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#### Major article

# Prevalence of *Staphylococcus aureus* methicillin-sensitive and methicillin-resistant nasal and pharyngeal colonization in outpatients in Lebanon

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Key Words: Staphylococcus aureus Methicillin-resistant Staphylococcus aureus Methicillin-sensitive Staphylococcus aureus Nose and throat carriage **Background:** There is an increasing concern about methicillin-resistant *Staphylococcus aureus* (MRSA) infections in the community. This study aimed to evaluate the rate of *S aureus* nasopharyngeal colonization in outpatients as the primary endpoint, and also to study the impact of several possible risk factors, including recent hospitalization, recent surgical procedures, and antibiotic intake.

**Methods:** A total of 1,526 consecutive outpatients underwent surveillance cultures after completing a questionnaire. Isolated *S aureus* strains were tested for antibiotic susceptibility. The Pearson  $\chi^2$  test was used for statistical analysis. The differences were considered to be statistically significant at a *P* value <.05.

**Results:** Out of the 1,526 outpatients tested, 133 (8.7%) carried *S aureus* in the nose and/or throat. Only 2 of those cases were MRSA, and both were isolated from the nose. One hundred thirty-one patients had methicillin-sensitive *S aureus*, 13 with simultaneous carriage in the nose and throat. Among the risk factors, a relative working in health care, presence of an intravascular device, recent dental procedure, and health club use were significantly associated with an increased risk of *S aureus* colonization, with *P* values of .00, .02, .04, and .00, respectively, calculated by the  $\chi^2$  test.

**Conclusions:** The prevalence of MRSA is still low in our study population within the Lebanese community. The only significant risk factors playing a role in increasing the carriage of *S aureus* were related to health care exposure.

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Methicillin-resistant *Staphylococcus aureus* (MRSA) was described in 1961, shortly after the introduction of methicillin, and outbreaks of MRSA were already being reported by the early 1960s. Methicillin resistance is mediated by PBP-2a, a penicillin-binding protein encoded by the *mecA* gene that allows the organism to grow and divide in the presence of methicillin and other betalactam antibiotics. The *mecA* gene is located on a mobile genetic element known as the staphylococcal chromosome cassette (SCCmec).<sup>2</sup>

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Community-acquired (CA) MRSA is most often associated with skin and soft tissue infections in young, healthy individuals with no recent health care exposure.<sup>3</sup> Most CA-MRSA strains are sensitive to non—beta-lactam antibiotics, although a multidrug-resistant isolate has been described among men who have sex with men.<sup>4</sup> This strain contains the pUSA03 plasmid and carries resistance genes for beta-lactams, fluoroquinolones, tetracycline, macrolide, clindamycin, and mupirocin.<sup>4</sup> Most CA-MRSA strains carry SCCmec type IV or V, and frequently carry genes for the cytotoxin Panton-Valentine leukocidin that confers enhanced virulence.<sup>4</sup>

CA-MRSA was initially reported among injection drug users in the early 1980 and has since become the most frequent cause of skin and soft tissue infections presenting to US emergency departments and ambulatory clinics.<sup>5</sup> Community outbreaks have

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been reported in multiple settings, including native and aboriginal communities, sports teams, child care centers, military personnel, men who have sex with men, and prison inmates and guards. These observations have led to identification of risk factors with relatively poor predictive value for CA-MRSA, including skin trauma (eg. lacerations, abrasions, tattoos, injection drug use), cosmetic body shaving, incarceration, sharing of unclean equipment between users, and physical contact with others who have MRSA colonization or infection. Pets may play a role as a source of transmission. Many patients with CA-MRSA have no identifiable risk factors, however.

CA-MRSA infections also have been observed with increasing frequency among patients in hospital settings, because patients who acquire CA-MRSA strains in the community may require hospitalization and subsequently transmit such strains to other hospitalized patients. Skin and soft tissue remain the predominant sites of CA-MRSA infection, although CA-MRSA also can cause severe invasive diseases, such as necrotizing fasciitis, wound infections, otitis media and otitis externa, osteomyelitis, urinary tract infection, endocarditis, sepsis, and necrotizing pneumonia. S

The present study aimed to evaluate the rates of nasopharyngeal colonization of methicillin-sensitive *S aureus* (MSSA) and MRSA in a population of individuals in an outpatient department as the primary endpoint. Secondary endpoints focused on evaluating the impact of several possible risk factors, including recent hospitalization (in the 6 months before culture), recent surgical procedure, antibiotic intake, and rate of staphylococcal carriage.

#### **METHODS**

Consecutive patients of all age groups presenting to the outpatient laboratory between December 15, 2010, and May 30, 2011, for laboratory testing or for first hospital admission in the preoperative evaluation unit for ophthalmology for presurgical screening workup were recruited for nasal and pharyngeal swab culture. Cultures were performed after the patient provided written informed consent and completed a questionnaire. Those patients represented a random sample of minimally health care—exposed group of individuals from the general Lebanese population. Patients were recruited when they presented to the preoperative evaluation unit responsible for presurgical workup screening for ophthalmologic surgery in a university-affiliated tertiary care center in Beirut.

The questionnaire elicited information on the following risk factors: health care—related activity, close contact with someone working in health care, recent hospitalization (in the previous 6 months), recent nursing home admission, outpatient medical care admission in the previous year, skin or soft tissue infection in the previous 6 months, other skin diseases, dental surgery in the previous year, chronic illness (diabetes, renal failure, malignancy, or HIV-positive status), intravascular device or prosthesis, antimicrobial use within the previous 3 months, inhaled aerosol use in the previous 3 months, nasal spray use within the previous 3 months, injection device use in the previous 3 months, oral contraception, corticosteroid use, use of a health club facility, sharing of shaving material, tattoo, smoking, and alcohol and recreational drug intake.

Two samples for culture were obtained from a nose swab and a throat swab. The swabs were inoculated directly on mannitol salt medium and incubated for 24 hours at 37°C. Methods for isolation and identification of *S aureus* are described elsewhere. <sup>10,11</sup> The specificity of the reaction is ensured by simultaneous use of DR0596 Staphylase Test Reagent (Oxiod, Hampshire, UK; rabbit fibrinogensensitized sheep red blood cells) and DR0597 Staphylase Control Reagent (Oxiod; unsensitized sheep red blood cells). <sup>10,11</sup> All tests were run along with a control strain of *Staphylococcus aureus* ATCC 29213.

**Table 1**Demographic and clinical characteristics of enrolled patients

Characteristic	Value
Total number of patients	1,526
Patient location, n (%)	
Beirut	699 (47.2)
Mount Lebanon	540 (35)
North	78 (5.1)
South	141 (9.2)
Bekaa	68 (4.5)
Age, years, mean $\pm$ SD	$50.73\pm19.7$
Sex, n (%)	
Male	718 (47.1)
Female	808 (52.9)
S aureus carriage, n (%)	132 (8.6)
MSSA	130 (8.5)
MRSA (all detected in the nose)	2 (0.1)
Site of S aureus carriage, n (%)	
Nose alone	119 (7.8)
Throat alone	27 (1.8)
Nose and throat	13 (0.9)

Antibiotic susceptibility testing on identified isolates were done as described elsewhere  $^{12,13}$  through a disk diffusion assay. The following antibiotics were included: penicillin 10  $\mu g$ , oxacillin 5  $\mu g$ , cephalotin 30  $\mu g$ , cefoxitin 30  $\mu g$ , erythromycin 15  $\mu g$ , clindamycin 2  $\mu g$ , ciprofloxacin 5  $\mu g$ , rifampicin 5  $\mu g$ , fuscidic acid 10  $\mu g$ , teicoplanin 30  $\mu g$ , vancomycin 30  $\mu g$ , tetracycline 30  $\mu g$ , and tigecycline 15  $\mu g$ .

Resistance to oxacillin was evaluated by cefoxitin disk susceptibility testing  $^{14}$  and by plating isolates on an oxacillin plate containing 6  $\mu g/mL$  of oxacillin in Mueller-Hinton medium. All incubations were done at  $36^{\circ}\text{C}$ , and all readings were performed at 24 hours and 48 hours.  $^{15}$ 

No genetic study was done for *S aureus* type characterization. However, all strains demonstrating resistance to oxacillin were saved for reference and for future polymerase chain reaction analysis for *mec A* mutations.

For statistical analysis, data were collected, pooled, and analyzed using SPSS version 16.0 (SPSS, Chicago, IL). The  $\chi^2$  test was used for comparing categorical variables between groups except when expected values within cells were <5, in which case Fisher's exact test was used. A P value <.05 was considered to indicate statistical significance. If significance was found, then a subsequent logistic regression was performed to adjust for confusion factors (age, gender, and location of patient).

#### **RESULTS**

A total of 1,526 patients (718 males and 808 females) were included in this study. The patients ranged in age from 1 to 88 years, with a mean age of 51 years. One hundred and thirty-three were found to carry *S aureus* in the nose and/or throat. Only 2 of those cases were MRSA, and both were isolated from the nose. One hundred and thirty-one patients had MSSA, 13 with simultaneous recovery in the nose and throat and 119 with recovery only from the nose. The sex distribution of *S aureus* carriers was 87 of 718 males (12.12%) and 46 of 808 females (5.69%) (Table 1).

Logistic regression revealed no significant differences in the rate of *S aureus* carriage among the different districts ( $\chi^2 = 16.3$ ; P = .43).

The impact of the various identified risk factors on staphylococcal colonization is shown in Table 2. Among the risk factors, only intravascular device or prosthesis placement was significantly associated with an increased risk of *S aureus* colonization ( $\chi^2 = 5.93$ ; P = .024).

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