JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Original Article

Incidence and antibiotic susceptibility of MRSA infections in a Saudi Arabian Hospital: a 10-year surveillance study

Arif Mansour Al-Hamad[1], Afaq Ali Alfaraj[1], Jaffar Ahmed Altowaileb[1], Sameer Mahdi Al-Shamlan[1], Hussam Hassan Leskafi[1], Fatimah Abdullah Alsubeikhy[1], Hussein Radhi Abbas[1]

[1] *Division of Clinical Microbiology, Pathology and Laboratory Medicine, Qatif Central Hospital, Qatif, Saudi Arabia*

Abstract

Introduction: Methicillin-resistant *Staphylococcus aureus* (MRSA) infections remain prevalent and are associated with significant morbidity and mortality. The aim of the present study was to investigate the epidemiology of MRSA infections and antibiotic susceptibility in Qatif, Saudi Arabia.

Methodology: All patients who had positive culture for *S. aureus* from January 1, 2006 through December 31, 2015 were enrolled and analyzed in WHONET, a free database software developed by the World Health Organization (WHO). Patients' data were collected from electronic medical records and traditional chart reviews to determine whether MRSA acquisition was likely to have been in the community or in the healthcare facility. Susceptibility results for community-associated (CA)-MRSA were compared with isolates from healthcare setting.

Results: A total of 3395 patients with *S. aureus* infections were analyzed, with an overall annual MRSA incidence of 25 cases per 100,000 patients (27% of total *S. aureus isolates*). While the majority (64%) of MRSA infections occurred in healthcare setting, CA-MRSA isolation increased steadily from 23% in 2006 to 60% in 2015, exceeding rate of isolation of healthcare-associated (HA)-MRSA. Skin and soft tissue, the lung and blood stream were the most common sites of infection, with 20% to 35% of MRSA infections occurring in pediatric patients. In the inpatient setting, the majority of infections due to MRSA were in surgical wards and critical care units. Compared with CA-MRSA, HA-MRSA isolates turned out to be more frequently resistant against ciprofloxacin, clindamycin, erythromycin, tetracycline, and trimethoprim/sulfamethoxazole.

Conclusions: *Staphylococcus aureus* continues to cause multiple site infections with a relatively stable methicillin-resistance rate, but the isolation of MRSA from the community is increasing.

Key words: MRSA; antibiotic resistance; susceptibility; WHONET.

J Infect Dev Ctries 2018; 12(6):454-461. doi:10.3855/jidc.9778

(Received 24 September 2017 – Accepted 09 May 2018)

Introduction

Staphylococcus aureus is a major human pathogen capable of causing a wide range of clinical infections. It is a leading cause of skin and soft tissue infections, endovascular infections, pneumonia, septic arthritis, endocarditis, osteomyelitis, device-related infections, and sepsis [1,2]. Beta-lactam antimicrobial agents are the preferred drugs for serious *S. aureus* infections. However, since the introduction of methicillin into clinical use, methicillin-resistant *S. aureus* (MRSA) isolates have emerged worldwide as important nosocomial pathogens, and the prevalence of these isolates in the community is now increasing substantially [3-5]. In the United States of America, it was reported that the number of MRSA infections in hospitals has doubled nationwide, from approximately 127,000 in 1999 to 278,000 in 2005, while at the same time annual deaths increased from 11,000 to more than 17,000 [6]. In 2011, 80,461 invasive MRSA infections and 11,285 related deaths occurred in the USA, and an estimated annual economic burden of between $1.4 billion and $13.8 billion was attributed to community-acquired MRSA [7,8]. It was estimated that MRSA infections within the healthcare setting alone affect more than 150,000 patients annually in the European Union, with an additional cost of 380 million Euros [9].

Although MRSA infections were initially exclusively associated with the hospital setting, a change in epidemiology occurred in the 1990s when infections began to emerge among previously healthy individuals who had no prior hospital association [3-5]. Patients with community-associated MRSA (CA-MRSA) infections have often lacked risk factors known for patients with healthcare-associated MRSA (HA-MRSA) infections. These include recent hospitalization, dialysis, nursing-home residence, and

other comorbid conditions such as diabetes, chronic renal failure, and chronic pulmonary diseases which bring them into contact with healthcare settings [3,4,10]. Clusters of CA-MRSA infection have been described among prisoners, sports players, children, injection drug users, homeless persons, nursing homes and long term rehabilitation centers [3,11].

The substantial spread of CA-MRSA infections has increased the challenge of selecting empirical antimicrobial treatments in outpatient settings. In addition to most beta-lactams, MRSA is also commonly resistant to erythromycin, clindamycin, fluoroquinolones, trimethoprim/sulfamethoxazole and tetracycline. However, a good number of MRSA isolates acquired outside of healthcare settings remain susceptible to these agents [12,13]. These reports prompted us to review the incidence of *S. aureus* infections, including MRSA, in Qatif, a metropolitan area with more than half million population in the Eastern Region of Saudi Arabia. In this study, we describe the epidemiology of MRSA infections and antibiotic susceptibility patterns at Qatif Central Hospital from January 1, 2006 to December 31, 2015.

Methodology

Study setting

The study was conducted at a 335-bedded district general hospital serving more than half million population. In addition, the hospital is situated between two industrial cities and provides care for road traffic accidents victims. Adult patient care included 8-bedded intensive care unit, 6-bedded intermediate intensive care unit, internal medicine, general surgery, obstetrics and genecology, neurosurgery and orthopedic surgery. Pediatric patients' services included medical, intensive and neonatology care. The hospital also had a very busy emergency department and outpatient clinics serving as referrals from primary care centers and two small 50-bedded hospitals in the city. There was an active infection control team in the hospital with a microbiology results-ward liaison approach of surveillance. Only critical care patients were screened routinely for nasal, axilla and groin MRSA colonization, but these specimens were not included in the analyses, as they were likely to represent colonization rather than infection. Patients' data were collected from electronic medical records and traditional chart reviews to determine whether MRSA acquisition was likely to be healthcare- or community-associated. HA-MRSA infection was defined in accordance with the previously published criteria [14] and included nosocomial infection or the presence of any of the following risk factors: (1) residence in a long-term care facility, (2) use of central intravenous catheters or long-term venous access devices, (3) use of urinary catheters, (4) use of other long-term percutaneous devices, and/or (5) need for any form of dialysis. Nosocomial infection was defined as an isolate obtained from a sample collected from a patient with infection >48 h after hospital admission [15]. We defined colonization as a positive microbiological culture result in the absence of clinical features of infection. All patients who had positive culture for *S. aureus* from January 1, 2006 to December 31, 2015 were enrolled in the study.

Susceptibility testing and data analyses

Identification and susceptibility testing were performed routinely using the automated system BD Phoenix™, Becton Dickinson, Riyadh, Saudi Arabia. Inpatients with positive cultures were screened for colonization and cultured on Mannitol Salt Agar, and subsequently tested using cefoxitin disk on Mueller Hinton Agar as per the Clinical and Laboratory Standards Institute (CLSI) M100 guidelines. The same culture, identification and susceptibility testing methods and screening policy were followed over the study period. All results were entered routinely in WHONET [16], a free Windows-based database software developed by the World Health Organization (WHO) for the management and analysis of microbiology laboratory data with a special focus on the analysis of antimicrobial susceptibility test results. The software has been developed since 1989 by the WHO Collaborating Centre for Surveillance of Antimicrobial Resistance based at the Brigham and Women's Hospital in Boston, and is used by clinical, public health, veterinary, and food laboratories in over 90 countries to support local and national surveillance programs. Data generated by WHONET facilitate clinical decision support, antimicrobial use policy, infection control and outbreak detection, identifying laboratory test performance, and characterization of local microbial and resistance epidemiology. In addition, it promotes local, national, regional, and global collaborations through the exchange of data and sharing of experiences. Analyses were performed using the WHONET to determine the number of patients with positive culture to include non-duplicate data from clinical specimens. Total number of patients and the number of patients based on location, site of infection, service and age group were determined and analyzed. In addition, antimicrobial susceptibility results were analyzed. Only the first isolate within a month interval

was included if a patient had multiple or repeated isolates. Susceptibility data for CA-MRSA isolates were compared with HA-MRSA isolates.

Results

A total of 3395 patients with *S. aureus* infections were analyzed, with an annual incidence of 68.7 cases (ranging from 50 to 100.4) per 100,000 patients (Figure 1). Of the total *S. aureus* isolates, annual MRSA rates ranged from 24% to 30%, with an overall rate of 27% (903/3395). There was no specific trend and the annual incidence of MRSA fluctuated between 16.9 and 36.2 per 100,000 patients, with an overall annual incidence of 25 cases per 100,000 patients.

The incidence of MRSA was higher in the healthcare setting, ranging from 250 in 2011 and 800 in 2006 per 100,000 inpatients per year (Figure 2). A total of 581 (64%) HA-MRSA infections had been identified over the study period, compared with 322 (36%) CA-MRSA infections. There was a declining trend for HA-MRSA infections until 2012, when there was a slight increase in the incidence for two years followed by a decrease in 2015. In contrast, MRSA isolation from outpatient setting increased in 2013 to 10.9 cases per 100,000, compared with 8.5 or less in th years before 2013. The rate of CA-MRSA isolation increased from 23% of total MRSA in 2006 to 60% in 2015, exceeding rate of isolation from healthcare setting.

Figure 3 shows the different locations for MRSA infected patients. In the hospital setting, the vast majority of infections due to MRSA were in surgical wards (24%), followed by intensive care unit (ICU) (13%). The number of cases from medical wards and intermediate intensive care unit (IICU) were 97 (11%) and 45 (5%), respectively. Amongst pediatric patients, pediatric medical ward (PMW) had the highest isolation of 40 (4%) cases, followed by 23 (3%) and 16 (2%) from pediatric intensive care unit (PICU) and neonatal intensive care unit (NICU), respectively. The least MRSA isolation was from cardiac care unit (CCU) and obstetric ward (OBW), with an isolation of 10 (1%) and 11 (1%), respectively. In the outpatient setting, 125 (14%) and 65 (7%) MRSA cases were identified from outpatient clinics and emergency department (ED), respectively. In addition, nearly all patients with positive MRSA culture from hospital 1 (22) and hospital 2 (36) were from outpatient setting, collectively account for 6% of the total MRSA isolates.

The vast majority of MRSA isolates were from skin/soft tissue infections, followed by similar numbers of isolation from blood and lower respiratory tract (Figure 4). A total of 1972 *S. aureus* skin/soft tissue infection episodes were recorded, 532 (27%) were caused by MRSA. There were 126 and 124 cases of MRSA bloodstream infections and lower respiratory tract infection, respectively. Other specimen types were less common and represented 25 cases or less.

Of the 903 MRSA isolations, 72% (650/903) occurred in adult patients, with an overall annual incidence of 24.7per 100,000 adult patients, compared with a similar incidence of 26.5 per 100,000 pediatric patients (Figure 5). Incidence in pediatric patients fluctuated between 14.8 in 2011and 39.5 in 2006 per 100,000 pediatric patients. In contrast, a slightly decreasing incidence trend was observed for adult patients.

Figure 1 Incidence of *Staphylococcus aureus* infections and rate of methicillin resistance. MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*.

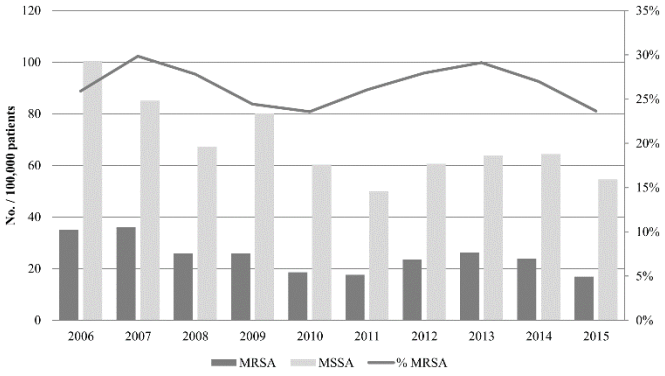

Figure 2 Incidence of healthcare-associated methicillin-resistant *Staphylococcus aureus* (HA-MRSA) and community-associated (CA)-MRSA infections along with percentage of CA-MRSA isolation.

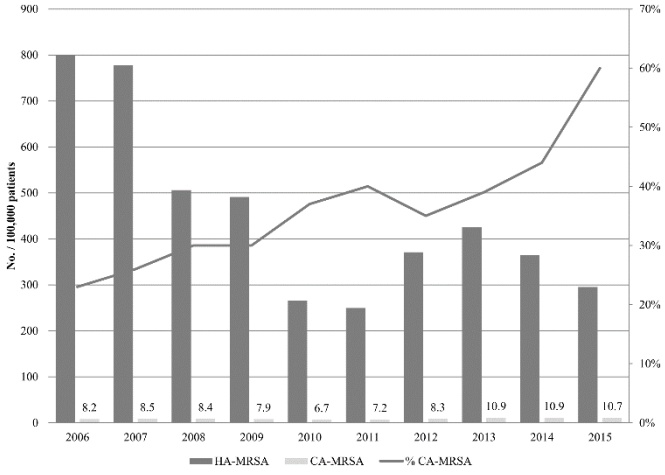

Figure 3 Number of patients with positive methicillin-resistant *Staphylococcus aureus* (MRSA) culture from different locations over a 10-year period. OPD, outpatient department; ICU, intensive care unit; FSW, female surgical ward; MSW, male surgical ward; ED, emergency department; MMW, male medical ward; FMW, female medical ward; IICU, intermediate ICU; PMW, pediatric medical ward; RDU, renal dialysis unit; PICU, pediatric ICU; NICU, neonatology ICU; CCU, cardiac care unit; OBW, obstetric ward.

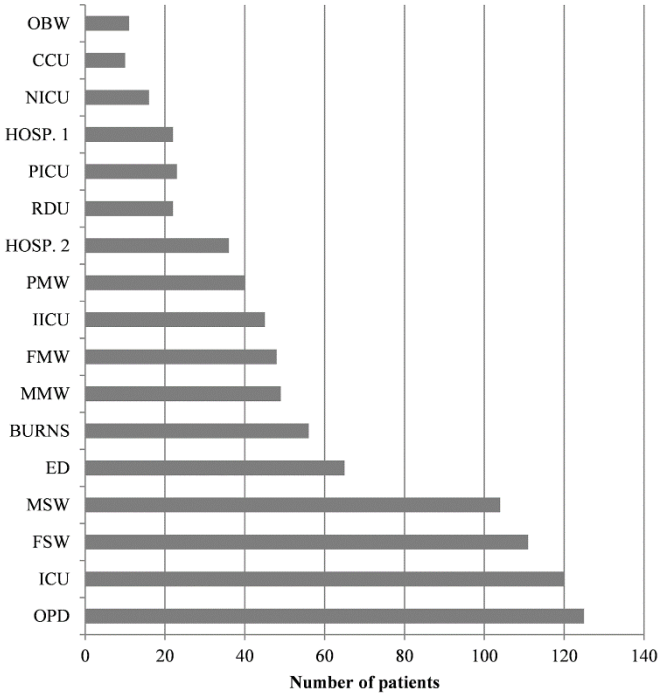

Figure 4 Distribution of origin of methicillin-resistant *Staphylococcus aureus* over a 10-year period.

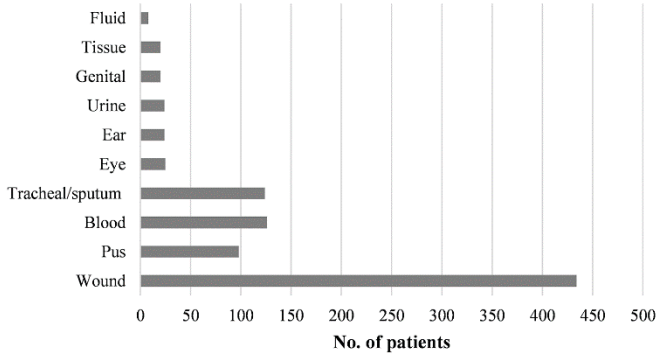

Figure 5 Incidence of adult and pediatric patients with methicillin-resistant *Staphylococcus aureus* (MRSA) positive culture.

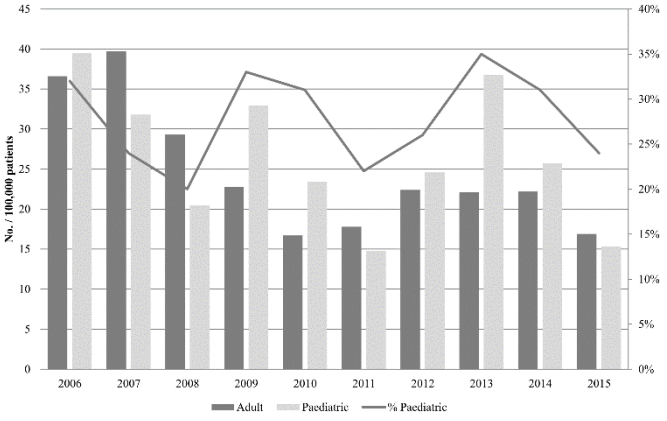

Figure 6 Comparison of susceptibility data between healthcare-associated methicillin-resistant *Staphylococcus aureus* (HA-MRSA) and community-associated (CA)-MRSA for non-beta lactam antibiotics. Susceptibility percentage data presented with 95% confidence intervals. CIP, ciprofloxacin; SXT, trimethoprim/sulfamethoxazole; CLI, clindamycin; ERY, erythromycin; TET, tetracycline.

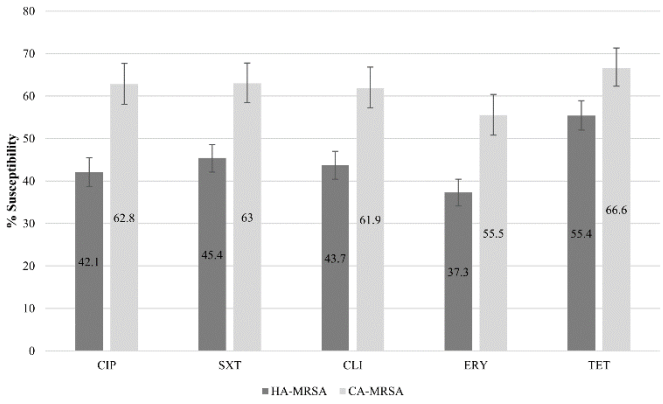

Figure 6 shows comparison of susceptibility data between HA-MRSA and CA-MRSA for non-beta lactam antimicrobial agents. HA-MRSA isolates clearly showed a more complex resistance profile than the CA-MRSA isolates against all antibiotics tested. Forty four percent and 85% of HA-MRSA isolates were susceptible to gentamicin and rifampicin, respectively, compared with 62% and 92% for CA-MRSA. All *S. aureus* isolates, including MRSA, were fully susceptible to vancomycin and linezolid (data not shown).

Discussion

The epidemiology of MRSA is constantly changing, and both circulating clones and their antibiotic resistance profiles vary considerably throughout regions and countries [17]. Appropriate empiric treatment of infections, based on knowledge of local circulating pathogens, is known to lead to better patient outcomes [18]. Therefore, epidemiologic information gathered through ongoing surveillance is essential to support clinicians and infection control committees in their efforts to prevent and treat infection. In this study, of the total 3395 *S. aureus* infections detected, 903 (27%) MRSA cases were identified. A systematic review and meta-analysis published in 2013, which included MRSA data from five regions in Saudi Arabia from 2002 up to 2012, revealed that MRSA had an estimated prevalence of 35% out of the 22,793 *S. aureus* isolates analyzed [19]. This percentage was higher than prevalence reported in Lebanon, Bahrain and Kuwait, but lower than prevalence percentage of >50% reported from Jordan, Oman, Egypt and Iran [19]. Prevalence of MRSA varied dramatically among different regions in Saudi Arabia, ranging from 5% in Dhahran to 95% in Riyadh. Despite the fact that the reasons for this geographic variation are unknown, a study by Van Belkum et al., confirmed that a single clone of MRSA is responsible for 93% of the isolates tested [20]. In addition, environmental and host factors may play a role for this variation in incidence. In the past few decades, the prevalence of MRSA among both nosocomial and community acquired infections has increased throughout the world and due to the development of multidrug resistance among *S. aureus* isolates, treatment of these infections has become problematic [3-5]. This worsening resistance trend is seen in countries with large health resources as well as countries with modest ones.

Although our data show that the rate of MRSA isolation was relatively stable for the past decade, the incidence of CA-MRSA has increased in the recent years. This was paralleled with a decrease in the incidence of HA-MRSA infections. While the explanation for this shift in the incidence of MRSA is not clear, it is suggested that enhanced infection control measures reduced infectious outbreaks due to MRSA in the healthcare settings [21]. In addition, a successful clone may be spreading in the community, capable of causing infections in individuals without risk factors for MRSA infection. In 2006, one specific clone of USA300 was reported to be the single most frequent cause of skin and soft tissue infections reported to U.S. emergency departments [22]. It is believed that this successful spread of this specific clone was due to higher virulence and increased transmissibility characteristics, as compared to traditional HA-MRSA. Furthermore, CA-MRSA are genetically distinct from HA-MRSA isolates and contain a novel cassette element, SCCmec IV and exotoxin, Panton-Valentine leukocidin (PVL). Although there has been intensive research in the last decade, the molecular basis of CA-MRSA virulence is still a matter of controversy [22]. In addition, CA-MRSA isolates have been reported from several other countries, including countries with historically low prevalence of MRSA [23,24]. However, the epidemiology of MRSA has become increasingly complex as CA-MRSA and HA-MRSA isolates have co-mingled both in the community and in healthcare facilities [25,26].

In our study, most (n = 655; 72.5%) MRSA infections were from healthcare setting, originating from adult critical care (18%) and surgical (24%), internal medicine (11%), pediatric (7%) and neonatology (1.7%) wards. In 2002, Madani reported a similar rate (75%) of MRSA inpatient acquisition and similar prevalence in the intensive care units (17%) at a university hospital in Jeddah, Saudi Arabia [27]. However, his finding showed a higher prevalence in medical ward (27%), but lower rate of isolation from outpatient department (18%), suggesting an increase in the isolation for MRSA from outpatient setting. Worldwide, most CA-MRSA cases are mild skin and soft tissue infections, although requirement for hospitalization due to severe cases remains high and is estimated to be between 16% and 44% [24]. Indeed, because of the increased virulence, especially the presence of PVL toxin, CA-MRSA may cause severe infections such as necrotizing pneumonia or necrotizing fasciitis. Of note, skin and soft tissue infections and pneumonia caused by MRSA can serve as a source of blood stream infections, and are associated with higher mortality rates, longer hospital admissions, and greater

hospital costs than infections caused by MSSA isolates [24,28,29].

We found that the vast majority of MRSA isolates were cultured from wound and pus specimens, confirming that skin and soft tissue infections were the most common presentation of MRSA infection. In addition, our analyses showed that the incidence of MRSA was similar in adult and pediatric patients, suggesting that the epidemiology of MRSA is age independent. However, MRSA-related hospitalizations in older individuals are more likely to be caused by HA-MRSA even when they are hospitalized for skin and soft-tissue infections. One reason for this could be that older individuals are more likely to visit healthcare facilities or live in long-term care facilities. However, a prospective cohort study, collecting all clinical MRSA isolates from 30 of 31 hospitals in California in order to characterize differences in pediatric and adult MRSA strains, showed significantly more genetic diversity among adult MRSA isolates than among pediatric isolates [30]. This could be due to different degrees of contact; for example, adults may have more diverse MRSA encounters (travel, work, social venues, and health care facilities). In contrast, children are often healthier and are more likely to encounter MRSA in the community through exposure to high-density environments such as schools and day care [30].

The treatment of MRSA is challenging because of its resistance to antimicrobial agents. In addition to being resistant to most beta-lactams, MRSA isolates are typically resistant to multiple classes of antibiotics. In this study, the antibiotic susceptibility results of MRSA against ciprofloxacin, clindamycin, erythromycin, tetracycline and trimethoprim/sulfamethoxazole were less resistant in community compared to the healthcare setting, similar to previously reported observation [31,32]. However, in a study conducted in Oman in 2015, antibiotic susceptibility tests revealed that the HA-MRSA isolates remained sensitive to most antibiotics, but there was a high rate of resistance against erythromycin [48%] and clindamycin [29%] [33]. In addition, recent evidence suggests that CA-MRSA isolates can acquire multiple resistance genes, though in general most CA-MRSA isolates are still susceptible to numerous antibiotics to which HA-MRSA is routinely resistant [4]. These results will be of local clinical relevance to guide empiric treatment of MRSA infections. In a study conducted in Northern Australia, Tong et.al. revealed that inducible clindamycin resistance was present in 52 (22%) of 239 non-multidrug resistant MRSA, defined as resistant to less than 3 non-beta lactam antibiotics. All isolates were susceptible to trimethoprim/sulfamethoxazole and rifampin, and most were susceptible to tetracycline (97%) [34]. Another study found that all MRSA isolates tested were susceptible to doxycycline, tigecycline, trimethoprim/sulfamethoxazole and vancomycin [12].

Conclusion

The present study included incidence of MRSA and rates of the total *S. aureus* infections, with detailed stratifications based on location, specimen type and age as well as community versus hospital acquisition of infection. Although automated system used for identification and susceptibility testing was subjected to validation process upon installation and after major maintenance, limitations included lack of confirmation of MRSA by the detection of *mecA/mecC* genes by PCR and molecular typing to detect specific clones. No attempts were made to determine the mortality rates due to MRSA infections, risk factors or the presence of virulence factors e.g. PVL toxin.

However, the results of this study showed the importance of regular surveillance of epidemiologically important pathogens such as MRSA. In addition, monitoring antibiotic susceptibility pattern is of paramount importance to guide empiric antibiotic therapy. There should also be an effective infection control committee to coordinate implementation of its policies, especially the use of empiric antibiotic therapy based on local susceptibility patterns and the prevalence of specific pathogens. Educational awareness should be encouraged to update healthcare workers with new intervention strategies. Although vancomycin-resistant MRSA has not been detected at our institution, the unique ability of *S. aureus* to acquire and transfer antibiotic resistance calls for urgent and well-coordinated surveillance program to combat this situation.

Funding

No funding sources.

References

1. Lowy FD (1998) *Staphylococcus aureus* infections. N Engl J Med 339: 520-532.
2. Tong SY, Davis JS, Eichenberger E, Holland TL, Fowler VG Jr. (2015) *Staphylococcus aureus* infections: epidemiology, pathophysiology, clinical manifestations, and management. Clin Microbiol Rev 28: 603-661.
3. David MZ, Daum RS (2010) Community-associated methicillin-resistant *Staphylococcus aureus*: epidemiology and clinical consequences of an emerging epidemic. Clin Microbiol Rev 23: 616-687.

4. Klein EY, Sun L, Smith DL, Laxminarayan R (2013) The changing epidemiology of methicillin-resistant *Staphylococcus aureus* in the United States: a national observational study. Am J Epidemiol 177: 666-674.
5. Wood JB, Smith DB, Baker EH, Brecher SM, Gupta K (2012) Has the emergence of community-associated methicillin-resistant *Staphylococcus aureus* increased trimethoprim-sulfamethoxazole use and resistance?: a 10-year time series analysis. Antimicrob Agents Chemother 56: 5655-5660.
6. Klein E, Smith DL, Laxminarayan R (2007) Hospitalizations and deaths caused by methicillin-resistant *Staphylococcus aureus*, United States, 1999-2005. Emerg Infect Dis 13: 1840-1846.
7. Lee BY, Singh A, David MZ, Bartsch SM, Slayton RB, Huang SS, Zimmer SM, Potter MA, Macal CM, Lauderdale DS, Miller LG, Daum RS (2013) The economic burden of community-associated methicillin-resistant *Staphylococcus aureus* (CA-MRSA). Clin Microbiol Infect 19: 528-536.
8. Centers for Disease Control and Prevention (2013) Antibiotic Resistance Threats in the United States. Available: https://www.cdc.gov/drugresistance/threat-report-2013/index.html. Accessed 22 August 2017.
9. Kock R, Becker K, Cookson B, van Gemert-Pijnen JE, Harbarth S, Kluytmans J, Mielke M, Peters G, Skov RL, Struelens MJ, Tacconelli E, Navarro Torné A, Witte W, Friedrich AW (2010) Methicillin-resistant *Staphylococcus aureus* (MRSA): burden of disease and control challenges in Europe. Euro Surveill *15*: 19688.
10. Herold BC, Immergluck LC, Maranan MC, Lauderdale DS, Gaskin RE, Boyle-Vavra S, Leitch CD, Daum RS (1998) Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. JAMA 279: 593-598.
11. Farley JE (2008) Epidemiology, clinical manifestations, and treatment options for skin and soft tissue infection caused by community-acquired methicillin-resistant *Staphylococcus aureus.* J Am Acad Nurse Pract 20: 85-92.
12. Levesque S, Bourgault AM, Galarneau LA, Moisan D, Doualla-Bell F, Tremblay C (2015) Molecular epidemiology and antimicrobial susceptibility profiles of methicillin-resistant *Staphylococcus aureus* blood culture isolates: results of the Quebec Provincial Surveillance Programme. Epidemiol Infect 143: 1511-1518.
13. Huang H, Flynn NM, King JH, Monchaud C, Morita M, Cohen SH (2006) Comparisons of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA) and hospital-associated MSRA infections in Sacramento, California. J Clin Microbiol 44: 2423-2427.
14. Seybold U, Kourbatova EV, Johnson JG, Halvosa SJ, Wang YF, King MD, Ray SM, Blumberg HM (2006) Emergence of community-associated methicillin-resistant *Staphylococcus aureus* USA300 genotype as a major cause of health care-associated blood stream infections. Clin Infect Dis 42: 647-656.
15. Garner JS, Jarvis WR, Emori TG, Horan TC, Hughes JM (1988) CDC definitions for nosocomial infections, 1988. Am J Infect Control 16: 128-140.
16. Stelling JM, O'Brien TF (1997) Surveillance of antimicrobial resistance: the WHONET program. Clin Infect Dis 24 Suppl 1: 157-168.
17. Guzman-Blanco M, Mejia C, Isturiz R, Alvarez C, Bavestrello L, Gotuzzo E, Labarca J, Luna CM, Rodriguez-Noriega E, Salles MJ, Zurita J, Seas C (2009) Epidemiology of methicillin-resistant *Staphylococcus aureus* (MRSA) in Latin America. Int J Antimicrob Agents 34: 304-308.
18. Kollef MH (2000) Inadequate antimicrobial treatment: an important determinant of outcome for hospitalized patients. Clin Infect Dis 31 Suppl 4: 131-138.
19. AL-Yousef SA, Mahmoud SY, Eihab MT (2013) Prevalence of methicillin-resistant *Staphylococcus aureus* in Saudi Arabia: Systemic review and meta-analysis. Afr J Clin Exper Microbiol 14: 146-154.
20. Van Belkum A, Vandenbergh M, Kessie G, Qadri SM, Lee G, van den Braak N, Verbrugh H, and al-Ahdal MN (1997) Genetic homogeneity among methicillin-resistant *Staphylococcus aureus* strains from Saudi Arabia. Microb Drug Resist 3: 365-369.
21. Marimuthu K, Pittet D, Harbarth S (2014) The effect of improved hand hygiene on nosocomial MRSA control. Antimicrob Resist Infect Control 3: 34.
22. Otto M (2012) MRSA virulence and spread. Cell Microbiol 14: 1513-1521.
23. Chambers HF, Deleo FR (2009) Waves of resistance: *Staphylococcus aureus* in the antibiotic era. Nat Rev Microbiol 7: 629-641.
24. Chatterjee SS, Otto M (2013) Improved understanding of factors driving methicillin-resistant *Staphylococcus aureus* epidemic waves. Clin Epidemiol 5: 205-217.
25. Liu C, Graber CJ, Karr M, Diep BA, Basuino L, Schwartz BS, Enright MC, O'Hanlon SJ, Thomas JC, Perdreau-Remington F, Gordon S, Gunthorpe H, Jacobs R, Jensen P, Leoung G, Rumack JS, Chambers HF (2008) A population-based study of the incidence and molecular epidemiology of methicillin-resistant *Staphylococcus aureus* disease in San Francisco, 2004-2005. Clin Infect Dis 46: 1637-1646.
26. D'Agata EM, Webb GF, Horn MA, Moellering RC Jr., Ruan S (2009) Modeling the invasion of community-acquired methicillin-resistant *Staphylococcus aureus* into hospitals. Clin Infect Dis 48: 274-284.
27. Madani TA (2002) Epidemiology and clinical features of methicillin-resistant *Staphylococcus aureus* in the University Hospital, Jeddah, Saudi Arabia. Can J Infect Dis 13: 245-250.
28. Dryden M (2008) Complicated skin and soft tissue infections caused by methicillin-resistant *Staphylococcus aureus*: epidemiology, risk factors, and presentation. Surg Infect 9 Suppl 1: 3-10.
29. Kaye KS, Engemann JJ, Mozaffari E, Carmeli Y (2004) Reference group choice and antibiotic resistance outcomes. Emerg Infect Dis 10: 1125-1128.
30. Hudson LO, Murphy CR, Spratt BG, Enright MC, Terpstra L, Gombosev A, Hannah P, Mikhail L, Alexander R, Moore DF, Huang SS (2012) Differences in methicillin-resistant *Staphylococcus aureus* strains isolated from pediatric and adult patients from hospitals in a large county in California. J Clin Microbiol 50: 573-579.
31. Raygada JL, Levine DP (2009) Methicillin-resistant *Staphylococcus aureus*: A growing risk in the hospital and in the community. Am Health Drug Benefits 2: 86-95.
32. Nicolle L (2006) Community-acquired MRSA: a practitioner's guide. CMAJ 175: 145.
33. Hurley JC (2003) Comparison of mortality associated with methicillin-susceptible and methicillin-resistant *Staphylococcus aureus* bacteremia: an ecological analysis. Clin Infect Dis 37: 866-868; author reply 868-869.
34. Tong SY, Bishop EJ, Lilliebridge RA, Cheng AC, Spasova-Penkova Z, Holt DC, Giffard PM, McDonald MI, Currie BJ,

Boutlis CS (2009) Community-associated strains of methicillin-resistant *Staphylococcus aureus* and methicillin-susceptible *S. aureus* in indigenous Northern Australia: epidemiology and outcomes. J Infect Dis 199: 1461-1470.

Corresponding author
Arif Al-Hamad, PhD, DipHIC
Division of Clinical Microbiology, Qatif Central Hospital, PO Box 18476, Qatif 31911, Saudi Arabia
Phone: +966 (3) 8361000 Ex. 4306
Fax: +966 (3) 8360040
E-mail: arifhamad@doctors.org.uk

Conflict of interests: No conflict of interests is declared.