department, was varied. Among MRSA strains, four were MLSB inducible. Conclusions: There is an urgent need to improve effective control measures for preventing the spread of MRSA.

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1. Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) poses serious global public health problems (Aliberti *et al.,* 2016). Globally, MRSA is one of the major causes of hospital acquired infections (Visalachy *et al.,* 2016). The prevalence of MRSA among health care workers (HCWs) has been reported in various countries (Sassmannshausen *et al.,* 2016). The carriage of MRSA in HCWs in a non-outbreak setting was reported to be higher when compared to an outbreak setting (Dulon *et al.,* 2014). Recently, Al-Humanidan *et al.* (2015) reported risk factors of nasal carriage of *Staphylococcus aureus* and MRSA among health care staff in central Saudi Arabia, but there are a very limited number of reports from other regions of Saudi Arabia (Al-Yousef and Taha, 2016), and there are very few reports around the world, especially the occupational related carriage of MRSA among HCWs (Dulon *et al.,*, 2014). The average prevalence of MRSA in HCWs has been estimated to be 4.6% (Albrich and Harbarth, 2008). Transmission of MRSA through hand contamination is considered one of the most important modes (Cimolai, 2008) and other modes of transmission of MRSA have been reported through the clothes and equipment of HCWs (Henderson, 2006). Indeed, the mass screening of health care workers for MRSA carriage is an ongoing controversy in relation to various issues, such as advantages, disadvantages and ethical issues, but detection of MRSA in health care workers is necessary, especially in critical care areas in the hospital (Simpson *et al.,* 2007). Different rules were followed by various countries; for example, in European countries, the screening of HCWs were conducted for MRSA carriage in epidemiological situations (Coia *et al.,* 2006), and the Netherlands advocates that staff screen only after each contact with an MRSA positive patient. Apart from this approach, there are recent reports of increasing macrolide (erythromycin) lincosamide (clindamycin) streptogramin resistance B (quinupristin dalfopristin) (Vallianou *et al.,* 2015; Pereira *et al.,* 2016) and inducible clindamycin resistance among *S. aureus* clinical isolates (Lall *et al.,* 2014). Nevertheless, to date, there is no information on macrolide-lincosamide-streptogramin B resistance and inducible clindamycin resistance (MLSB inducible) among nasal carriage of *S. aureus* isolates from HCWs in

Saudi Arabia. Hence, the following study was conducted to rule out the prevalence of the nasal carriage of MRSA including macrolide-lincosamide-streptogramin B resistance and inducible clindamycin resistance in various occupational groups and medical specialists in health care settings in Saudi Arabia.

2. Materials and Methods

Sample collection and processing

Nasopharyngeal swabs were collected from 174 HCWs (physicians, nurses, lab specialists and workers) from different departments (Table 1) of a tertiary care hospital, Jazan Province, Saudi Arabia. Among the health care workers, 114 were males and 60 were females of different nationalities. All of the information pertaining to research was collected and informed consent was obtained from all HCWs. Ethical approval was obtained from the Ministry of Health, Saudi Arabia. All of the swabs were collected in transport media and transported immediately to a microbiology lab for processing.

Each swab was inoculated in 1 mL of enrichment broth (Iyer *et al.,* 2014) and incubated at 35 °C for 24 hours. After 24 hours, they were sub-cultured on blood agar (Hi Media, Mumbai) and incubated at 35 °C for 24 hours. After 24 hours, beta hemolytic colonies were picked for further characterization by Gram stain, the catalase test and the coagulase test (Brown *et al.,* 2005).

Automated method

All coagulase positive strains were further identified using the VITEK 2 microbial identification and susceptibility system (bioMérieux, Marcy l'Etoile, France) (Brown DF *et al.,* 2005). The VITEK 2 system automatically detects the growth of bacteria and the sensitivity of bacteria. The VITEK 2 system works within the guidelines of the Clinical and Laboratory Standards Institute (CLSI). For the identification of gram-positive cocci, the Gram-positive reagent card (GP ID card; bioMérieux, Marcy l'Etoile, France) was used, and the antibiotic sensitivity test reagent card (AST-P; bioMérieux, Marcy l'Etoile, France) was used. *S. aureus* strain ATCC (25923) was used as a control in our study.

Statistical methods

The data were analyzed by the Statistical Package for Social Science software (SPSS v20.0; IBM Crop, Armonk, N.Y., USA). The values were expressed as the mean, standard deviation and percentages wherever necessary.

3. Results

Epidemiological data

Out of the 174 samples, 27% (47) of HCWs carry *S. aureus* in the anterior nares, and 12.1% (21) were MRSA. MRSA carriage in male HCWs was 4% (7) out of 60 male HCWs, whereas in female HCWs, it was 8% (14) out of 114 female HCWs. MRSA nasal carriage was found in 9.2% (16) of HCWs belonging to the 20- to 30-year-old age group followed by 1.7% (3) of HCWs belonging to the 30- to 40-year-old age group, and 0.6% (1) of both age groups of HCWs belong to the 40- to 50-year-old and 50- to 60-year-old age group. Nonetheless, MRSA carriage in HCWs and according to working departments was 3.4% (6) from the hemodialysis unit, 1.7% (3) from the orthopedic unit, 1.1% (2) from the burn unit, 1.1% (2) from ICU unit, 1.1% (2) from medicine unit, 1.1% (2) from the laboratory unit and 0.6% (1) from each unit belonging to dental, ENT, gynecology and neurology. Interestingly, MRSA carriage was found in 2.9% (5) of doctors, 7.5% (13) of nurses and 0.6% (1) of laboratory staff (Table 1). The nasal carriage of methicillin sensitive *Staphylococcus aureus* (MSSA) in HCWs is shown in Table 1.

Antibiotic resistance pattern in MRSA isolates

MRSA isolates from HCWs were resistant to penicillin (100%), oxacillin (100%), gentamycin (28.6%), erythromycin (19%), clindamycin (23.8%), tetracycline (23.8%), Trimethoprim/sulfamethoxazole (SXT) (23.8%), ciprofloxacin (28.6%) and levofloxacin (4.8%). Some strains of the MRSA isolates were shown with intermediate sensitivity to ciprofloxacin (4.8%), levofloxacin (14.3%) and nitrofurantoin (4.8%) (Table 2).

Among the isolated MRSA stains (21), 12 strains belong to modification of the penicillin binding protein (PBP) (mecA) and are resistant to streptogramins, four strains belong to the modification of PBP (mecA) and were macrolide-lincosamide-streptogramin B (MLSB) inducible, four strains belong to modification of PBP (mecA and ACQ pase) and one strain was inconsistent (Table 3).

Antibiotic resistance pattern in MSSA isolates

MSSA strain isolates were resistant to penicillin (80.8%), erythromycin (7.7%), clindamycin (7.7%), tetracycline (15.4%) and SXT (3.8%) (Table 2). MSSA strain isolates showed intermediate sensitivity to ciprofloxacin (7.7%) and nitrofurantoin (3.8%).

Out of the 26 strains of MSSA, 18 strains were resistant to streptogramins (SGA-SGB), two strains were vancomycin intermediate *Staphylococcus aureus* (VISA) and resistant to streptogramins (SGA-SGB), one strain was VISA (Hetero-VISA, ACQ pase or modification of PBP and resistant to streptogramins; SGA-SGB), one strain was one ACQ pase or modification of PBP, one strain was ACQ pase or

modification of PBP and resistant to streptogramins (SGA-SGB), one strain was MLSB inducible and one strain ACQ pase or modification of PBP and MLSB inducible (Table 3).

Table 1. Summary of HCWs nasal carriage of *Staphylococcus aureus* when working in a tertiary care hospital in Jazan Province, Saudi Arabia.

Participant group		Total number (%)	Nasal carrier		
			MSSA n (%)	MRSA n (%)	Total number of SA (%)
All participants		174 (100)	26 (14.9)	21(12.1)	47 (27)
Gender	Male	60 (34.5)	13 (7.5)	7 (4.0)	20 (11.5)
	Female	114 (65.5)	13 (7.5)	14(8.0)	27 (15.5)
Age	20-30 yrs	122 (70.1)	18 (10.3)	16 (9.2)	34 (19.5)
	30 - 40 yrs	33 (19.0)	7 (4.0)	3 (1.7)	10 (5.7)
	40-50 yrs	16 (9.2)	1 (0.6)	1 (0.6)	2 (1.2)
	50 - 60 yrs	3 (1.7)	0 (0.0)	1 (0.6)	1 (0.6)
Department	Burn	11 (6.3)	1 (0.6)	2 (1.1)	3 (1.7)
	Cardio	3 (1.7)	1 (0.6)	0 (0.0)	1 (0.6)
	Dental	8 (4.6)	2 (1.1)	1 (0.6)	3 (1.7)
	ENT	3 (1.7)	0 (0.0)	1 (0.6)	1 (0.6)
	Gynecology	13 (7.5)	2 (1.1)	1 (0.6)	3 (1.7)
	Hemodialysis	25 (14.4)	4 (2.3)	6 (3.4)	10 (5.7)
	Housekeeping	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
	ICU	12 (6.9)	0 (0.0)	2 (1.1)	2 (1.1)
	NICU	15 (8.6)	1 (0.6)	0 (0.0)	1 (0.6)
	Medicine	18 (10.3)	7 (4.0)	2 (1.1)	9 (5.1)
	Neurology	5 (2.9)	0 (0.0)	1 (0.6)	1 (0.6)
	Orthopedic	18 (10.3)	3 (1.7)	3 (1.7)	6 (3.4)
	Pediatric	4 (2.3)	1 (0.6)	0 (0.0)	1 (0.6)
	Surgery	11 (6.3)	1 (0.6)	0 (0.0)	1 (0.6)
	OPD	2 (1.1)	1 (0.6)	0 (0.0)	1 (0.6)
	Laboratory	18 (10.3)	2 (1.1)	2 (1.1)	4 (2.2)
	Psychology	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)
	Isolation	3 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)
	Endoscopy	2 (1.1)	0 (0.0)	0 (0.0)	0 (0.0)
Occupation	Doctor	38 (21.8)	4 (2.3)	5 (2.9)	9 (5.2)
	Nurse	111 (63.8)	31 (17.8)	13 (7.5)	44 (25.3)
	House keeping	5 (2.9)	2 (1.1)	0 (0.0)	2 (1.1)
	Lab. technician	12 (6.9)	2 (1.1)	1 (0.6)	3 (1.7)

MSSA, methicillin sensitive *Staphylococcus aureus*; MRSA, methicillin resistant *Staphylococcus aureus*; SA, *Staphylococcus aureus*

Table 2. Antibiotic-resistance among MSSA and MRSA isolates from HCWs

Antibiotics	MSSA total n= 26 (%)			MRSA total n= 21 (%)		
	S	R	I	S	R	I
Penicillin	4 (15.4)	21(80.8)	-	-	21(100)	-
Oxacillin	26 (100)	-	-	-	21(100)	-
Gentamycin	26 (100)	-	-	15 (71.4)	6 (28.6)	-
Erythromycin	24 (92.3)	2 (7.7)	-	17 (81.0)	4 (19.0)	-
Inducible clindamycin resistance	-	2(7.7)	-	-	4 (19.0)	-
Clindamycin	24 (92.3)	2 (7.7)	-	16 (76.2)	5 (23.8)	-
Vancomycin	26 (100)	-	-	21 (100)	-	-
Tetracycline	22 (84.6)	4 (15.4)	-	16 (76.2)	5 (23.8)	-
SXT	25 (96.1)	1 (3.8)	-	16 (76.2)	5 (23.8)	-
Rifampicin	26 (100)	-	-	21(100)	-	-
Ciprofloxacin	24 (92.3)	-	2 (7.7)	14 (66.7)	6 (28.6)	1(4.8)
Levofloxacin	26 (100)	-	-	18 (85.7)	1(4.8)	2 (14.3)
Linezolid	26 (100)	-	-	21(100)	-	-
Nitrofurantoin	25 (96.1)	-	1 (3.8)	20 (95.2)	-	1 (4.8)

MSSA, methicillin sensitive *Staphylococcus aureus*; MRSA, methicillin resistant *Staphylococcus aureus*
S, sensitivity; R, resistance; I, intermediate
SXT= Trimethoprim/sulfamethoxazole

Table 3. **Type of antibiotic-resistant strains isolated among MSSA and MRSA isolates from HCWs**

Bacterial strains	Type of resistance strain	Number of antibiotic resistant strain
26 MSSA	Macrolides/lincosamides/streptogramins	18 (resistant to streptogramins- SGA-SGB)
	Glycopeptides + macrolides/ lincosamides/ streptogramins	2 (VISA and resistant to streptogramins- SGA-SGB)
	Glycopeptides + beta-bactams + macrolides/lincosamides/streptogramins	1 (VISA, Hetero-VISA, ACQ pase or modification of PBP and resistant to streptogramins -SGA-SGB)
	Glycopeptides + beta-bactams + macrolides/lincosamides/streptogramins	1 (VISA, ACQ pase or modification of PBP and resistant to streptogramins- SGA-SGB)
	Beta-lactams	1 (ACQ pase or modification of PBP)
	Beta-lactams + macrolides/lincosamides/streptogramins	1 (ACQ pase or modification of PBP and resistant to streptogramins-SGA-SGB)
	Macrolides/lincosamides/streptogramins	1 (MLSB inducible)
	Beta-lactams + Macrolides/lincosamides/streptogramins	1 (ACQ pase or modification of PBP and MLSB inducible)
22 MRSA		
	Beta-lactams + macrolides/lincosamides/streptogramins	12 (Modification of PBP (mecA) and resistant to streptogramins-SGA-SGB)
	Beta-lactams + macrolides/lincosamides/streptogramins	4 (Modification of PBP (mecA) and MLSB inducible)
	Inconsistent	1 (Inconsistent)
	Beta-lactams	4 (Modification of PBP (mecA) and ACQ pase)

MSSA, methicillin sensitive *Staphylococcus aureus*; MRSA, methicillin resistant *Staphylococcus aureus*.
SGA-SGB, streptogramins A- streptogramins B.
ViSA, vancomycin intermediate *Staphylococcus aureus;* MLSB inducible, macrolide-lincosamide-streptogramin B resistance and inducible clindamycin resistance.
PBP, penicillin binding protein; *mecA* gene.

4. Discussion

Globally, MRSA has become a major nosocomial pathogen (Dou *et al.,* 2016).

There is considerable improvement in the delivery of health care in a tertiary care hospitals throughout the world, but there are still reports of

nasal colonization of MRSA (4.6%) among health care workers (Orellana *et al.,* 2016) (Visalachy *et al.,* 2016). This colonization presents a significant risk of pathogen transmission (Bingham *et al.,* 2016), and recently, there have been reports of a nosocomial MRSA outbreak in a neonatal intensive care unit (Steensels *et al.,* 2016).

Castro *et al.* (2016) reported the prevalence of nasal carriage of MRSA in health care professionals in a Portuguese hospital. These researchers observed a nasal carriage rate of 17.2% MRSA in health care professionals, whereas a MRSA prevalence of 12.1% was observed among HCWs in the present study, which is less when compared to 18% that was reported previously from Saudi Arabia (Al-Humaidan *et al.,* 2015). However, our results are within the international range of MRSA carriage of 6-18% among HCWs. MRSA nasal colonization in HCWs is more common when compared to the general population due to contact exposure with patients who are MRSA carriers. In the present study, nasal carriage of MRSA was higher among female HCWs compared with that of male HCWs and similar results were reported in an earlier study from Saudi Arabia (Ahmed S, 2010). A greater percentage of nasal carriage of MRSA in HCWs belongs to the 20- to 30-year-old age group (9.2%) followed by the 30- to 40-year-old (1.7%), the 40- to 50-year-old (0.6%) and the 50- to 60-year-old (0.6%) age groups. However, occupational related nasal carriage of MRSA was found in more than 1% in HCWs working in a hemodialysis unit (3.4%), orthopedic unit (1.7%), burn unit (1.1%), ICU unit (1.1%), medicine unit (1.1%), and laboratory unit (1.1%), whereas it was less than 1% in HCWs working in gynecology (0.6%), neurology (0.6%), ENT (0.6%) and dental (0.6%). Nasal carriage of MRSA in HCWs workers was varied according to their working units. A previous study reported a decreasing order of carriage of MRSA in HCWs working in a burn unit followed by an ICU unit and out-patient department from Saudi Arabia because they collected samples from only three units (Iyer *et al.,* 2014). Elie-Turenne *et al.* (2010) reported occupational related nasal carriage of MRSA in HCWs working in emergency departmental works (4.7%), the ICU unit (1.6%), emergency medical services (0.4%) and neonatal intensive care units (0.02%) (Mangini E et al., 2013). The present study indicates future research should focus on effective control mechanisms in different units, where we observed a higher percentage of nasal carriage of MRSA among HCWs (Lindberg and Lindberg, 2012).

Dulon *et al.* (2013) reported that the nasal carriage of MRSA in physicians was 5.3%, whereas in the present study it was 2.9% and reported to be 3.8% in Elie-Turenne *et al.* (2010). Tsao *et al.* (2015) reported that the nasal carriage of MRSA in nurses was 15.6%, whereas in the present study it was 17.8% and reported to be 10.5% in Elie-Turenne *et al.* (2010). This study is in agreement with previous study reports, which showed that among HCWs, nursing groups experience the highest risk for MRSA colonization (Sassmannshausen *et al.,* 2016).

Among MRSA isolates from HCWs, resistance to penicillin (100%), oxacillin (100%), gentamycin (28.6%), ciprofloxacin (28.6%), clindamycin (23.8%), tetracycline (23.8%), SXT (23.8%), erythromycin (19%), and levofloxacin (4.8%) (Table 2) were reported, whereas in another study from Saudi Arabia, MRSA isolates were found to be resistant to penicillin (100%), oxacillin (100%), gentamycin (2.8%), clindamycin (69.4%), tetracycline (11.1%), and erythromycin (72.2%). Castro A et al. (2016) reported that the majority of nasal carriage of MRSA was found to be resistant to beta-lactams, erythromycin and ciprofloxacin. Among the MSSA strain isolates from HCWs, resistance was found for penicillin (80.8%), tetracycline (15.4%), erythromycin (7.7%), clindamycin (7.7%), and SXT (3.8%) (Table 2). It was found that isolates of MRSA strains were highly resistant to various antibiotics compared to MSSA isolates. The *mecA* gene, which is present in the staphylococcal (MRSA) cassette chromosome, codes for a penicillin-binding protein (PBP2a) and prevents the action of beta-lactam antibiotics (Al-Humaidan *et al.,* 2015).

Among the 21 isolated MRSA strains, four strains belong to the modification of PBP (mecA) and are MLSB inducible (Table 3). Out of the 26 strains of MSSA, two strains were vancomycin intermediate *Staphylococcus aureus* (VISA) and resistant to streptogramins (SGA-SGB), one strain was VISA (Hetero-VISA, ACQ pase or modification of PBP and resistant to streptogramins; SGA-SGB), one strain was MLSB inducible and one strain was ACQ pase or modification of PBP and MLSB inducible (Table 3). Among *Staphylococci*, the mechanism is the gene *msr A* that encodes the efflux pump, or another mechanism is the modification of the drug binding site on ribosomes that promotes resistance to macrolides, lincosamides and the streptogramins B group (MSLB resistance) (Leclercq, 2002). These three drug classes share an *erm* gene (routinely *erm* A or *erm* C), which encodes methylation of the 23S rRNA binding site (Aktas *et al.,* 2007). MLSB inducible resistance is resistant to erythromycin but appears sensitive to clindamycin (Gupta *et al.,* 2009).

Isolation of VISA and its precursor hetero-VISA (hVISA) among MSSA from HCWs was not reported earlier from Saudi Arabia. VISA is due to the accumulation of mutations and not to the *van* gene, which mediates resistance in Enterococci and

Staphylococci. It exhibits a diverse and intriguing genetic mechanism to express its resistance phenotype (Hiramatsu *et al.,* 2014). Isolation of resistance strains is highly variable with regard to the geographic locality. It is worth noting from a recent report that states that role of nasal MRSA carriage of HCWs in nosocomial outbreaks was associated with improper nursing care practices (Stock *et al.,* 2016). The present study presents data regarding antibacterial resistance, which will provide guidance to take appropriate measures to limit the risk of MRSA cross-contamination by HCWs.

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