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Antimicrobial Susceptibility Patterns of *Staphylococcus aureus* in Decubitus Ulcer Infections

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Abstract

Objective: Decubitus ulcers, also called bedsores or pressure ulcers, are skin and soft tissue injuries caused by sustained or prolonged pressure on the skin. *Staphylococcus aureus* (*S. aureus*) is one of the most frequently isolated bacteria in patients with decubitus ulcer infection. In this study, we aimed to retrospectively determine the antimicrobial susceptibility profile of *S. aureus* strains isolated from wound swab cultures of patients hospitalized in various wards.

Methods: Wound swab cultures were examined from patients with clinical signs of decubitus ulcer infection during inpatient treatment in different wards with various diagnoses between January 2009 and October 2019. In these samples, the antimicrobial susceptibility profile data of 132 *S. aureus* strains belonging to 132 different patients who were considered clinically significant were included in our study.

Results: Among all specimens, 132 (13.83%) *S. aureus* positivity cases were included in our study. The methicillin-resistant (MRSA) rates were 43.85% (24/56) in male patients and 57.14% (32/56) in female patients with decubitus ulcer infection. Of the *S. aureus* strains, 42.42% (56/132) were MRSA and 57.58% (76/132) were methicillin-susceptible (MSSA). Linezolid was found to be the most effective antibiotic among MRSA strains, whereas all MSSA strains were susceptible to amoxicillin + clavulanic acid, rifampicin, and cefoxitin.

Conclusion: Antimicrobial resistant strains such as MRSA may be encountered in half of *S. aureus* infections and may complicate treatment options. We conclude that infections and antimicrobial resistance profiles should be routinely monitored.

Keywords: *Staphylococcus aureus*, MRSA, MSSA, decubitus ulcers

INTRODUCTION

Decubitus ulcers, also called bedsores or pressure ulcers, are skin and soft tissue injuries resulting from continuous or prolonged pressure applied to the skin. Ulcers occur in bony parts of the body, and lesions mostly occur in people with conditions that reduce mobility and make it difficult to change posture (1). They are serious complications resulting from multiple morbidities and immobilization. Decubitus ulcers are rare among bedridden patients owing to the conscious use of pressure-reducing measures and increased mobilization. However, not all decubitus ulcers can be considered preventable or potentially treatable (2). Complications of decubitus ulcers are associated with significant morbidity and mortality. Bacterial infection is the most common complication associated with decubitus ulcers. Infection of the decubitus ulcer may lead to soft tissue and bone infections, such as cellulitis, abscess formation, bursitis, and osteomyelitis, in the bone under the wound bed (3). Decubitus ulcers are most commonly seen in the lower half of the body, along bony prominences, such as the sacrum and

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heels, in bedridden patients. Blood flow to compressed tissue is restricted, and toxic metabolites begin to accumulate over time, while nutrient distribution stops, leading to cell death. In addition, as circulation is restricted, the immunologic response around the wound becomes ineffective, and the ability to heal is compromised (4). *S. aureus* is one of the bacteria frequently isolated in patients with decubitus ulcer infection. *S. aureus* is known to be a common colonizing microorganism in human epithelium, especially in the nose. However, in decubitus ulcers, *S. aureus* may colonize and be a source of infection in the region. It has different virulence factors that help it cause serious infections ranging from decubitus ulcer infection to osteomyelitis and bacteremia (5). *S. aureus* isolates with an auxiliary penicillin-binding protein (PBP2a/PBP2c encoded by *mecA* or *mecC* genes) for which β-lactam agents have low affinity, except for the novel class of cephalosporins having anti-methicillin-resistant (MRSA) activity (ceftaroline and ceftobiprole). European Committee on Antimicrobial Susceptibility Testing's (EUCAST) MRSA definitions: "isolates that test resistant to benzylpenicillin but susceptible to cefoxitin are susceptible to β-lactam β-lactamase inhibitor combinations, the isoxazolylpenicillins (oxacillin, cloxacillin, dicloxacillin and flucloxacillin) and nafcillin." The susceptibility of staphylococci to cephalosporins is inferred from the cefoxitin susceptibility, except for cefixime, ceftazidime, ceftazidimeavibactam, ceftibuten, and ceftolozanetazobactam, which do not have breakpoints and should not be used for staphylococcal infections. For agents given orally, care to achieve sufficient exposure at the site of the infection should be exercised. If cefotaxime and ceftriaxone are reported for methicillin-susceptible (MSSA) staphylococci, these should be reported "susceptible, increased exposure". Some MRSA *S. aureus* are susceptible to ceftaroline and ceftobiprole" (6). Decubitus ulcer infection is an important reservoir for MRSA in hospitals, and these patients are known as high-risk patients for MRSA bacteremia. MRSA detection may contribute to prolonged hospitalization and poor prognosis in these patients. Along with *S. aureus*, Gram-negative bacilli are the most common bacterial pathogens in infected decubitus ulcers (7).

However, it is known that a biofilm layer that protects the pathogen from the effects of many antibiotics can form in decubitus ulcer infections, which contributes to the secretion of toxins by the pathogen that cause more damage to the skin and surrounding tissues and the emergence of multidrug-resistant strains, such as MRSA, making the treatment of infected decubitus ulcers difficult (8). One of the methods used to characterize organisms as multidrug-resistant is based on *in vitro* antimicrobial susceptibility test results, when they test "resistant to multiple antimicrobial agents, classes or subclasses of antimicrobial agents". The definition most frequently used for Gram-positive and Gram-negative bacteria is "resistant to three or more antimicrobial classes" (9). In this study, we aimed to retrospectively determine the antimicrobial susceptibility profile of *S. aureus* strains detected as causative agents of decubitus ulcer infection in wound swab cultures of patients hospitalized in various wards.

METHODS

In our study, we examined wound swab cultures obtained from patients with clinical signs of decubitus ulcer infection during inpatient treatment in different wards with various diagnoses between January 2009 and October 2019. In these samples, the antimicrobial susceptibility profile data of 132 *S. aureus* strains belonging to 132 different patients who were considered clinically significant were included in our study. The data and antimicrobial susceptibility profiles of these strains were retrospectively collected through the hospital information management system. Among consecutive samples from the same patient, only the first positive result was included in the study; results from other repeat strains of the same patient were excluded. Because this was a retrospective study, informed consent was not required. Ethics committee approval was obtained for the use of retrospective antimicrobial susceptibility profile data of *S. aureus* strains [Private Medical Park Fatih Hospital Academic and Ethics Committee (approval number: 2021-1-2, date: 26.04.2021)].

The presence of infection at the ulcer site was based on clinical signs and symptoms (erythema, edema, pain, foul odor, fever, etc.). In addition, the wound was considered infected when the ratio of polymorphonuclear cells to squamous epithelial cells was ≥2:1 after Giemsa staining in the smear of wound swab material (10). To isolate and identify *S. aureus*, wound swab culture samples were cultured on 5% sheep blood agar medium in the laboratory. The preparations prepared from the samples were stained with Gram stain. All suspected strains were identified using the Vitek 2 Compact system (Biomerieux, Marcy-l'Étoile, France), and antimicrobial susceptibility profiles were studied. Antimicrobial susceptibility results were evaluated according to the Clinical Laboratory Standards Institute criteria before 2016 and the EUCAST criteria after 2016. The *S. aureus* ATCC 25923 reference strain was used for quality control in all procedures (11,12).

Statistical Analysis

Only descriptive statistical methods were used in this study.

RESULTS

Our study included 954 specimens from patients hospitalized in various wards between January 2009 and October 2019, from which wound swab cultures were obtained during hospitalization. Among all specimens, 132 (13.83%) *S. aureus* positivity detected as the causative agent of decubitus ulcer infection were analyzed. The mean age of female patients with decubitus ulcer infection who were positive for *S. aureus* was 64.94±12.12 years and the mean age of male patients was 66.08±13.85 years. The rate of MRSA was 43.85% (24/56) in male patients and 57.14% (32/56) in female patients with decubitus ulcer infection. Table 1 presents the distribution of antimicrobial susceptibility profiles of the strains. Of the *S. aureus* strains, 42.42% (56/132) were MRSA and 57.58% (76/132) were MSSA. Linezolid was the most effective antibiotic for all strains, and 99.24% were found to be susceptible. This antibiotic was followed by levofloxacin with 80.30% and cefazolin with 79.55%.

The distribution of antimicrobial susceptibility profile of MRSA and MSSA strains included in this study are presented in Table 2. Linezolid was the most effective antibiotic among MRSA strains, and 98.21% of the strains were susceptible. All MSSA strains were susceptible to amoxicillin + clavulanic acid, rifampicin, and cefoxitin. Ampicillin + sulbactam (98.68%) and gentamicin (92.11%) followed these antibiotics with high susceptibility rates.

Table 1. Distribution of antimicrobial susceptibility profiles of the *S. aureus* strains included in the study

	***S. aureus* (n=132)**			
	S		**R**	
	n	**%**	**n**	**%**
Amoxicillin/clav.	76	57.58%	56	42.42%
Ampicillin/sulbactam	76	57.58%	56	42.42%
Erythromycin	40	30.30%	92	69.70%
Gentamicin	78	59.09%	54	40.91%
Clindamysin	82	62.12%	50	37.88%
Cotrimoxazol	66	50.00%	66	50.00%
Levofloxacin	106	80.30%	26	19.70%
Linezolid	131	99.24%	1	0.76%
Methicillin	76	57.58%	56	42.42%
Rifampicin	76	57.58%	56	42.42%
Cefazolin	105	79.55%	27	20.45%
Cefoxitin	76	57.58%	56	42.42%
Ciprofloxacin	100	75.76%	32	24.24%
Tetracyclin	58	43.94%	74	56.06%

S. aureus: Staphylococcus aureus, S: Susceptible, R: Resistant

Table 2. Distribution of antimicrobial susceptibility profiles of MRSA and MSSA strains included in the study

	MRSA (n=56)				**MSSA (n=76)**			
	S		**R**		**S**		**R**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Amoxicillin/clav.	0	0.00%	56	100.00%	76	100.00%	0	0.00%
Ampicillin/sulbactam	1	1.79%	55	98.21%	75	98.68%	1	1.32%
Erythromycin	1	1.79%	55	98.21%	39	51.32%	37	48.68%
Gentamicin	8	14.29%	48	85.71%	70	92.11%	6	7.89%
Clindamysin	24	42.86%	32	57.14%	58	76.32%	18	23.68%
Cotrimoxazol	28	50.00%	28	50.00%	38	50.00%	38	50.00%
Levofloxacin	47	83.93%	9	16.07%	59	77.63%	17	22.37%
Linezolid	55	98.21%	1	1.79%	76	100.00%	0	0.00%
Methicillin	0	0.00%	56	100.00%	76	100.00%	0	0.00%
Rifampicin	0	0.00%	56	100.00%	76	100.00%	0	0.00%
Cefazolin	31	55.36%	25	44.64%	74	97.37%	2	2.63%
Cefoxitin	0	0.00%	56	100.00%	76	100.00%	0	0.00%
Ciprofloxacin	37	66.07%	19	33.93%	63	82.89%	13	17.11%
Tetracyclin	32	57.14%	24	42.86%	26	34.21%	50	65.79%

MRSA: Methicillin-resistant, MSSA: Methicillin-susceptible, S: Susceptible, R: Resistant

DISCUSSION

Decubitus ulcer infections are a common complication in patients with reduced mobility. They often develop in elderly patients and in patients with debilitating diseases and spinal cord injury (13). The microbiota of the decubitus ulcer site is often polymicrobial and complex and can be colonized by multidrug-resistant Gram-negative bacilli and bacteria such as MRSA. This region may be a reservoir for resistant microorganisms and may turn into local infections due to the effects of these bacteria, and it is also known that it may turn into bacteremia and become an important cause of mortality in hospitalized patients (10). In our study, we retrospectively determined the antimicrobial susceptibility profile of *S. aureus* strains found to be causative agents in patients with decubitus ulcer infections over an 11-year period. In international studies were analyzed; Nery Silva Pirett et al. (7) reported that MRSA was detected in 43.5% of 145 patients. They reported that 42% of patients with MRSA were male and 58% were female. The mean age of patients with MRSA was reported to be 64.2±16.3 years (7). In 2024, Sharp (14) reported that MRSA was colonized in 48% of decubitus ulcers in elderly people over 65 years old staying in residential aged care facilities. Their data were similar to those of our study (7,14). Braga et al. (15) reported that *S. aureus* positivity was detected in 20.7% of 145 patients. Dana and Bauman (3) analyzed studies published between 1996 and 2004 and found that *Staphylococcus* species were reported as causative agents in 23% of the studies. Binsuwaidan et al. (16) reported *S. aureus* as the most frequently isolated bacteria in 2023 and stated that 28% of these *S. aureus* isolates were generally sensitive to clindamycin, mupirocin, trimethoprim, and linezolid. MRSA was detected 60.3% (35 out of 58 *S. aureus* strains) of these ulcers. In our study, 13.83% *S. aureus* (and 42.42% of MRSA) was detected, and although this rate is lower than that reported in the literature, the fact that our samples originated from a private hospital may be the reason for this difference. Chronic wounds or pressure ulcers are characterized by colonization by microorganisms, and infections are known to develop in 5% to 80% of cases due to various factors (17). The observation of a polymicrobial and heterogeneous population of microbes in a pressure ulcer infection as a chronic wound can be attributed to the presence of virulence factors, such as biofilms, especially in the causative strains. Therefore, *S. aureus*, *Streptococcus pyogenes*, *Pseudomonas aeruginosa*, and *Peptostreptococcus* spp. are frequently encountered. Multiresistant strains, such as MRSA, *Acinetobacter* spp., and *Pseudomonas* spp., are also frequently detected as dominant agents (17). When national studies are examined; Öztin et al. (18) detected *S. aureus* infection in 7 patients in Erzurum within a 1-year period. Öztürk and Öztin (11) reported that they detected *S. aureus* positivity in 2 (3.7%) of the wound cultures of 42 patients in their study conducted in Erzurum in 2018. They reported that these strains were 100% resistant to ampicillin and ciprofloxacin, 50% resistant to gentamicin, and sensitive to tigecycline (11). Öztürk et al. (19) detected *S. aureus* in 2 (7.69%) patients in their study conducted in Ankara in 2019-2020. They reported 50% ampicillin, 50% ciprofloxacin, and 50% gentamicin resistance in these strains. Turhanoğlu et al. (20) reported that 41.4% of the microorganisms isolated from wound cultures between 2010 and 2015 were *S. aureus*. In this study, similar to our study, 100% susceptibility was found for linezolid, teicoplanin, and vancomycin. Cirit et al. (21) reported 13.7% (150/1093) positivity for *S. aureus* in wound cultures between 2010 and 2012. They reported that 27.3% of these strains were MRSA. They detected 100% susceptibility to teicoplanin and vancomycin. Erdiren et al. (22) reported 15.4% *S. aureus* positivity in wound cultures in a four-year period. They were 100% sensitive to linezolid, teicoplanin, and vancomycin. It can be seen that our study is similar to the literature data. Linezolid was found to be effective against these infections.

Study Limitations

Wound cultures were collected at different times and with different methods; therefore, we collected the patients belonging to the most common method, i.e., swab culture method. If appropriate conditions exist, the preferred method for wound culture is to excise and sample the deep tissue. This is a limitation for our study.

CONCLUSION

In conclusion; *S. aureus* can be a causative agent of decubitus ulcer infections. It should be kept in mind that antimicrobial resistant strains, such as MRSA, may be encountered in half of *S. aureus* infections and may complicate treatment options. Although newer antibiotics, such as linezolid, currently appear to be active *in vitro* for the treatment of these infections, it is clear that these strains may lose their *in vivo* activity because of their biofilm properties, and new antimicrobial options are needed. We believe that these infections and antimicrobial resistance profiles should be routinely monitored.

Footnote

Ethics Committee Approval: Ethics committee approval was obtained for the use of retrospective antimicrobial susceptibility profile data of *S. aureus* strains [Private Medical Park Fatih

Hospital Academic and Ethics Committee (approval number: 2021-1-2, date: 26.04.2021)].

Informed Consent: A retrospective study, informed consent was not required.

Authorship Contributions

Concept: A.B., Ö.Ü., M.D., Design: A.B., Ö.Ü., S.G., M.D., Data Collection or Processing: A.B., M.G.E., S.G., Analysis or Interpretation: A.B., M.G.E., Ö.Ü., Literature Search: A.B., S.G., Writing: A.B., M.G.E., M.D.

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