

# PREVALENCE OF METHICILLIN-RESISTANT *STAPHYLOCCOCUS AUREUS* AND ASSOCIATED RISK FACTORS ON ADMISSION TO A SPECIALIST CARE EYE HOSPITAL

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**Background:** *Staphylococcus aureus* is known to be a frequent pathogen in hospital settings, with its well-known and resistant forms to the anti-staphylococcal penicillins. Reports on community carriage outside hospital settings have been feared to be on the increase due to the frequency of reported cases on admission to hospitals. We undertook this study to determine the prevalence of, and to establish predictors for, nasal carriage of methicillin-resistant *S. aureus* (MRSA) at the time of admission to a specialist care eye hospital.

**Materials and Methods:** A prospective survey was conducted at King Khaled Eye Specialist Hospital (KKESH), Riyadh, during three differing weeks randomly selected from the year 1999. The first 100 patients admitted during those three weeks were selected according to inclusion criteria. The hospital is a 220-bed tertiary ophthalmic care facility, with an average 7,500 admissions per year. Nasal bacterial swabs were taken within 48 hours of admission and tested for all strains of *S. aureus* and sensitivity to methicillin. Detailed interviews were conducted about medical history and habitual environment.

**Results:** Of 306 nasal cultures tested, none was isolated for MRSA and 102 (33%) were sensitive to methicillin (MSSA). We found 0% nasal carriage rate for MRSA. Respondents had difficulty with questions related to antibiotic administration. No identifiable medical or environmental risk factors could be found.

**Conclusion:** Nasal swabs of patients admitted to KKESH did not reveal MRSA colonization, indicating that MRSA may not be prevalent in the community at present.

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**Key Words:** Antibiotics, community carriage, nasal, *Staphylococcus aureus*, methicillin-resistant *Staphylococcus aureus*.

Strains of *Staphylococcus aureus* resistant to methicillin were first described soon after the introduction of this antibiotic. Methicillin, the first of the anti-staphylococcal penicillins, was soon replaced by cloxacillin and flucloxacillin, but it rapidly became evident that strains of *S. aureus* that were resistant to methicillin were invariably resistant to the latter two, as well as cephalosporins.<sup>1</sup> *S. aureus* is known to be a frequent pathogen in hospital settings and forms of the pathogen resistant to methicillin are common isolates. In US hospitals, the prevalence of methicillin-resistant *S. aureus* (MRSA) increased from 2.4% in 1975 to 29% in 1991.<sup>2</sup>

Classically, MRSA has been a nosocomial problem associated with long hospital stays, numerous or prolonged antibiotic courses, the presence of invasive devices and proximity to an already infected or colonized patient.<sup>3</sup> There is also evidence that prolonged community carriage is increasing from studies in the USA and Japan.<sup>4,6</sup> In three reports on the epidemiology of MRSA at institutions in Canada, Switzerland and the USA, 20%-62% of patients colonized with this organism were detected within 48-72

and previous receipt of a fluoroquinolone,<sup>12</sup> organ transplantation, employment in health care, pressure sores, tube feeding, and hospitalization within the preceding year.<sup>13</sup> Troillet et al.<sup>4</sup> found that significant predictors of carriage were: prior detection of MRSA, open wounds, diabetes mellitus, treatments by injection, prior nursing home stays, visits at home by a nurse, and prior antibiotic treatments. In that case-control study, they also found that MRSA cases had stayed for longer periods in hospitals and had received longer antibiotic treatments within a year compared to controls.<sup>4</sup> Warshawsky et al. found that hospital contact was the single most important risk factor for the acquisition of MRSA.<sup>14</sup>

Community-acquired MRSA has been rarely reported, however, there is evidence of its occurrence.<sup>15-17</sup> It is unclear whether community acquisition of MRSA is truly occurring or whether findings simply represent acquisition associated with some contact with health care setting or health care providers. In a study carried out in Detroit, USA, during the 1980s, Saravolatz et al reported on a community-acquired MRSA epidemic which originated among parenteral drug abusers and disseminated among the general population.<sup>17</sup> Recent contact or cohabitation with a health care worker has also been recognized as a risk factor for the spread of MRSA, especially in overcrowded communities with low health standards and sanitation.<sup>18</sup>

In Saudi Arabia, many recent publications have identified the problem in district hospitals from various regions and reported on the increasing resistance of strains genetically identified in the Kingdom.<sup>19-23</sup> Most recently, community carriage in Saudi Arabia has been reported with

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Numerous risk factors for long-term or community carriage have been reported, including the presence of skin lesions,<sup>10</sup> wounds,<sup>11</sup> history of multi-site MRSA carriage,

a prevalence rate of 26.1% among healthy adults in Abha.<sup>24</sup> *Staphylococcus aureus* has been isolated from swimming pools and beaches in Saudi Arabia—a factor that may be of importance in potentiating carriers in the community.<sup>25</sup>

## Materials and Methods

The survey was carried out over three different weeks (to prevent possible seasonal bias), during 6-12 February, 24-30 April, and 20-24 November, 1999 at King Khaled Eye Specialist Hospital (KKESH). This tertiary ophthalmic facility has a 220-bed capacity with an average 7,500 admissions per year of patients referred from various regions of the Kingdom. At each start date all consecutive admissions identified by midnight census were noted with the aim of enrolling the first 100 admissions. Patients who refused enrollment, short-stay patients (non-admitted), and patients whose cultures were not obtained within the designated time of 48 hours were excluded

### Laboratory Protocol

A nasal culture from every consenting patient was obtained within 48 hours of admission. Nasal cultures were collected by using rayon swabs (Euromed culture tube with media). The swab was pre-moistened by breaking the ampoule of the transport media. The swab was then inserted into a single naris (approximately 1 cm) and rotated five times according to published methods.<sup>26</sup> Each tube was labeled and taken to the hospital's laboratory. Within two hours of arrival at the laboratory, each culture sample was direct-plated onto blood agar and mannitol salt agar. One-half of each plate was inoculated by turning the swab while rubbing it over the agar to expose all surfaces. A sterile loop was then used to streak the inoculum over the remaining half of the plate in at least two separate quadrants to achieve maximum isolation. Plates were incubated in air at 35°C for up to 48 hours. Plates were examined daily for characteristic white to yellow, opaque, butyrous, entire and convex colonies. Negative plates were discarded after 48 hours. *Staphylococcus aureus* was identified from suspicious colonies by gram stain, catalase and coagulase testing.<sup>26</sup>

All *Staphylococcus* isolates were screened for methicillin resistance by inoculation of Mueller-Hinton agar supplemented with salt and oxacillin 6 µg/mL, according to National Committee for Clinical Laboratory Standards (NCCLS) guidelines<sup>27</sup> and held for a full 24 hours. Cultures were not tested for multi-resistance to other antibiotics.

Wound cultures (in addition to the nasal culture), when obtained, were processed by laboratory routine, by plating directly onto sheep blood agar. *S. aureus* isolates were screened for methicillin resistance according to methods described above.

Laboratory personnel recorded culture results by patient medical record number in a log. The usual protocol of

notification of the attending physician and application of infection control measures would have been applied if a case of MRSA had been isolated. Those cultures were treated with additional sensitivities and minimal inhibition concentrations (MIC), determined by Etest® methodology (AB Biodisk, Solna, Sweden).<sup>28</sup> Using this specific methodology, the MIC interpretive breakpoint of oxacillin-resistant *S. aureus* strain is stated as  $\geq 4$  and sensitive strains as  $\leq 2$ .<sup>28</sup>

### Questionnaire Protocol

Interviews were carried out according to a specified questionnaire that covered the following: time since last hospitalization; length of time hospitalized in the preceding 12 months; time since last outpatient visit; antibiotic usage history including time since last antibiotic treatment and route; and for any medical condition requiring parenteral treatment. Patients were also asked if a member of their household had been hospitalized in the last six months. The questionnaire also included three questions regarding living conditions and habitat: number of persons living under the same roof; presence of running tap water; and number of toilets.

### History Protocol

After admission, medical records were reviewed for possible risk factors, such as immunodeficiency, malignancy, diabetes, renal disease requiring dialysis, any medical condition requiring lengthy immunosuppressive therapy and history of positive MRSA culture.

## Results

From a total of 313 patients, seven were excluded based on exclusion criteria, resulting in a net enrollment of 306 patients comprising 175 males (57%) and 131 females (43%). The mean age of the patients was 53.6 years (range 1-100), and 42 (14%) were under 12 years. The majority of nasal swabs (89%) were done prior to the patient being seen by the medical internist, while the others (11%) were taken within 24 hours of admission. Nasal carriage of *S. aureus* was detected in 102 patients (33%) and all were methicillin/oxacillin sensitive. No *S. aureus* was isolated in 204 (67%) of our sample. We could not find any nasal carriage of MRSA in our studied population.

Five of the 306 patients who reported open wound, had wound cultures taken in addition to the nasal culture. Three were swabbed at pre-admission, 1 within 48 hours, and 1 had the usual nasal swab but no wound swab. These four wound cultures did not grow *S. aureus*; 3 cultures were from the negative nasal swab group and 1 was from the methicillin-sensitive nasal swab group.

The questionnaire revealed that enrolled patients found it difficult to answer questions relating to antibiotic administration. The initial question was: "Have you ever taken penicillin or any other antibiotic?" The majority, 164

(54%) answered yes; 113 (37%) answered no, and 29 (9%) did not know. In other words, 46% were unable to provide any data. On subsequent questions, respondents could not answer questions relating specifically to timing, duration, and route of antibiotic treatment. Of the 164 patients who said they had had antibiotics in the past, 41 (25%) could not remember the date, 81 (49%) stated they had the antibiotics prior to a month previously, 25 (15%) within the month; and 17 (10%) said they had had antibiotics within the week. Regarding periods of antibiotic administration, 78 (48%) replied the period was less than 1 week, 52 (32%) replied it was more than 1 week, 15 (9%) said it was more than 2 weeks; and 19 (12%) could not recall the duration. On the route of administration: 136 (83%) said they had taken their antibiotics by mouth, 21 (13%) by injection, and 7 (5%) reported taking a combination of oral/injection of antibiotics. When asked about any treatment by injection in the past for any reason, 155 (51%) answered positively.

Important questions relevant to developing resistance (previous hospitalization of the patient or a member of the family as well as visiting an outpatient unit in the recent past) received favorable responses with only 2% not providing data. Most (190 or 62%) of the respondents had not been hospitalized nor stayed in a nursing home within the past year, while 116 (38%) had been hospitalized within the year. Of those hospitalized, 65 (56%) were in-patients for <1 week, 39 (34%) for 1-4 weeks, and 6 (5%) for more than 4 weeks, while another 6 (5%) were unsure and were thus excluded. As for outpatient visits to a medical center, 276 (90%) had visited an outpatient center but the majority of visits (40%) were prior to a period of at least 1 month from the interview date. As for members within the family being hospitalized during the last 6 months, only 16% gave a positive history of previous admission to hospitals of a family member.

Living conditions and sanitation were questioned to establish whether overcrowding and lack of certain facilities could contribute to exposure to a carrier within the same household. Family sizes ranged from 1-40 members under the same roof. The majority of households had between 7-10 members (mean 8.6). The majority had piped water either from an outside well or reservoir or both. Only 7% of families did not have running water in their homes, with water being carried manually into the house from an outside well. The number of indoor toilet facilities in any household varied from none (2%) to 1 (6%), to >1 toilet (92%).

Medical questions were devised to detect contributing factors, if any, to being a carrier of resistant strains of *S. aureus*, in line with published reports.<sup>18</sup> Of the 306 patients, 201 were classified as healthy, 88 were diabetic (with 9% insulin dependent), 5 had malignant disease, 5 were immunodeficient, 4 were immunosuppressed, and 3 were on dialysis. No identifiable medical or environmental risk factors could be found.

## Discussion

*Staphylococcus aureus* resistance to antibiotics is causing worldwide concern particularly to methicillin. When penicillin was introduced in 1944, over 95% of *Staphylococcus* isolates were susceptible to the drug. Today, the proportion has shrunk to 10%.<sup>29</sup> During the early 1950s, resistance began to develop to this so-called wonder drug, however, the introduction of beta-lactamase stable antibiotics in the early 1960s briefly overcame this resistance. The introduction and use of gentamycin during the late 1960s and early 1970s halted the development of MRSA. However by the late 1970s, gentamycin-resistant MRSA had emerged.<sup>29</sup>

Antimicrobial resistance is an inevitable consequence of antimicrobial use. This resistance makes infections more difficult and more expensive to treat. Also it may increase complications and lengthen hospital stay.<sup>30</sup>

Methicillin-resistant *S. aureus*, known to be a nosocomial infection, has long been suspected to have spread to the community. This has led to several studies to assess community carriage for MRSA.<sup>7-9</sup> These reports highlighted new and important predisposing factors within societies that may facilitate spread in the community.<sup>18</sup> Overcrowded and low sanitary living conditions, and parenteral drug abuse have been thought to be responsible for a major outbreak in the Detroit area, USA, in the 1980s.<sup>17</sup> Recent changes in health trends from hospital-based care to extended-care facilities and nursing homes with early discharge of patients as well as the indiscriminate prescribing and easy availability of antibiotics in some societies were suggested to play major roles in the development and spread of MRSA.<sup>26</sup>

At our institution, during a period of eight years (1989 - 1996), the percentage of MRSA for all *S. aureus* isolates per year ranged from 1.9% -6.6% (KKESH internal statistics). There were four patients with MRSA-positive cultures in 1997 who were infected or colonized prior to admission. The suspicion of a possible community carriage in the presence of major risk factors within the community prompted us to investigate MRSA carriage or infection on admission in this present study.

Our results differ from some of the above published articles possibly due to a variety of factors. King Khaled Eye Specialist Hospital is a tertiary care center that mostly serves elective ocular surgical procedures. Acute cases form a small percentage of all admissions. Most multiple trauma patients and patients who require intensive care during their ocular management are not accepted for care at KKESH. Hence, our sample population is specialty-oriented and mainly non-emergent. Also, demographic characteristics, societal norms, as well as cultural habits may have impacted on our results.

The aim of the survey was primarily to identify nasal carriage of MRSA on admission to KKESH and also to identify possible risk factors as indicators of resistance. Our

results showed no carriers of MRSA and only 33% of the patients showed methicillin-sensitive *S. aureus* (MSSA) nasal carriage.

Our questionnaire was designed to establish frequency of possible medical and social risk factors for developing resistance. In spite of the presence of significant risk factors in our studied population for community carriage or acquisition of MRSA (for example, risk factors of “40% positive for hospitalization in the last year” and “90% positive for contact with a health care setting by an outpatient visit”), it is evident that this did not predispose to an acquisition in our studied sample.

Respondents had difficulty in answering questions about antibiotic usage, consequently antibiotic usage history and its importance as a risk factor was not determined. This is interesting in light of the theory that misuse or inappropriate use of antibiotics by patients with unrestricted access to antibiotics, as is the case in Saudi Arabia, is a possible contributing factor to increasing prevalence of antibiotic resistance.<sup>26</sup> It is not known whether antibiotic therapy promotes colonization of patients with multiple-resistant *S. aureus* strains or serves as an indication of increased susceptibility.

Our sample also differs from quoted studies in the few numbers of patients identified with potential medical risk factors: immunodeficiency (5), immunosuppression (4), malignancy (5), open wounds (5), or renal disease requiring dialysis (3). Diabetes was the only medical variable that was commonly found in our studied population (29%). Diabetes does not appear to be an independent risk factor for the carriage of MRSA in our study group.

Although not specifically considered, cultural habits and societal norms in our studied population may contribute to the favorable findings. For example, although drug abuse has been reported, we believe the majority of drug abusers in our society are possibly inhaling or ingesting drugs rather than injecting them. Additionally, extended nursing facilities and home nursing in general is in its infancy in our health care system and as yet could not contribute to communal spread of MRSA. The questions on living and sanitary conditions did not give any predictors for MRSA acquisition or carriage in view of the nasal culture results.

In conclusion, this survey was an attempt to explore community or long-term carriage of MRSA in patients at admission to a tertiary eye care facility. This random sample of patients referred from different regions of Saudi Arabia did not reveal nasal carriage of MRSA, which may indicate that community or long-term carriage of MRSA and community acquisition of MRSA may not be prevalent in our society at present. Further more extensive studies in appropriate settings are recommended.

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