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REVIEW ARTICLE OPEN ACCESS

Staphylococcus aureus as Food-Borne Disease: An Ongoing Threat in Public Health in the Kingdom of Saudi Arabia

Mashael Alghizzi and Ashwag Shami*

Department of Biology, College of Sciences, Princess Nourah bint Abdulrahman University, P.O. Box 84428, Riyadh 11671, Saudi Arabia.

Abstract

Majority of the global population have been affected by food-borne diseases, and *Staphylococcus aureus* is one of the causes of this disease. *S. aureus* can be transmitted through contaminated food and is a risk to universal human health because of its ability to produce toxins-staphylococcal enterotoxins. Additionally, methicillin resistant *Staphylococcus aureus* (MRSA) furthered public health concerns. Although MRSA has been identified in food worldwide, little information is available on this topic locally and internationally. This review presents information on MRSA that was collected as evidence of such infections globally and in Saudi Arabia.

Keywords: Saudi Arabia, Food-born Disease, MRSA, Antibiotics, *PVL, SCCmec, MecA*

***Correspondence:** ayshami@pnu.edu.sa

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INTRODUCTION

Staphylococcal species are opportunistic pathogens that can cause various types of infections with varying levels of severity. *S. saprophyticus* is the second main cause of urinary tract infections, and *S. simulans*, *S. warneri,* and *S. haemolyticus* can cause device-related infections. Additionally, *S. aureus* is a serious human pathogen that can cause lethal diseases such as pneumonia, endocarditis, toxic shock syndrome, and sepsis (Figure 1). Moreover, *S. aureus* and *S. epidermidis* can cause nosocomial infections in indwelling devices.[1] *S. aureus* can cause alternative diseases, particularly methicillin-resistant *Staphylococcus aureus* (MRSA), which forms approximately 13–74% of *S. aureus* infections.

MRSA infection and colonization can be negatively affected by factors such as obesity; however, the mechanism has not yet been revealed.[2] According to origin of the outbreaks, MRSA is divided into two groups: healthcare-associated MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA).[3] CA-MRSA clones differ from country-to-country; e.g., ST8 (USA300) and ST1 (USA400) clones were found essentially in the USA and Canada, whereas ST80 clones were found in Europe.[4] Although the MRSA USA300 clone was mainly found in the USA and Canada, it was also infrequently detected in wild pig meat in Germany, Switzerland, and Spain.[5] The probability of MRSA infection in patients colonized with CA-MRSA (13%) are lower than those with HA-MRSA (37%). Hence, patients colonized with HA-MRSA exhibit longer recovery time than those colonized with CA-MRSA.[6] Additionally, the major cause of this infectious disease is that *S. aureus* is resistant to several types of antibiotics, and the susceptibility of HA-MRSA to antibiotics is lower than that of CA-MERSA.[7,8]

Livestock is considered a major source of staphylococci species, particularly *S. aureus*, causing livestock-associated MRSA (LA-MRSA). Thus, LA-MRSA can occur by direct contact with animals or by use of animal products obtained from animals such as lambs, calves, and goats. However, the spread rate of *S. aureus* was lower in calves (12.5%) and goats (1 %) than in lambs (30%). LA-MRSA was first discovered in France and the Netherlands and was found in pig populations

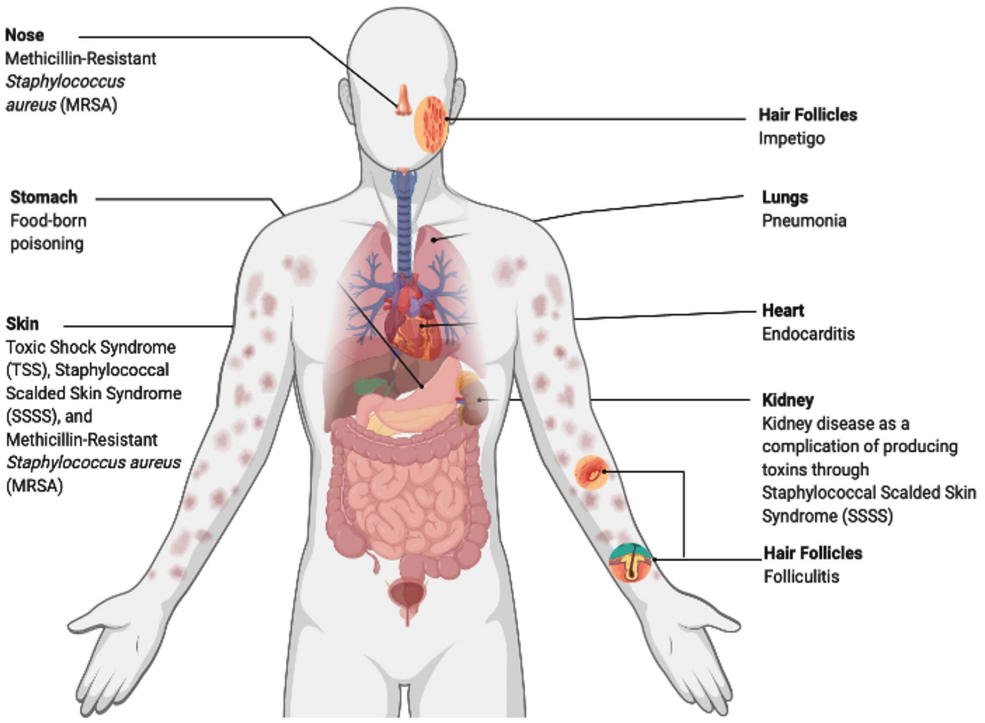

Figure 1. Infections caused by *Staphylococcus aureus*

in several countries of Europe. Furthermore, CA-MRSA, HA-MRSA and LA-MRSA clones vary between countries; e.g., the CC398 clone was detected in Europe and the USA, whereas the CC9 clone was found in Asia.[5, 9]

Pathogenesis of Staphylococcal Disease and Virulence Factors

Genetically, one of the many types of staphylococcal cassette chromosome *mec* complex gene (*SCCmec*) would be sufficient to induce an MRSA infection. Elements of *SCCmec* carry *mecA* gene, which encodes penicillin-binding protein 2a (PBP2a) that is responsible for bacterial resistance to methicillin, as shown in Figure 2. PBP2a has low similarity to beta-lactamases, which are responsible for resistance against extended-spectrum cephalosporins, monobactams, penicillins, and carbapenems.[10,11,12]

Furthermore, the Panton-Valentine Leukocidin (*PVL*) gene is a genetic marker of MRSA (first identified in 2003) (Figure 2). Strains that produce *PVL* may cause skin infection or serious diseases such as pneumonia. However, *PVL* gene was more prevalent in CA-MRSA than in HA-MRSA and was found in approximately 60%–100% of CA-MRSA strains. Consequently, *PVL* develops the pathogenicity of CA-MRSA strains, and the prevalence of *PVL* between strains relies on mobile genetic elements, particularly bacteriophages.[8,13,14] *S. aureus* also causes Staphylococcus scalded skin syndrome by producing the epidermolytic toxins A and B, which affect the skin all over the body. It commonly affects children aged <5 years, in addition to adults with kidney disease.[15]

Some species of Staphylococci can cause a very prevalent disease called food-borne poisoning that occurs after consumption of contaminated food. It is mainly caused by *S. aureus* or occasionally by other Staphylococcus species, such as *S. intermedius*. Symptoms (vomiting, fever, nausea, diarrhea, dizziness, low blood pressure, and headache) present 30 min to 8 h post consumption of contaminated food.[16] *S. aureus* live in various habitats and can contaminate foods such as sandwich fillings, salads, milk, sausages, canned meat, cheeses, and cooked meals.[17] However, staphylococci can be killed by different methods for food preservation, such as cooking food with high heat and pasteurization.[18] Bacteria can also contaminate food during food preparation and milk processing or storage. Consequently, Staphylococci produce enterotoxins, which include more than 20 types of toxins.[16]

Statement of the Problem

MRSA infections spread rapidly throughout Saudi Arabia. A group of clinicians reported that the percentage of such infections in King Fahad Medical City in Riyadh reached 50% during 2011, and there are no sufficient studies addressing this problem.[19] Although MRSA in Saudi Arabia was discovered in the 1990s, the number of studies on MRSA infection in Saudi Arabia is limited compared to that in other countries around the world.[20] According to PubMed, there were only 141 studies conducted on MRSA in Saudi Arabia over past 5 years (2015–2019), of which majority have been conducted on HA-MRSA. Nevertheless, until May 2014, there were only 12 articles on

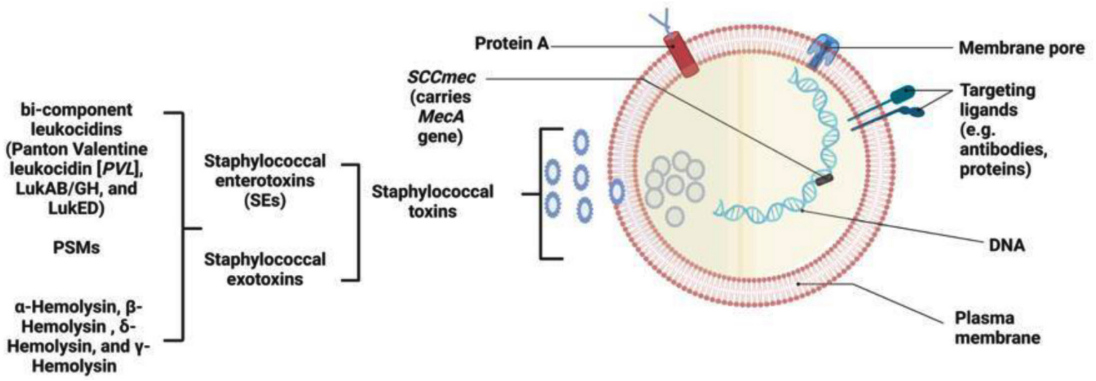

Figure 2. virulence factors of *Staphylococcus aureus*

MRSA infections, of which ten were published in Riyadh and Dammam.[10] Despite conducting investigations and discussions on HA-MRSA, there is still a shortage in the number of studies on HA-MRSA in children, and surprisingly, HA-MRSA is primarily found in men than in women.[21] Based on the prevalence of CA-MRSA, the number of patients significantly increased from 9.9 per 10,000 in 2001 to 67 per 10,000 in 2008.[21,22] Furthermore, between 2000 and 2008, the spread rate of CA-MRSA in the eastern region of Riyadh increased six-fold.[19] Furthermore, CA-MRSA samples collected from Qatif city, Saudi Arabia, showed that CA-MRSA percentages increased gradually from 23% in 2006 to 60% in 2015.[23] There is still a lack of studies that aimed to investigate LA-MRSA.[24]

MRSA in the Capital City of Saudi Arabia

According to the Center of Disease Control, two in 100 individuals develop MRSA infections, and 33% of persons colonize with *Staphylococcus.*[25] *S. aureus* strains (n=135) have been collected from main public health centers and hospital laboratories in Riyadh city between 2008 and 2009 to examine the presence of CA-MRSA infections. As a result, scientists have announced that the CA-MRSA infection rate was amplified in Riyadh city.[22] Al Yousef *et al*. reported that 94% of MRSA strains have been detected in Riyadh.[26] In addition, all 37 isolates of *S. aureus*, which were collected from King Khalid University Hospital in Riyadh (2007), were MRSA, and only two of them carried *mecA* gene. [27]

Moreover, *SCCmec* type IV was tested in Riyadh to determine the type of strains; subsequently, CC22-MRSA-IV was found to be a common strain associated with strains collected from India and the Middle East rather than that from the Western European countries.[28] Senok *et al.* obtained 117 samples of MRSA infections over a 6-year period (2009–2015) in Riyadh city and examined them to identify the most derived strains related to CA-MRSA; CC5, CC22, CC6, and CC80 (13, 12, 15, and 35 strains, respectively) were the most commonly identified strains. This study identified three new MRSA clones in Saudi Arabia (CC15-MRSA).[29]

Alaklobi *et al.* estimated the growth of CA-MRSA levels among children in Riyadh city, which ranged from 0%–9%, and 164/824 samples in this study were colonized with *S. aureus*; however, only 38 samples were MRSA, and 23% of the MRSA infections were reported in children.[30] In addition, another study examined 100 raw retail

Figure 3. Spread of HA-MRSA and CA-MRSA in Saudi Arabia

meat samples: 24 lamb (mutton), 24 camel, 23 beef, and 29 poultry (chicken parts) in Riyadh. Of the 100 meat samples, 25 were contaminated with *S. aureus*. While meat samples from poultry assets were recorded to have the lowest contamination among the tested samples, the meat sample from camel had the highest level of contamination.[24] Moreover, 80 camel milk samples were collected from different places throughout Riyadh city, and strains of bacteria that carried the 16s RNA gene similar to many pathogens such as MRSA were found.[31]

MRSA in Different Cities of Saudi Arabia

As shown in figure 3, MRSA's types have been spotted in variant cities of Saudi Arabia such as Dhahran, Dammam, Medina, Jeddah, Taif, Asir, etc. In 2019; moreover, Farah *et al.* reported that there was a high level of multidrug resistance among seven different locations and 12 hospitals in Saudi Arabia. During the same period, HA-MRSA cases declined significantly from 0.17/1000 to 0.03/1000.[25] In Saudi Arabia, HA-MRSA was first discovered, followed by CA-MRSA and LA-MRSA. However, CA-MRSA has been reported to be less serious than HA-MRSA; hence, researchers in Saudi Arabia are more focused on HA-MRSA.[32,33] In addition, investigators have tended to use *PVL* as an indicator of CA-MRSA presence, which has been recorded to be present at high levels in Riyadh since 2012.[19,32]

Additionally, a group of scientists in Riyadh and Taif focused on CA-MRSA and found that since *SCCmec* IV and V can easily be transmitted among organisms, they are predominant than *SCCmec* I, II, and III.[22,34]

Owing to the Hajj season, 31 studies were conducted in Mecca, Mina, and Medina, and the authors examined food workers, hospitalized patients, and pilgrims between 2000 and 2015. Subsequently, a sharp increase in MRSA infections in pilgrims was observed (from 1% in 2000 to 63% in 2015). The rate of MRSA isolated from food handlers has also increased remarkably (i.e., from 0% in 2001 to 20% in 2014).[35]Additionally, certain restaurants in Makkah city have tested and reported that the food samples were contaminated with *S. aureus.* [33] In addition, many food samples (e.g., raw milk and cheese) in Makkah City were found to have a significant incidence of multidrug-resistant *S. aureus* and coagulase-negative staphylococci.[36]

The western region of Saudi Arabia has been similarly investigated by El amin and Faidah, and the most isolated MRSA infections (87%) were from soft tissue, skin, and wounds. In addition, the prevalence of HA-MRSA was 53%, whereas that of CA-MRSA was 31.5%.[37] Approximately 5% of MRSA infections were also reported in Madinah city by Ghanem *et al*. during the time of fourteen-month. Most of them were isolated from men (237 MRSA strains), including 37 recovered strains from nasal swabs, 120 strains from sputum, and 124 strains from wound swabs. Moreover, MRSA isolated from catheter tips and pus samples was higher in women than in men, and the rate of MRSA infections reached a peak in the summer season throughout the Hajj term (51%), which decreased during other seasons: 21% in autumn, 18.5% in winter, and 10% in spring.[38]

Apart from Mecca city, different cities in Saudi Arabia have been examined for MRSA infections; e.g., a study conducted in Qatif city from January 1, 2006, to December 31, 2015, highlighted that 25/100,000 patients were diagnosed with MRSA infection, and 20%–35% of all patients in the examined city were children.[23] Moreover, MRSA was detected in 101 samples from public health centers and large hospital laboratories in Jeddah city between August 2009 and May 2011. MRSA strains carry *mecA* gene and are positive for *PVL*; therefore, the common type of *SCCmec* in that study was type V, followed by type III (42.5% and 39%, respectively).[39] Four different strains of *S. aureus* (CC22, CC8, CC5, and CC80) were isolated from 206 nasal swabs (103 from Saudi Arabia and 103 from Egypt). The prevalence of MRSA in Saudi Arabia was lower than that in Egypt (12% and 15%, respectively). In this study, *mecA* gene was positive, and the most common types of *SCCmec* were IVa and V.[40]

A recent study in Jeddah city, conducted by Al-Zahrani *et al*. recorded the highest ratio of MRSA infections (CA-MRSA comprised majority of the infections). During Hajj, pilgrims travel from Jeddah to Mecca, which lead to a rise in MRSA cases (>61%), and these cases majorly include foreigners (from Pakistan, Sudan, Syria, Yamen, Somalia, Egypt, and Chad).[41]

In addition, a 7-year study from 2001 to 2008 was conducted in the eastern region of Saudi Arabia, which revealed that the rate of CA-MRSA infections increased from 9.9/10,000 in 2001 to 67/10,000 in 2008. This investigation was divided into two stages. The presence of CA-MRSA was 67 (20%) and 176 (59%) in the first (2001–2004) and second stages (2005–2008), respectively.[42] Furthermore, Dhahran city in Saudi Arabia was among the places that attracted the attention of researchers for further investigation of MRSA. Khanfar *et al.* reported 878 cases of MRSA infections from the Saudi Aramco Dhahran Health Center between 2004 and 2009; 777 (88%) and 101(11.5%) cases were CA-MRSA and HA-MRSA infections, respectively.[43] Approximately 30% of MRSA strains have been discovered in approximately 90 minced meat and vegetable sandwiches collected from fast-food canteens in Al-Ahsa city.[44]

Throughout the southern region of Saudi Arabia, from Asir Central Hospital and Abha General Hospital, 210/9831 infectious samples contained *S. aureus*. The samples were collected from three dissimilar sources (ten from the hospital environment, 100 from community-acquired infections, and 100 from hospital-acquired infections). Hence, the hospital environment is a serious threat to all hospital staff, visitors, and hospitalized patients in terms of MRSA dissemination.[45]

Several CA-MRSA + HA-MRSA and LA-MRSA infections have been reported in several cities of Saudi Arabia. For example, 20 isolates from 775 nasal swabs and 235 milk samples taken from a goat farm in eastern Saudi Arabia were MRSA. The maximum prevalence of MRSA in this study was 2%, and most of them were from mastitic milk (9%) and a few were from normal milk (0.6%).[46] Furthermore, in Al-Hasa city, 20 out of 187 fresh raw camel meat samples consisted of *S. aureus* strains, and three of 20 isolates were reported as MRSA.[47]

In Qassim city, 90/400 animal-derived samples (from goat, sheep, cow, and camels) were identified as LA-MRSA (57%). The smallest level of LA-MRSA isolates was from cow and goat samples, whereas the highest level was from sheep and camel samples.[48]

Reasons of MRSA Infection

Bhedi *et al.* stated that the presence of MRSA infections in poultry meat is attributed to many factors, such as dropping meat handling levels in selling shops, hygiene, and sales practices.[49] Globally, food handlers are also considered a major cause of food contamination; e.g., in Dhaka city, street food is served with bare hands. Thus, approximately 50–70% of ready-to-eat food (RTE) handlers are transmitters of *S. aureus.* Moreover, 32% and 1% of food handlers of Zimbabwe and Hong Kong, respectively, are infected with *S. aureus*. Another study in China confirmed that 3–6% of Hong Kong butchers were affected by LA-MRSA ST9.[50,51]

CONCLUSION

This literature review revealed that the rate of MRSA prevalence has significantly increased worldwide, with the emergence of MRSA in food handlers, food samples, and animal-derived food. In Saudi Arabia, studies have emphasized that HA-MRSA is more serious, even though the susceptibility of HA-MRSA to antibiotics is lower than that of CA-MERSA. Lastly, it is worth mentioning that more studies on MRSA are required because of their impact on public health.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

AUTHORS' CONTRIBUTION

All authors listed have made a substantial, direct and intellectual contribution to the work, and approved it for publication.

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None.

DATA AVAILABILITY

All datasets generated or analyzed during this study are included in the manuscript.

ETHICS STATEMENT

Not applicable.

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