

# Epidemiology and clinical features of methicillin-resistant *Staphylococcus aureus* in the University Hospital, Jeddah, Saudi Arabia

Tariq A Madani MD

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**OBJECTIVE:** To describe the prevalence, demography and clinical characteristics of patients who were colonized or infected with methicillin-resistant *Staphylococcus aureus* (MRSA) in 1998 at King Abdulaziz University Hospital, Jeddah, Saudi Arabia.

**PATIENTS AND METHODS:** Results of MRSA-positive cultures of clinical specimens obtained as part of investigations for suspected infections were retrieved from the King Abdulaziz University Hospital Infection Control Department's records. Charts of patients were reviewed.

**RESULTS:** Of 292 *S aureus* isolates identified, 111 (38%) were MRSA, or 6.0 MRSA isolates/1000 admissions, which represented a marked increase over MRSA prevalence in 1988 (less than 2%). Nosocomial acquisition occurred in 74.8% of isolates. All age groups were affected, but 45.9% of patients were in the 'extremes of age' group (younger than one or older than 60 years of age). The prevalence was highest in the medical ward (27%), followed by the paediatrics combined medical and surgical ward (20.7%), the outpatient department (18%), the adult surgical ward (17.1%) and the intensive care units (17.1%). Two-thirds

(66.7%) of cases represented infection and the remainder represented colonization. Surgical wounds (31.1%), the chest (27%) and endovascular catheters (20.3%) were the most common sites of infection. Bacteremia occurred in 27% of patients. Local signs (68.9%) and fever (60.8%) were the most common clinical manifestations. Respiratory distress and septic shock occurred in 28.4% and 6.8% of cases, respectively. Of 74 patients with MRSA infection and 37 patients with MRSA colonization, 91.9% and 56.8% received antibiotics in the preceding six weeks, respectively ( $P < 0.0001$ ). The total mortality of patients with MRSA infection was 60.8%; 37.8% of deaths were the result of MRSA infection and 23% were the result of other diseases.

**CONCLUSIONS:** The prevalence of MRSA is high and rapidly increasing at King Abdulaziz University Hospital, as it is worldwide. Control measures to prevent the spread of MRSA in hospitals should continue with reinforcement of hygienic precautions and development of policies to restrict the use of antibiotics.

**Key Words:** Colonization; Infection; MRSA; Saudi Arabia; *Staphylococcus aureus*

*Résumé à la page suivante*

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King Abdulaziz University Hospital, Jeddah, Saudi Arabia

Correspondence: Dr Tariq Ahmed Madani, Department of Medicine, King Abdulaziz University Hospital, PO Box 80215, Jeddah 21589, Saudi Arabia. Telephone 011-9665-568-3107, fax 011-9662-640-3975, e-mail tmadani@health.net.sa

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## Épidémiologie et manifestations cliniques des infections à *Staphylococcus aureus* résistant à la méthicilline dans un hôpital universitaire de Djeddah, en Arabie saoudite

**OBJECTIF :** Décrire la prévalence et les manifestations cliniques des infections à *Staphylococcus aureus* résistant à la méthicilline (SARM) ainsi que la démographie des patients qui ont été infectés ou colonisés par le microbe en 1998, au King Abdulaziz University Hospital, à Djeddah, en Arabie saoudite.

**PATIENTS ET MÉTHODE :** Nous avons parcouru les dossiers des patients du service de lutte contre les infections du King Abdulaziz University Hospital situé à Djeddah, en Arabie saoudite, et nous avons retenu ceux dont les résultats de culture de spécimens cliniques se sont avérés positifs à l'égard du SARM dans le cadre de l'évaluation de cas soupçonnés.

**RÉSULTATS :** Sur 292 isolats de *Staphylococcus aureus* identifiés, 111 (38 %) étaient de type SARM, soit 6,0 isolats de SARM/1 000 admissions, ce qui représente une hausse marquée par rapport à la prévalence du SARM observée en 1988 (moins de 2 %). Dans 74,8 % des isolats, l'infection était d'origine nosocomiale. L'infection a touché tous les groupes d'âge, sauf que 45,9 % des patients appartenaient aux groupes d'âge

« extrêmes » (moins de un an ou plus de 60 ans). La prévalence la plus élevée a été observée dans les salles d'hôpital (27 %), suivies des salles de soins médicaux et chirurgicaux pour enfants (20,7 %), du service de consultations externes (18 %), du service de chirurgie pour adultes (17,1 %) et de l'unité de soins intensifs (17,1 %). Les deux tiers des cas (66,7 %) étaient infectés, les autres, colonisés. Les plaies opératoires (31,1 %), le thorax (27 %) et les cathéters endovasculaires (20,3 %) se sont révélés les sièges d'infection les plus fréquents. Vingt-sept pour cent des patients présentaient une bactériémie. Les manifestations cliniques les plus courantes étaient les signes locaux (68,9 %) et la fièvre (60,8 %). Il y a eu détresse respiratoire et choc septique dans 28,4 % et 6,8 % des cas respectivement. Des 74 patients infectés à SARM et des 37 patients colonisés à SARM, 91,9 % et 56,8 % d'entre eux respectivement avaient reçu des antibiotiques au cours des six semaines précédentes ( $p=0,0001$ ). Le taux de mortalité chez les patients infectés à SARM s'est établi à 60,8 %; 37,8 % d'entre eux sont morts des suites de l'infection à SARM et 23 %, des suites d'autres maladies.

**CONCLUSION :** La prévalence du SARM est forte et augmente rapidement au King Abdulaziz University Hospital, phénomène d'ailleurs observé à l'échelle mondiale. Il faudrait donc, d'une part, continuer d'appliquer des mesures de lutte contre la propagation du SARM dans les hôpitaux et, d'autre part, renforcer les précautions hygiéniques et élaborer des politiques pour limiter l'utilisation des antibiotiques.

*Staphylococcus aureus* is one of the most common pathogens, known for causing a variety of infections ranging from relatively benign skin infections to life-threatening systemic illnesses such as pneumonia, endocarditis, septic arthritis, osteomyelitis and subcutaneous or visceral abscesses. *S aureus* is usually sensitive to cloxacillin (or methicillin), amoxicillin/clavulinate, first-generation cephalosporins, erythromycin, clindamycin and glycopeptides, such as vancomycin and teicoplanin. Methicillin-resistant *S aureus* (MRSA) is important because it is also usually resistant to the aforementioned antibiotics, with the exception of glycopeptides, which can only be administered intravenously. MRSA is primarily a nosocomial pathogen that emerged in the 1980s as a major cause of infection and colonization in hospitalized patients (1,2). More recently, this organism has been implicated as a cause of community-acquired infections in people with recognized predisposing risk factors, such as recent contact with a health care facility or nursing home residence, or parenteral substance abuse (3-7). Community-acquired MRSA infections in the absence of identified risk factors have also been increasingly reported (7-12). The prevalence of MRSA has increased worldwide over the past decade, with marked variations in different regions. It is generally high in the United States (13), southern European countries (14,15) and Japan (16), but is low (less than 10% of *S aureus* isolates) in Sweden, Denmark and the Netherlands (14,17,18). In the United States, the prevalence of MRSA increased from 2% in 1974 to approximately 50% in 1997 (19-21). In England and Wales, resistance to methicillin among *S aureus* isolates recovered from blood or cerebrospinal fluid was stable at about 1.5% of isolates from 1989 to 1991, but increased thereafter to 13.2% in 1995 (22). Currently, in hospitals in the United Kingdom, the prevalence of MRSA has reached epidemic levels, and incidents involving MRSA have risen

12-fold since 1991 and were responsible for 37% of all *S aureus* infections in 1999, compared with only 3% in 1991 (23). A prevalence of more than 30% was also observed in other southern European countries, including Spain, France and Italy (14). A high prevalence of MRSA has also been reported from Malaysia (24), Ethiopia (25) and other developing countries such as Kenya, Sri Lanka and Tunisia (26).

The prevalence of MRSA in Saudi Arabia is not well defined. The present study describes the prevalence of MRSA, and the demographic and clinical characteristics of patients who were colonized or infected with this organism in 1998 at King Abdulaziz University Hospital, Jeddah, Saudi Arabia.

### DATA AND METHODS

#### Institution and patient population

The King Abdulaziz University Hospital is a tertiary care teaching hospital with a bed capacity of 265. The hospital had 18,492 admissions in 1998, the year of the present retrospective review. From 1978 to 1996, the hospital was run in temporary buildings. In late 1996, the hospital moved to permanent buildings. Hospital units included adult and paediatric medical, surgical and intensive care units, and an obstetrics and gynecology unit. The hemodialysis unit was not open during the study period, and there is, as yet, no burn unit. MRSA infections were treated with vancomycin. Patients with MRSA-positive cultures from any body specimen were identified from January 1, 1998 to December 31, 1998 for the present review.

#### Data collection

During the study period, specimens for bacterial culture were obtained as part of septic screening for suspected infections. Surveillance cultures specific for MRSA colonization were not completed during this period. All

MRSA-positive culture results were obtained from the Infection Control Department's records. MRSA isolated from more than one site (eg, sputum and blood) from the same patient was counted only once. Charts of all patients with positive cultures were reviewed using standardized data collection methods. Information collected included patient demographics, mode of acquisition (nosocomial- or community-acquired), hospital units where patients stayed, comorbidities, surgery and other invasive procedures, presence of foreign devices, receipt of prophylactic or therapeutic antibiotics in the preceding six weeks, previous hospitalization, clinical significance of MRSA (colonization versus infection), site and clinical manifestations of infections, complications, and outcome.

### Microbiological methods

Susceptibility testing of *S aureus* isolates to oxacillin was performed using a 1 µg oxacillin disk diffusion method (Oxoid Limited, United Kingdom) according to published guidelines (27). Oxacillin resistance was demonstrated by a zone of inhibition of 10 mm or less. Strains with borderline zones of inhibition (11 mm to 12 mm) were tested by E-test (AB Biodisk, Sweden) to determine the minimum inhibitory concentration (MIC). Strains with MICs of 4 µg/mL or greater were considered to be resistant, those with MICs of 2 µg/mL or less were considered to be sensitive, and those with MICs between 2 µg/mL and 4 µg/mL were considered to be intermediate (28).

### Definitions

MRSA isolates were considered to be community acquired if they were recovered within 72 h of admission, and nosocomial if they were recovered after that period.

The clinical significance of MRSA isolation from different body specimens was classified as either infection or colonization based on the presence or absence of a potential source of MRSA infection, the patient's clinical status and other relevant data. In the absence of any potential source or clinical evidence of infection, MRSA was considered to be colonizing the site from which a specimen was obtained.

The source of infection was determined on the basis of clinical evidence and recovery of MRSA from an infected site.

Outcome of patients with MRSA infection was classified into four categories: recovery without complications, recovery following complications such as septic shock or respiratory failure, death due to MRSA infection, or death unrelated to MRSA infection. MRSA-attributable mortality was defined as death directly related to clinically and microbiologically documented MRSA infection or any of its complications (eg, septic shock and acute respiratory distress syndrome).

### Data analysis

The Statistical Package for Social Sciences program (SPSS, Inc, United States) was used for data analysis. Yates-

corrected  $\chi^2$  test was used for comparison of proportions (categorical data).

## RESULTS

The total number of *S aureus* isolates that were isolated during the study period was 292, of which 111 (38%) were MRSA isolated from 111 patients, which translates to six (111/18,492 × 1000) MRSA isolates/1000 admissions. Twenty-eight (25.2%, or 1.5/1000 admissions) isolates were community acquired and 83 (74.8%) isolates were nosocomial. Sixty-five (58.6%) patients were male and 46 (41.4%) were female, with a mean age of 31.8 ± 25.8 years. Twenty (18%) patients were younger than one month of age, nine (8.1%) were between one and 12 months of age, 60 (54.1%) were between one and 60 years of age, and 22 (19.8%) were older than 60 years of age. Fifty-three (47.7%) patients were citizens of Saudi Arabia and 58 (52.3%) were not. The clinical characteristics of patients are summarized in Table 1. MRSA caused infection in 74 (66.7%) cases, and in the remaining 37 (33.3%) patients, it represented colonization. Surgical site infections (31.1%), pneumonia (27%) and endovascular catheter infections (20.3%) were the most common types of infection. Bacteremia occurred in 20 (27%) patients with microbiologically documented primary sites of MRSA infection. Local signs (68.9%), such as erythema, purulent discharge, tenderness of wounds or endovascular catheter sites, and fever (60.8%) were the most common clinical manifestations of MRSA infection. Respiratory distress and septic shock occurred in 28.4% and 6.8% of cases, respectively. Of 74 patients with MRSA infection and 37 patients with MRSA colonization, 68 (91.9%) and 21 (56.8%) patients received antibiotics in the preceding six weeks, respectively (P<0.0001, odds ratio 8.6, CI 2.7 to 28.7). Of 111 patients with MRSA infection or colonization, 53 (47.7%) had at least one comorbidity, 39 (35.1%) had one comorbidity, and 14 (12.6%) had two comorbidities.

Twenty-nine of 74 (39.2%) patients with MRSA infections recovered completely from their infections; 21 (28.4%) patients had an uneventful recovery, whereas the remaining eight (10.8%) patients recovered following complications, such as septic shock and/or respiratory failure requiring mechanical ventilation. The total mortality of patients with MRSA infection was 60.8% (45 of 74); 37.8% (28 of 74) died as a result of MRSA infection and 23% (17 of 74) as a result of other diseases.

## DISCUSSION

The present study at the King Abdulaziz University Hospital demonstrated a high prevalence of MRSA (38% of all *S aureus* isolates). The prevalence has increased gradually from less than 2% in 1988 (unpublished data) to the current rate of 38%. The organism affected all age groups, but almost half (45.9%) of the patients were in the 'extremes of age' group (younger than one or older than 60 years). There was no predilection for any sex or nationality. Three-quarters (74.8%) of cases were nosocomial, and the

**TABLE 1**  
**Clinical characteristics of 111 patients with methicillin-resistant *Staphylococcus aureus* (MRSA) infection or colonization**

Characteristics	Number of patients (%)
Nosocomial acquisition	83 (74.8)
Community acquisition	28 (25.2)
Comorbidities	53 (47.7)
Diabetes mellitus	24 (21.6)
Malignancy	12 (10.8)
End-stage renal failure	10 (9.0)
Cerebrovascular accident	8 (7.2)
Heart failure	7 (6.3)
Chronic obstructive pulmonary disease	5 (4.5)
HIV infection	2 (1.8)
Past history of MRSA infection or colonization	21 (18.9)
Previous hospitalization	20 (18.0)
Unit	
Medical ward	30 (27)
Paediatrics (medical and surgical) ward	23 (20.7)
Outpatient department	20 (18)
Surgical ward	19 (17.1)
Intensive care unit	12 (10.8)
Neonatal intensive care unit	7 (6.3)
Clinical significance	
MRSA infection	74 (66.7)
MRSA colonization	37 (33.3)
Type of infection (n=74 patients)	
Central venous catheter infection	10 (13.5)
Peripheral venous line infection	5 (6.8)
Surgical site infection	23 (31.1)
Pneumonia	20 (27)
Urinary tract infection	3 (4.1)
Others	13 (17.6)
Bacteremia (n=74 patients)	20 (27)
Clinical manifestations of MRSA infections (n=74 patients)	
Fever	45 (60.8)
Shock	5 (6.8)
Respiratory distress	21 (28.4)
Local signs	51 (68.9)
Outcome (n=74 patients)	
Recovery	29 (39.2)
Death due to MRSA infection	28 (37.8)
Death due to other causes	17 (23)

remainder (25.2%) were community acquired. The prevalence was highest in the medical ward (27%), followed by the paediatrics combined medical and surgical ward (20.7%), the outpatient department (18%), the adult surgical ward (17.1%), the intensive care unit (10.8%) and the

neonatal intensive care unit (6.3%). Approximately two-thirds (66.7%) of cases represented infection and one-third (33.3%) represented colonization. This high infection to colonization ratio was similar to what has been observed by other researchers (29). For instance, in an American MRSA outbreak, 260 of 286 (90.9%) affected patients were infected and not simply colonized (29). Health care facilities that routinely perform MRSA surveillance cultures, which were not undertaken at the King Abdulaziz University Hospital during this study period, obviously have a substantially lower infection to colonization ratio due to the detection of more colonized patients. Therefore, this information is essential for the appropriate comparison of the MRSA prevalence and infection to colonization ratio of different centres.

Once confined mainly to hospitals, MRSA has recently been increasingly implicated in community-acquired infections and colonization in patients with predisposing risk factors such as recent contact with a health care facility or nursing home residence, or parenteral substance abuse (3-7), as well as in patients without any recognized predisposing risk factors (7-12). For instance, in two hospitals in the United States in the early 1990s, 28% to 67% of patients with MRSA colonization had probable community acquisition (30,31). In five Canadian tertiary acute care teaching hospitals in three provinces, patients with MRSA isolates present at admission accounted for 62% of MRSA isolations from 1990 to 1992 (11). In a university hospital in the United States, 36 of 87 (41%) patients with MRSA had community acquisition; of those, eight (22%) had no identified risk factors (32). In a paediatric hospital in the United States, eight and 35 cases of community-acquired MRSA infections were identified in the time periods of 1988 to 1990 and 1993 to 1995, respectively. One (12.5%) and 25 (71.4%) cases had no identified risk factors, respectively, and the prevalence of community-acquired MRSA without identified risk increased from 0.1/1000 admissions in 1988 to 1990 to 2.6/1000 admissions in 1993 to 1995 (12). At the King Abdulaziz University Hospital, the prevalence of community acquisition of MRSA (25.2% or 1.5/1000 admissions) was moderately high compared with published data. These studies, collectively, suggest that MRSA may be more widespread in the general population than has been previously appreciated.

Risk factors that have been associated with MRSA acquisition include older age, prolonged hospitalization, prior antibiotic therapy, more severe underlying disease and degree of disability, surgical procedures, presence in an intensive care or burn unit, having a surgical wound infection, intravascular devices, mechanical ventilation, tracheostomy, pressure ulcers, or exposure to other infected or colonized individuals (1,2,33-38). Not only does antibiotic therapy predispose patients to colonization with MRSA, but it also increases the risk of invasive disease and infection, as demonstrated by the present study, in which significantly more patients with MRSA infection than those with MRSA colonization received antibiotics before posi-



tive MRSA culture (91.9% versus 56.8%,  $P < 0.0001$ ). Other host factors associated with progression from colonization to infection include recent hospitalization, preceding surgical or wound debridement, and the number of invasive procedures (39).

The body sites that were most frequently affected by overt MRSA infection were surgical sites (infections, 31.1%), the chest (pneumonia, 27%), and endovascular catheter sites (infections, 20.3%). Approximately 25% of patients with MRSA infections had bacteremia, but only 6.8% had overt septic shock. The total mortality of patients with MRSA infections was high (60.8%), as was the mortality attributable to MRSA infection (37.8%). It was generally believed that MRSA strains were not more virulent than methicillin-susceptible *S aureus* (MSSA) strains (20,40,41). Recent data, however, suggest that MRSA bacteremia is associated with a significantly higher mortality rate than MSSA bacteremia (42-44). For instance, Romero-Vivas et al (42) compared 100 cases of

MSSA bacteremia and 84 cases of MRSA bacteremia; the mortality rates were 32% and 58.3%, respectively ( $P < 0.01$ ), and methicillin resistance was found to be independently associated with mortality.

## CONCLUSIONS

The prevalence of MRSA is high and rapidly increasing at the King Abdulaziz University Hospital, as it is worldwide. One can foresee a time in the near future when the majority of *S aureus* isolates is resistant to methicillin, as happened with penicillin, a drug to which almost all isolates of *S aureus* are resistant. Attempts to control the spread of MRSA in hospitals should continue with reinforcement of hygienic precautions and infection control measures (45). Hospitals should also develop policies to restrict the use of antibiotics and to establish monitoring systems for rapid identification of epidemics and determination of factors that are responsible for spread and colonization to allow for a more targeted approach.

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