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New epidemiology of *Staphylococcus aureus* infections in the Middle East

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Abstract

Staphylococcus aureus is a bacterial pathogen that is distributed worldwide and represents an increasing problem, both in hospitals and in the community. Global transmission of methicillin-resistant *S. aureus* (MRSA) has been the subject of many studies. Determining the incidence of colonization with community-acquired MRSA in hospitalized patients and outpatients has been the aim of several studies conducted in the Middle East (western Asia). The local epidemiology within countries in this region is changing, owing to the introduction of new strains with the intercontinental exchange of several clones. Sequence type 80-MRSA-IV is one common clone detected in different countries within the region showing country-based differences, and hence more likely to form clonal lineages. MRSA is endemic in this region, and the burden and the difficulty in detecting imported strains are increasing. This is also increasing the risk of domestic and global transmission. To counter the threat associated with the high incidence of MRSA carriage and infections, systematic surveillance of both hospital and community isolates is required, along with appropriate measures designed to limit their spread. Additionally, antibiotic stewardship is needed to contain the further development of the observed resistance and to help in preserving antibiotics as precious therapeutic resources. It is critical for countries in this region to establish both national and international initiatives to develop better measurements designed to limit and control the spread of infections. Finally, more sequence-based studies are needed to better understand the pathogenicity and epidemiology of these important pathogens.

Keywords: Epidemiology, methicillin-resistant *S. aureus*, Middle East, resistance, ST80-MRSA-IV
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Introduction

Staphylococcus aureus is a major human pathogen that causes a broad range of serious community-acquired and nosocomial diseases in humans, from minor skin infections to severe infections such as septicaemia [1]. The increasing prevalence of methicillin-resistant *S. aureus* (MRSA) and its ability to spread in hospitals and the community have posed a major challenge for infection control [2].

Since the introduction of methicillin for the treatment of penicillin-resistant *Staphylococcus* strains in 1959, MRSA has emerged as an important hospital-associated pathogen, because of increased morbidity and mortality rates, healthcare costs, and length of hospital stays [3,4]. Hospital-associated MSRA (HA-MRSA) infections arise in individuals with predisposing risk factors, such as surgery or the presence of an indwelling medical device. In contrast, many community-acquired MRSA (CA-MRSA) infections arise in otherwise healthy individuals who do not have such risk factors, and are known to be epidemic in some countries [5,6]. These features suggest that CA-MRSA are more virulent and transmissible than are traditional HA-MRSA [5,6].

The epidemiology of MRSA varies considerably on a global basis, and the spread of several CA-MRSA clones and their dissemination into hospitals have made understanding the epidemiology more difficult [1]. CA-MRSA lineages are genotypically and phenotypically unrelated to multidrug-resistant HA-MRSA, and have recently started to replace the once pandemic HA-MRSA clones (clonal complex (CC)5, CC8, CC22, CC36, and CC45) in healthcare facilities [7,8]. CA-MRSA infections have been dominated by five lineages:

sequence type (ST)1-IV (USA400), ST8-IV (USA300), ST30-IV (Pacific/Oceania; South West Pacific clone), ST59-IV/V (USA1000, Taiwan), and ST80-IV (European CA-MRSA), each being geographically restricted [6]. However, these originally continent-specific clones have spread to other parts of the world; ST1 clone USA400, for example, has been detected in Europe and Asia. Some Panton–Valentine leukocidin (PVL)-positive clones, such as ST1 and ST30, are pandemic, having been detected in America, Europe, and Asia [5]. ST80, known as the European clone, has also been reported in Libya, Jordan, and Lebanon [9,10].

Global transmission of MRSA linked to international travel has been the subject of many studies [9–11]. However, in countries with a high prevalence of MRSA, imported cases of MRSA are not easily distinguished from the domestic background prevalence. Information about the epidemiology of MRSA in non-European countries of the south-eastern Mediterranean has been sparse. Borg *et al.* [11] collected the largest dataset on the epidemiology of MRSA in this region, and showed the significant presence of MRSA in this part of the world, with many hospitals showing evidence of endemicity. It is worth noting that healthcare in such countries is more concentrated in urban areas. The reported catchment populations can therefore be underestimated, as it is difficult to estimate the proportion of the population coming from the rural areas to a particular hospital in the city [11].

The purpose of this review is to summarize what has recently been reported about the epidemiology of CA-MRSA in the Middle East, specifically covering western Asia, and touch upon the clinical spectrum of infectious syndromes associated along with resistance patterns.

Epidemiology of MRSA in the Middle East

The incidence of patient colonization with CA-MRSA has been the aim of several studies conducted in the region. Epidemiological data on CA-MRSA carriage and infection in the Middle East are limited; there is no information on the MRSA population structure, and little attention has been paid to the molecular epidemiology of this pathogen. CA-MRSA infections have changed markedly, and are expanding to also become causative agents of nosocomial infections. Recently, several studies have reported on MRSA carriage and/or infection coming from different countries in the south-eastern Mediterranean region.

Palestine

A study conducted throughout the Gaza strip by Biber *et al.* [12] revealed widespread CA-MRSA carriage, whereby 30% of healthy children and their parents carried *S. aureus*. Ninety-four MRSA were identified, and further molecular characterization revealed the predominance of CC22, which included 70 strains. The SCC*mec* type of the Gaza strain was IVa, whereas nine pulsed-field gel electrophoresis-related isolates carried SCC*mec* V, and seven of these belonged to ST22. Interestingly, eight of the 94 MRSA were PVL-positive and belonged to ST80-MRSA-IV. The authors hypothesized that the origin of the Gaza clone was either an HA-MRSA that spread in the community, or a local ST22-methicillin-sensitive *S. aureus* (MSSA) that evolved into a novel CA-MRSA clone. In a study conducted to determine the carriage rate and characteristics of CA-MRSA in patients admitted to Ramallah Governmental Hospital, a total of 843 swabs were obtained from patients who had no contact with healthcare workers at the time of hospital admission. For comparison purposes, the study also included samples collected from 72 volunteer healthcare workers working in close contact with patients in the internal medicine wards. The study revealed that the rate of *S. aureus* colonization at the time of admission was 26%, and that the rate of MRSA carriage was 2% [13]. Among the healthcare workers, *S. aureus* was detected in 21% and MRSA in 14%. Sabri *et al.* [14] also attempted to study the molecular epidemiology of MRSA circulating in Palestine, Jordan, and Iraq. Investigation of the genetic association between 12 representative MRSA from the predominant antibiotic resistance pattern revealed that 11 of these isolates shared a common *spa* type (t932) and were SCC*mec* type III. Few of the isolates were PVL-positive, being mainly hospital-acquired. This regional clustering was attributed to cross-border patient mobility. Finally, the prevalence of nasal carriage of *S. aureus* and MRSA was investigated among 360 healthy university students at An-Najah National University, Palestine [15]. The study also included 46 clinical MRSA obtained from three different health centres in northern Palestine within the same period of the study. Nasal carriage of *S. aureus* was detected in 24% of the students with MRSA, accounting for 9% of the isolates. Almost half of the MRSA belonged to SCC*mec* types IVa and V, and the other half belonged to SCC*mec* types II and III. SCC*mec* type IVa was found to be circulating among nasal carriers both in students and in healthcare workers.

Jordan

The incidence of colonization with CA-MRSA has also been the subject of several studies conducted in Jordan. Daghistani *et al.* [16] showed that 22.7% of nasal specimens collected from 132 healthy students were positive for *S. aureus*. The study included 80 *S. aureus* recovered randomly from wound specimens, and showed that toxic shock syndrome toxin-1 production was higher among the nasal isolates. More recently,