Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2022;47(2):580-588
DOI: 10.17826/cumj.1038002

ARAŞTIRMA / RESEARCH

Clinical characteristics and resistance patterns of *Staphylococcus aureus* infections in children at a tertiary care hospital in southern Turkey

Türkiye'nin güneyinde üçüncü basamak bir hastanede çocuklarda *Staphylococcus aureus* enfeksiyonlarının klinik özellikleri ve direnç paternleri

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Cukurova Medical Journal 2022;47(2):580-588

Abstract

Purpose: The aim of this study was to evaluate the clinical and demographic characteristics and resistance patterns to antistaphylococcal antibiotics of Staphylococcus aureus (*S. aureus*) isolates, which is a leading cause of invasive infections in children.

Materials and Methods: Patients who were under 18 years of age and who had *S. aureus* growth in abscess, wound, blood, cerebrospinal fluid, joint fluid and any other sterile body fluid cultures, who were followed up at Children's Health and Diseases Clinic in between July 2018 and July 2020 were included in the study.

Results: A total of 135 patients and cultures were included in the study. Community-acquired *S. aureus* (CA-SA) infection was present in 105 (77.7%) patients and hospital-acquired *S. aureus* (HA-SA) infections in 30 (22.3%). *S. aureus* was most commonly detected in skin and soft tissue infections. Skin and soft tissue infections were more common in patients with community-acquired disease, whereas bacteremia was more common in patients with nosocomial infection. Methicillin-resistant *S. aureus* (MRSA) isolates was encountered in 53.3% of all patients; Clindamycin resistance was found in 20% of all staphylococcal isolates and the ratio of mupirocin resistance was 14.4%.55.8% of all CA-SA and 46.7% of all HA-SA isolates were MRSA. Penicillin, mupirocin, erythromycin, and tetracycline resistance were significantly higher in MRSA isolates as compares to non-MRSA isolates. Mupirocin resistance was significantly higher in CA-SA isolates. The median length of hospital stay was 12 days. Length of hospital stay, duration of intravenous antibiotics use, mortality, and clindamycin resistance were

Öz

Amaç: Bu çalışmada çocuklarda invaziv enfeksiyonların önde gelen bir nedeni olan Staphylococcus aureus (*S. aureus*) izolatlarının klinik ve demografik özelliklerinin, antistafilokokal antibiyotiklere direnç durumlarının değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Temmuz 2018-Temmuz 2020 tarihleri arasında Çocuk Sağlığı ve Hastalıkları Kliniği'nde takip edilen, apse, yara, kan, beyin omurilik sıvısı, eklem sıvısı ve diğer steril vücut sıvısı kültürlerinde *S. aureus* üremesi olan 18 yaş altı hastaların dosya kayıtları retrospektif olarak incelendi.

Bulgular: 135 hasta çalışmaya alındı. Hastaların 105'inde (77.7%) toplum kökenli, 30'unda (22.3%) ise hastane kökenli *S. aureus* (HA-SA, Hospital Acquired *S. aureus*) enfeksiyonu mevcuttu. *S. aureus* en yaygın olarak cilt ve yumuşak doku enfeksiyonlarında saptandı. Toplum kökenlilerde cilt ve yumuşak doku enfeksiyonları, nozokomiyallerde ise bakteriyemi sık gözlendi. Tüm hastaların %53.3'ünde metisilin dirençli *S. aureus* (MRSA); %20'sinde klindamisin, %14.4'ünde mupirosin direnci saptandı. Toplum Kökenli *S. aureus*'ların (CS-SA, Community-acquired SA) %55,8'i, HA-SA'ların %46,7'si MRSA idi. MRSA olanlarda penisilin, mupirosin, eritromisin ve tetrasiklin direnci anlamlı derecede daha fazlaydı. CA-SA'larda mupirosin direnci anlamlı derecede daha fazlaydı. Yatış süresi median 12 gündü. Yatış süresi, IV antibiyotik alma süresi, mortalite, klindamisin direnci HA-MRSA enfeksiyonlarında anlamlı derecede daha yüksekti. *S. aureus* enfeksiyonlarında mortalite %2.2 iken, HA-SA enfeksiyonlarında mortalite %10 olarak saptandı.

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Geliş tarihi/Received: 23.12.2021 Kabul tarihi/Accepted: 12.03.2022

significantly higher in patients with HA-MRSA infections. While overall mortality was 2.2% in patients with *S. aureus* infections, when evaluated separately, it was 10% in patients with HA-SA infections.

Conclusion: Our CA-MRSA rates are quite high as compared to other reports, and clindamycin and mupirocin resistance seems to be an important problem in our region. Taking appropriate cultures at the right time is important in determining resistance patterns and guiding empirical treatment regimens.

Keywords:. Staphylococcus aureus, child, clinical characteristics, antibiotic resistance

Sonuç: Toplum kökenli MRSA oranlarımız oldukça yüksek olup; klindamisin ve mupirosin direnci bölgemizde önemli bir sorun olarak görünmektedir. Doğru zamanda, uygun kültür örneğinin alınması; direnç paternlerinin ve ampirik tedavi rejimlerinin belirlenmesinde önemlidir.

Anahtar kelimeler: Staphylococcus aureus, çocuk, klinik özellikler, antibiyotik direnci

INTRODUCTION

Staphylococcus aureus (SA) is the leading cause of both community-acquired and hospital-associated invasive infections in children. Although it is frequently encountered in skin, soft tissue and musculoskeletal system infections in children, it also causes septicemia, head and neck infections, infective endocarditis, pneumonia, ocular, catheter associated, ventriculo-peritoneal shunt and central nervous system infections[1]. Antimicrobial susceptibility tests are becoming increasingly crucial due to the increase in strains with multidrug resistance and the limited number of antimicrobial agents effective against methicillin-resistant *S. aureus* (MRSA)[2]. MRSA has traditionally been classified as hospital acquired (HA) and community-acquired (CA). MRSA was originally a pathogen associated with hospital-acquired infections, but has now become an increasingly common community-acquired pathogen. Serious increases in MRSA isolation rates have been reported in CA-MRSA strains without an underlying disease risk factor[3,4].

The prevalence of MRSA varies among countries, and resistance to erythromycin, clindamycin, tetracycline, trimethoprim-sulfamethoxazole (TMP-SMZ), quinolones, and aminoglycosides is commonly encountered in MRSA isolates. Clindamycin is being successfully used in the treatment of both invasive and non-invasive MRSA infections in children. This situation further increases the problem of clindamycin resistance in the hospital and the community. Mupirocin is the most effective antibiotic used for the topical treatment of methicillin-susceptible *S. aureus* (MSSA) and MRSA infections, for the decolonization of MSSA and MRSA in both patients and healthcare professionals, therefore is at great risk for the development of resistance due to its increasing use. For this reason, monitoring the development of mupirocin resistance is critical[5,6]. It is of great importance to know the antibiotic resistance patterns in the community and the hospital when starting empirical treatment for suspected SA infections.

We think that our MRSA rates are quite high due to the failure of empirical treatment with beta-lactam antibiotics in possible *S. aureus* infections in recent years and therefore we had to switch to glycopeptide or MRSA effective agents. So, the aim of this study was to identify and add to the literaturethe clinical features of infections with community-acquired and hospital acquired *S. aureus* isolates, MRSA and MSSA rates and resistance patterns to anti-staphylococcal antibiotics in our region and suggestan empirical treatment protocol forour population according to the study results.

MATERIALS AND METHODS

Study design and patient selection

This single-center, retrospective, observational study was conducted at Adana City Training and Research Hospital, which is a tertiary-care children's referral hospital in Adana. Approval for the study was obtained from the Clinical Research Ethics Committee of the Adana City Training and Research Hospital (Dated June 17, 2020 and numbered 936).

Based on the effect size of the studies in the literature, it is anticipated that a medium effect size (effect size=0.8) will be considered as a difference in the averages of the parameters in the studies examined; alpha significance level was calculated as 0.05 %95 Power, 105 patients in Group 1 (Community-acquired) and 30 patients in Group 2 (Hospital-acquired), a total of 135 patients. In this way, the patients who applied retrospectively in the last 2 years

were examined, and a sufficient number of them for the study was reached.

Data collection and variables

This 2-year retrospective study examined the pediatric patients (0-18 years old) who were followed up from July 2018 to June 2020 and whose abscess, wound, blood, cerebrospinal fluid (CSF), joint fluid and other sterile body fluid cultures were positive for *S. aureus* along with clinical symptoms of systemic infection. Patients who were older than 18 years of age, patients who had positive cultures but insufficient clinical data and patients with suspected asymptomatic decontamination were excluded.

The files were reviewed retrospectively. Age, gender, nationality, location of infection, area of culture, hospitalization period, oral and intravenous (IV) antibiotics used and their duration, surgical procedures perfomed, *S. aureus* antibiotic susceptibility test results, and prognosis were recorded in the leaflets.

Bacterial identification and antimicrobial susceptibility testing

Clinical samples were in cubated in the BACTEC 9240 (BD Becton, Dickinson and Company) blood culture system for blood and CSF samples by sample type. Then, like other samples, 5% sheep blood agar, Eosin Methylene Blue (EMB) agar and chocolate agar were inoculated, and the microorganisms grown after 18-24 hours incubation at 37°C were evaluated in terms of colony morphology and staining characteristics. Species identification of the isolates was determined by MALDI-TOF MS (BrukerDaltonics, USA) mass spectrometry. In order to determine antibiotic susceptibility, suspensions with 0.5 McFarland turbidity were prepared and investigated using MicroScanWalkAway 96 plus (Beckman Coulter, US) automated system panels. E-test method was used for the ones which required verification. Evaluations for antibiotic susceptibility were made according to the current criteria of the European Committee on Antimicrobial Susceptibility Testing (EUCAST)[7]. Methicillin resistance was evaluated as oxacillin MIC >2 mcg/mL. The growths that were resistant to methicillin or oxacillin in their antibiogram were evaluated as MRSA, and those susceptible to methicillin or oxacillin were considered as MSSA.

Definitions

HA-SA was defined as the presence of an invasive device at the onset of infection, a history of SA infection or colonization, a history of surgery, hospitalization or dialysis, and a positive culture result obtained from a normal sterile area obtained >48 hours after hospitalization[8]. CA-SA was defined as an isolate from either an outpatient, or an inpatient within 48 h of hospitalization, who had no medical history of *S. aureus* infection/colonization, hospitalization, surgery, dialysis or indwelling catheter last year[9].

Statistical analysis

SPSS (Statistical Package for the Social Sciences) 23.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum-maximum where appropriate). Pearson Chi-square and Fisher exact test statistics were used to compare categorical variables. Shapiro-Wilk test was used to determine whether the parameters in the study showed normal distribution. In comparison of continuous measurements between groups, distributions were controlled, and independent student's t-test was used in paired group analyses. Statistical significance level was taken as 0.05 in all tests.

RESULTS

We identified a total of 151 *S. aureus* isolates. However, 16 isolates were excluded because of contamination or insufficient clinical data. 135 patients were included in the study over a two-year period. 53.3% (n=73) of the patients were female, mean age was 60.38±66.95 months (median 27.5, range 0.19-211), 21.4% were Syrian refugees. Of the patients, 105 (77.7%) had community-acquired and 30 (32.3%) had hospital acquired SA infections. Of the 29 Syrian patients with SA infection, 20 (68.9%) were CA-SA. Demographic and clinical characteristics of the patients are shown in Table 1.

SA was most commonly detected in skin and soft tissue infections (STI). This was followed by bacteremia, lymphadenitis, and musculoskeletal infections. Otitis was detected in one patient and endocarditis in one patient. STI was common in community-acquired patients, and bacteremia was common in hospital acquired patients. The type and

location of community-acquired and hospital-associated *S. aureus* infections are shown in Table 2.

MRSA was found in 53.3% of all patients, when all the isolates were evaluated for antibiotic resistance, there was erythromycin resistance in 30.4%, clindamycin resistance in 20%, gentamicin resistance in 17.8%, and mupirocin resistance in 14.4%. Of all the isolates and the anti-staphylococcal drugs used, the lowest drug resistance was to TMP-SMZ, rifampicin and fucidic acid (5.2%, 4.4% and 2.4%, respectively). 55.8% of CA-SAs and 46.7% of HA-SAs were MRSA. The rate of clindamycin resistance was 27.4% for MRSA and 11.3% for MSSA isolates. Mupirocin resistance was found in 28.2% of patients with MRSA and 3.2% of patients with MSSA. Penicillin, mupirocin, erythromycin, and tetracycline resistance were significantly higher in those with MRSA as compared to MSSA (p=0.003, p=0.001, p=0.001, p=0.001 respectively) (Table 3). Rare of mupirocin resistance was higher in CA-SAs and rate of clindamycin resistance was higher in HA-SAs and the differences were statistically significant (p<0.005) (Table 4). No resistance against vancomycin and/or teicoplanin was observed in any of the strains (p<0.005). MRSA was detected in 66.3% of those with STI. The rate of MRSA positivity in the cultures taken from Syrian patients was noted to be 69%. Rate of oxacillin, gentamicin, and tetracycline resistance was statistically significantly higher in Syrian patients as compared to Turkish patients (p=0.049, p=0.008 and p=0.038 respectively), while rate of mupirocin resistance was significantly lower (p<0.05).

17% of the patients had been followed up on an outpatient basis. The median length of hospital stay was 12 (3-194 days) days. The mean duration of intravenous antibiotic use was 12.08±8.57 days. Length of hospital stay, duration of intravenous antibiotic use, rate of mortality associated with the isolate, and of clindamycin resistance were significantly higher with hospital associated-SA infections thanwith community-acquired SA infections (p<0.001) (Table 1).

Table 1. Demographic and clinical characteristics of the patients

		Community-acquired (n=105)	**Hospital-acquired (n=30)**	**p**
		n (%) Mean±SD	n (%) Mean±SD	
Gender	Male	48 (45.7)	14 (46.7)	0.926
	Female	57 (54.3)	16 (53.3)	
Age (month)		60.1±6.3	61.3±13.6	0.931
Ethnicity	Citizen of the Republic of Turkey	85 (81)	21 (70)	0.198
	Syrian refugee	20 (19)	9 (30)	
Hospitalization time		12.8±1.2	35.9±6.5	<0.001
Parenteral treatment duration		10.6±0.9	16.3±1.1	0.001
Oral treatment duration		7.8±0.2	5.3±1.2	0.075
Mortality		0 (0)	3 (10.0)	0.001

Table 2. Type of community-acquired and hospital acquired *S. aureus* infection

Site of infection		**Community-acquired n (%)**	**Hospital- acquired n (%)**	**Total n (%)**
Type of skin and soft issue infection	Cellulite	46 (44.7)	6 (20)	52 (38.5)
	Abscess	34 (32)	1 (3.3)	35 (25.5)
	Lymphadenitis	7 (6.8)	1 (3.3)	8 (5.8)
Blood stream infection		8 (7.8)	9 (30)	17 (12.1)
Catheter-associated infection		0 (0)	6 (20)	6 (4.4)
Musculoskeletal infection		7 (6.8)	1 (3.3)	8 (5.8)
V-P shunt infection		1 (0.9)	3 (10)	4 (2.9)
Endocarditis		0 (0)	1 (3.3)	1 (0.74)
Pneumonia		1 (0.9)	2 (6.7)	3 (2.2)
Otitis		1 (0.9)	0 (0)	1 (0.74)
Total		105 (100)	30 (100)	135 (100)

V-P: Ventriculo-peritoneal

Table 3. Antibiotic resistance status of MRSA and MSSA strains (n=135)

Antibiotic resistance	MRSA n=73 n (%)	MRSA n=62 n (%)	p
Penicillin	73 (100)	55 (88.7)	0.003
Clindamycin	20 (27.4)	7 (11.3)	0.013
Ciprofloxacin	6 (9.1)	1 (1.6)	NA
Erythromycin	33 (45.2)	8 (12.9)	0.001
Trimethoprim-sulfamethoxazole	3 (5.1)	0 (0)	NA
Mupirocin	18 (28.2)	2 (3.2)	0.001
Tetracycline	17 (25.1)	0 (0)	0.001

MRSA: Methicillin-resistant *Staphylococcus aureus;* MSSA: methicillin-susceptible *Staphylococcus aureus.*

Tablo 4. Antibiotic resistance status of community-acquired and hospital acquired strains

Antibiotic resistance	Community-acquired n=105 n (%)	Hospital- acquired n=30 n (%)	p
Oxacillin	59 (55.8)	14 (46.7)	0.378
Penicillin	100 (95.2)	28 (93.3)	0.678
Clindamycin	16 (15.2)	11 (36.7)	0.027
Ciprofloxacin	6 (5.8)	1 (3.3)	0.591
Erythromycin	30 (28.6)	11 (36.7)	0.618
Trimethoprim-sulfamethoxazole	3 (2.9)	0 (0)	0.347
Mupirocin	19 (18.1)	1 (3.3)	0.037
Tetracycline	13 (12.6)	4 (13.3)	0.918

The intravenous antibiotics used for treatment wereas follows: ampicillin-sulbactam+clindamycin combination (30.3%), vancomycin (20%), ampicillin-sulbactam (11.1%), clindamycin (6.6%), teicoplanin (6.6%), and linezolid (4%). Antibiotherapy changes were made in 25.2% of the patients according to the culture sensitivity results. When the use of oral antibiotics was considered, the drug/drugs of choice were TMP-SMZ (22.2%), amoxicillin-clavulanic acid (12.5%), cephalexin (11.8%), clindamycin (4.4%), ampicillin-sulbactam (2.9%), cefuroxime-axetil (2.2%), ampicillin-sulbactam+clindamycin (1.4%).

In terms of surgical procedures, incision and drainage was performed in 85 patients, arthroscopic lavagein three patients, tissue debridement in two patients, and extra-ventricular drainage in four patients. While the total mortality associated with SA infections was 2.2%, as could be expected, mortality associated with hospital-acquired SA was 10%. Mortality due to MRSA was noted to be 4.1%, whether it be HA- or CA-SA infection.

DISCUSSION

S. aureus infections are an increasing cause of morbidity and mortality despite appropriate treatment. SA can lead to serious invasive or noninvasive infections. It is known that 90-95% of community-acquired STI's in children have SA as the causative agent[10]. In Arıkan et al.[11] multicenter study, of all the 132 *S. aureus* isolates cultured, 45.4% was from STI, 37.8% from blood stream infections, and 8.3% from bone infections. Camacho-Cruz et al. [12] reported similar results in another study. In our study, in accordance with the literature, the most common causes of staphylococcal infections were found to be STIs, followed by bacteremia, osteoarticular and other sites. STI was more common in community-acquired patients, and bacteremia was common in hospital-associated patients. SA is a rare cause of acute otitis media in childhood and was detected in only one patient in our study.

In the past 20 years, there has been an epidemiological shift related to SA infections. While HA-SA infections have increased in the first decade, the rate of community-acquired STI's due to SA resistant to β-lactam antibiotics have increased in the second decade[13]. In the literature, the general rate of infection due to MRSA in children has been reported to be between 6% and 77.4%, and the rate of CA-MRSA infections has been reported to be between 7.1%-85.7%[11,14-17]. In conclusion, it has been reported that there is an increase in the rate of CA-

MRSA infections and a decrease in the rate of HA-MRSA infections[3,17,18]. Initially, MRSA a major problem as a causative agent of hospital-cquired infections, but in recent years there has been an emergence in CA-MRSA as a dominant cause of staphylococcal disease all over the world. In our study, the overall MRSA rate was found to be 53.3%, 55.8% for CA-SAs and 46.7% for HA-SAs, in agreement with the general literature. The rate of MRSA was higher in Syrian refugees living together in the same society. It is thought that factors such as high rates of hospital admission and hospitalization due to crowded living environments, poverty and poor hygiene conditions, and inappropriate and misuse of antibiotics cause this difference. The rate of MRSA varies between countries, regions, hospitals and even wards of the same hospital. These results demonstrate that CA-MRSA is a serious problem in our country as well. The high rates of antibiotic resistance in our study can be attributed to the high rates of antibiotic use in our country.

The most important problem associated with SA infections has been the development of resistance against more than one antibiotic class. Resistance developed within 2 years after the introduction of penicillin [19]. Subsequently, MRSA was clinically defined in 1960[20]. Along with MRSA, the problem of multi-antibiotic resistance has also begun to emerge. Methicillin resistance confers resistance to all β-lactamases. Therefore, MRSA is resistant to penicillin and cephalosporins. On the other hand, penicillin resistance is a major problem in MSSA strains. It has been reported to be as high as 65.3 to100% in our country[11,21,22]. In our study, as reported in the literature, penicillin resistance was found to be 100% in MRSA and 88.7% in MSSA isolates. MRSA isolates frequently show resistance to erythromycin, clindamycin, tetracycline, trimethoprim, sulfonamides, quinolones and aminoglycosides, apart from beta-lactam antimicrobials. Kumar et al.[23] reported that resistance to gentamicin and ciprofloxacin among the MRSA isolates was more than that in MSSAs in their study in children. Gurung et al.[24] reported that cefoxitin, gentamicin, amikacin, TMP-SMZ and erythromycin resistance was significantly higher in MRSA isolates compared to MSSA. In our study, the rate of erythromycin, tetracycline, and mupirocin resistance in MRSA isolates was found to be significantly higher than MSSA isolates (p=0.001). These rates vary from country to country and are crucial in the selection of antibiotics for treatment. Therefore, all staphylococci isolated from sterile body areas should be subjected to antimicrobial susceptibility testing for beta-lactam antibiotics (such as penicillin, cephalosporins), and for gentamicin, TMP-SMZ, tetracyclines, erythromycin, clindamycin, rifampicin, vancomycin, linezolid, and quinolones[25,26].

The problem of clindamycin resistance in MRSA strains is growing. Stein et al.[27] reported that prevalence of clindamycin resistance increased from 0.1% to 26.8% in a study involving community-acquired STIs in Israel. Khamash et al.[5] reported that rate of clindamycin resistance increased from 21% to 38% in MRSA isolates in children over the study period. In other studies, rate of clindamycin resistance in MRSA isolates has been reported to be 6%-23.3%[10,14,28]. In our study, rate of overall clindamycin resistance was 20%, and clindamycin resistance in MRSA strains was 27.4%. Clindamycin is a good alternative for the empirical treatment of CA-MRSA and MSSA infections. Taking into account the increasing rate of clindamycin resistance, it is prudent that each region and hospital determine its own resistance rates so as to guide empiric management.

MRSA finds its ecological niche in the human nose, as well as other body areas of healthcare workers and patients and this plays a major role in the induction and spread of infection. Mupirocin is the most effective antibiotic used for the topical treatment of SA infections, and decolonization of MSSA and MRSA. Its increased use, carries a great risk in terms of resistance development. In the literature, varying rates between 0.1% and 45% regarding mupirocin resistance have been reported [29-31]. In a meta-analysis by Dadashia et al.[6], a global increase in the prevalence of mupirocin resistance was reported in both all SAs and MRSA. In our study, while mupirocin resistance was 14.4% in all SA, it was found as 28.2% in MRSA. Mupirocin resistance was higher in community-acquired infections. Monitoring the resistance rate of mupirocin is critical in preventing the development of the disease. The fact that no mupirocin resistance had been detected in Syrian refugees living in the same community in our study may be due to its low accessibility and less frequent use. In conclusion, the rate of mupirocin resistance among *S. aureus* isolates varies according to geographic region and/or patient population.

The selection of appropriate antimicrobial agents in the treatment of staphylococcal infections is closely associated with the detection of bacterial resistance

patterns. With the increase in MRSA strains, the use of other antistaphylococcal antibiotics, especially clindamycin, has increased. Treatment options besides clindamycin, are limited. In our center, the lowest resistance rates were found for TMP-SMZ, rifampicin, and fusidic acid. Considering the intravenous antibiotics used in the treatment; The combination of ampicillin-sulbactam and clindamycin was used in 30% of infections, 6.6% of clindamycin, 20% of vancomycin and 1.4% of linezolid. Antibiotic changes were made in 25.2% of patients according to the culture results. TMP-SMX was the most commonly used antibiotic with a frequency of 22.2%. Glycopeptide antibiotics such as vancomycin are often used to treat MRSA strains. However, because of its widespread use and after the identification of a vancomycin intermediate-resistant *S. aureus* (VISA) strain in Japan in 1997, the concern for the development of vancomycin resistance increased[32]. Nonetheless, vancomycin resistance was not detected in any patient in our study. These results bring us face to face with the fact that if rational antibiotic selection and use is prioritised regarding glycopeptides and other antistaphylococcal antibiotics, we will encounter multi-drug resistant SA strains in the coming years. Today, glycopeptide antibiotics are life-saving options for infections with methicillin-resistant strains. However, it should not be the first choice for staphylococci other than MRSA to prevent acquisition of resistance.

It is known that MRSA tends to cause more serious and invasive infections. Infections due to MRSA leads to increased mortality, morbidity, length of hospital stay and increased costs [33-36]. In our study, length of hospital stay, duration of IV antibiotics, and mortality were significantly higher in HA-MRSA infections ($p<0.001$). The most important virulence factor in community-acquired MRSA strains is the synthesis of Panton-Valentine-leukocidin (PVL). Due to PVL, CA-MRSA invasive disease has a high mortality rate despite appropriate treatment [37]. In the meta-analysis of Cosgrove et al.[36] there was no significant difference in mortality rate between MRSA and MSSA in 24 of 31 studies, and the mortality rate of MRSA infections was higher in 7 of them. In studies conducted in the literature, mortality due to SA was reported as 0%-8%[8,15,38]. In a study by Crandall et al.[38] in USA, general mortality rate due to SA infections was reported as 3.6% and due to MRSA as 5.4%. Gomes et al.[16] found the overall mortality of SA infections to be 2.1% and the mortality of MRSA to be 16.7%. Consistent with the literature, in our study, mortality in all SA infections was 2.2%, while mortality due to MRSA was 4.1%. There are report simplying a higher overall mortality in MRSA infections.

Due to the fact that it being a retrospective study, the data limited. Patients' complaints, clinical severity, and MRSA risk factors could not be reviewed. There is a need for multicenter prospective studies in our country in order to determine the reasons for the high rates of antibiotic resistance, especially of MRSA, in our region, to find a solution, and guide empirical our treatment.

In conclusion, infections due to MRSA is common all over the world and its prevalence varies between countries. Today, MRSA, especially CA-MRSA, is a serious problem in our country as well as other parts of the world. Clindamycin and mupirocin resistance also poses a major problem for our region. With the increase in SA infections, both in the community and hospital setting, we can not emphasize enough the importance of taking appropriate culture samples on time and knowing the resistance patterns of the population in determining the empirical treatment regimen and guiding management of these patients.

Yazar Katkıları: Çalışma konsepti/Tasarımı: ÜÇ, ÜÇ, UÖ; Veri toplama: ÜÇ, AB; Veri analizi ve yorumlama: ÜÇ, ÜÇ, AB; Yazı taslağı: ÜÇ, ÜÇ, AB; İçeriğin eleştirel incelenmesi: ÜÇ, ÜÇ, AB, NÜ, UÖ; Son onay ve sorumluluk: AB, ÜÇ, ÜÇ, UÖ, NÜ; Teknik ve malzeme desteği: ÜÇ, ÜÇ; Süpervizyon: ÜÇ, AB; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Adana Şehir Eğitim ve Araştırma Hastanesi Klinik Araştırmalar Etik Kurulundan 17.06.2020 tarih ve 936/59 sayılı kararı ile etik onay alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: Concept/Design : ÜÇ, ÜÇ, UÖ; Data acquisition: ÜÇ, AB; Data analysis and interpretation: ÜÇ, ÜÇ, AB; Drafting manuscript: ÜÇ, ÜÇ, AB; Critical revision of manuscript: ÜÇ, ÜÇ, AB, NÜ, UÖ; Final approval and accountability: AB, ÜÇ, ÜÇ, UÖ, NÜ; Technical or material support: ÜÇ, ÜÇ; Supervision: ÜÇ, AB; Securing funding (if available): n/a.
Ethical Approval: For this study, ethical approval was obtained from the Clinical Research Ethics Committee of Adana City Training and Research Hospital with the decision dated 17.06.2020 and numbered 936/59.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

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