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Research Article

Investigations of Antibiotic Susceptibilities of *S. aureus* Strains Isolated from Various Clinical Samples

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Summary

Objective: *Staphylococcus aureus (S. aureus)* is a critical microorganism that causes a range of infections with high morbidity and mortality rates, including skin and soft tissue infections, urinary tract infections, endocarditis, pneumonia, septic arthritis, osteomyelitis, and sepsis in both community and healthcare settings. The objective of this study was to ascertain the antimicrobial resistance rates of methicillin-resistant *S. aureus* (MRSA) and Methicillin-susceptible *S. aureus* (MSSA) isolates derived from a range of clinical samples submitted to the Medical Microbiology Laboratory of our hospital and to examine the resistance profile specific to our hospital.

Methodology: The study included 229 *S. aureus* isolates collected between 2022 and 2023. The isolates were identified through the application of conventional methods and the MALDI-TOF-MS system (VITEK MS, bioMerieux France). The antimicrobial susceptibility of the isolates was determined by the BD Phoenix automated system (Becton Dickinson, USA) in accordance with the criteria set forth by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

Results: The MRSA rate in the one-year period was 25.77%. When the distribution of *S. aureus* isolates was analyzed, it was determined that blood cultures were the most common clinical specimens from which *S. aureus* was isolated. Resistance to glycopeptides and linezolid was determined in MRSA isolates, albeit at a low rate. No resistance to glycopeptide and linezolid was detected in MSSA isolates. MSSA isolates were found to have a more sensitive profile to other antibiotics than MRSA isolates. The highest resistance rate was detected against penicillin with 100% and 87.06% in MRSA and MSSA isolates, respectively. In addition, the most sensitive antibiotics were determined to be glycopeptide, linezolid, daptomycin, and aminoglycoside.

Conclusion: In conclusion, knowing the resistance profiles of *S. aureus* isolates in our hospital, will guide empirical treatment. Furthermore, the implementation of effective infection control measures and a cautious approach to antibiotic use will contribute to the management of MRSA infections.

Introduction

Staphylococci are common infectious agents worldwide, causing community-acquired severe or healthcare-associated infections. *S. aureus* is a critical microorganism that causes a range of infections with high morbidity and mortality rates, including skin and soft tissue infections, urinary tract infections, endocarditis, pneumonia, septic arthritis, osteomyelitis, and sepsis in both community and healthcare settings. *S. aureus* is the leading cause of serious infections, including bloodstream infections and infective endocarditis. In particular, methicillin-resistant *S. aureus* (MRSA) is a global concern due to its resistance to treatment and the gradual decrease in antibiotic options [1,2].

Antimicrobial resistance, a growing problem, has also emerged in *S. aureus*. Our treatment strategies for this species, which has developed resistance to many antibiotics, especially beta-lactam antibiotics, are gradually narrowing. Even moderately susceptible (VISA) and resistant (VRSA) strains to vancomycin, a glycopeptide effective in treating MRSA, have been reported. The spread of MRSA across Europe

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is accelerating, with a particularly rapid transmission from Mediterranean countries to Scandinavia. While 35% - 50% resistance rates have been observed in Turkey, Italy, Greece, and Portugal, this rate is around 5% in Scandinavian countries [1,3,4].

Monitoring antimicrobial resistance data, both in health care settings and in large-scale, multicentre settings is critical to addressing the problem of antimicrobial resistance. Retrospective analyses reveal trends in resistance development. In this study, the antibiotic resistance profile of *S. aureus* strains isolated over one year was analyzed retrospectively.

Method

The study included 229 *S. aureus* strains isolated in the microbiology laboratory of Necmettin Erbakan University Meram Medical Faculty, Konya, between 1 May 2022 and 31 April 2023. The samples were inoculated on eosin methylene blue (EMB) and 5% sheep blood agar media, and all petri dishes were incubated at 35±2 °C under aerophilic conditions for 20-24 hours. Blood cultures of the patients were evaluated using an automated blood culture detection system (DL-Bt240, Zhuhai Biotech Co. Ltd, China, and BACTEC Fx Top, Becton Dickinson Com, USA). Gram stains were performed on samples that gave a growth signal, and they were identified using conventional and automated methods (VITEK MS MALDI-TOF bioMerieux, Marcy l'Etoile, France and BACTEC Fx Top, Becton Dickinson Com, USA). Antibiotic susceptibilities were evaluated with Minimum Inhibitory Concentration (MIC) using an automated method (BACTEC Fx Top, Becton Dickinson Com, USA) according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints bacteria v12.0 and v13.1. Methicillin-resistant isolates were designated MRSA, and methicillin-susceptible isolates were designated MSSA.

Results

This study analyzed the resistance rates of *S. aureus* strains isolated from different clinical specimens to different antibiotics over one year. The distribution of the departments to which the specimens were sent was analyzed, and it was shown that MRSA isolates were isolated at higher rates in intensive care units and inpatient wards compared with MSSA isolates and in outpatient clinics. The distribution data according to the departments to which the samples were sent are shown in Table 1.

When analysing the types of specimens from which the strains were isolated, blood specimens (45.85%) were in the first place. Data on the distribution of isolates according to sample type are given in Table 2.

According to the data obtained from the antibiotic susceptibility testing of the bacteria we isolated, 59 (25.77%) of the 229 *S. aureus* strains were MRSA. The highest resistance rates for MRSA were for the antibiotics in the erythromycin (50.85%) and tetracycline (49.15%) groups. For MSSA, the highest resistance rates were found for penicillin-G (87.06%). The antibiotic resistance rates of the isolates are shown in Table 3.

Table 1: Distribution of samples sent from outpatient clinics, wards, and intensive care units.

Section	MRSA	MSSA	Total
Intensive Care	12 (29.27%)	29 (70.73%)	41
Inpatients Service	43 (29.05%)	105 (70.95%)	148
Polyclinics	4 (10%)	36 (90%)	40
Total	59	170	229

Table 2: Distribution of sample types.

Sample Type	Blood	Wound	BAL Fluid	Drainage	Abscess	Phlegm	Urine	Catheter	Other
Rates	105 (45.85%)	34 (14.85%)	22 (9.61%)	22 (9.61%)	12 (5.24%)	12 (5.24%)	10 (4.37%)	6 (2.62%)	6 (2.62%)

Table 3: Antibiotic susceptibilities of *S. aureus* isolates.

Antibiyotik	MSSA	MRSA	Toplam
Amikacin	2 (1.18%)	5 (8.47%)	7 (3.15%)
Ciprofloxacin	6 (3.53%)	11 (18.64%)	17 (7.42%)
Daptomycin	0 (0%)	0 (0%)	0 (0%)
Clindamycin	10 (5.88%)	4 (6.78%)	14 (6.11%)
Erythromycin	23 (13.53%)	30 (50.85%)	53 (23.14%)
Fosfomycin	2 (1.18%)	7 (11.86%)	9 (3.93%)
Gentamicin	4 (2.35%)	5 (8.47%)	9 (3.93%)
Fusidic Acid	8 (4.71%)	5 (8.47%)	13 (5.68%)
Levofloxacin	5 (2.94%)	11 (18.64%)	16 (7.51%)
Moxifloxacin	6 (3.53%)	11 (18.64%)	17 (7.42%)
Linezolid	0 (0%)	1 (1.69%)	1 (0.44%)
Penicillin-G	148 (87.06%)	59 (100%)	207 (90.39%)
Rifampicin	9 (5.29%)	7 (11.86%)	16 (7.51%)
Teicoplanin	0 (0%)	1 (1.69%)	1 (0.44%)
Tetracycline	11 (6.47%)	29 (49.15%)	40 (17.46%)
Trimethoprim/Sulfamethoxazole	2 (1.18%)	10 (16.95%)	12 (5.24%)
Vancomycin	0 (0%)	1 (1.69%)	1 (0.44%)
Total %	170(%74.23)	59 (25,77%)	229(%100)

Discussion

S. aureus is an important cause of both community-acquired and healthcare-associated infections. It can cause many local and systemic diseases, ranging from skin and soft tissue infections to bacteraemia [5]. In this study, the resistance rates of *S. aureus* strains isolated in a university hospital to various antibiotics were analyzed. When the distribution was analyzed by department, MRSA strains were isolated at higher rates in intensive care and inpatient wards, emphasizing the importance of strict implementation of infection control measures in these units. MSSA strains were more common in outpatient clinics, indicating that community-acquired infections are more often caused by MSSA.

In different studies conducted in Turkey, the proportion of the most frequently isolated *S. aureus* sample types varied [6-8]. Analyzing the distribution of sample types in this study, blood (45.85%) and wound (14.85%) samples were the most

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frequently isolated. The high isolation rate from blood samples indicates that bacteremia is an essential problem in *S. aureus* infections.

Although penicillin-G was effective in treating *S. aureus* for a time, significant resistance to this antibiotic later developed. Even when methicillin, which was developed later, was effective, MRSA strains resistant to this antibiotic emerged. When we evaluated the antibiotic susceptibility data in this study, 59 (25.77%) of the 229 *S. aureus* strains isolated during the one-year period were MRSA. This finding shows that MRSA remains an important pathogen in healthcare-associated infections and community-acquired infections. On the other hand, in various previous studies in Turkey and worldwide, MRSA rates were found to range widely between 12.2-71.7% and 0.9-74%, respectively [5]. These data show that the prevalence of MRSA may be lower due to infection control measures implemented in different centers or higher due to inappropriate antibiotherapy policies. In addition, 7 separate studies conducted in different years and different centers in Turkey are shown in Table 4. Considering the rates in this study, there is a possibility of a decrease in MRSA rates compared to previous years. However, conducting retrospective analyses in the same centers in this direction will contribute to the evaluation.

Antibiotic resistance rates clearly show that MRSA isolates are much more resistant than MSSA isolates. In parallel with our findings, many studies conducted in different centers in Turkey have found higher resistance rates in MRSA isolates than in MSSA isolates [5,8,9].

The resistance rates of MRSA strains known to be resistant to β-lactam antibiotics, especially oxacillin and penicillin-G, to other antibiotics are remarkable. Particularly high resistance rates to antibiotics such as erythromycin (50.85%) and tetracycline (49.15%) have also been observed in previous studies [5,8-11] and these drugs should be used with caution in the treatment of MRSA.

Low resistance rates were detected against antibiotics such as daptomycin (0%), linezolid (1.69%), and vancomycin (1.69%), which are alternative options of increasing importance due to the multidrug resistance often observed in MRSA isolates. In recent years, isolates resistant to glycopeptides have been reported from various centres worldwide, as well as from Turkey [12-14]. Especially The efficacy of vancomycin treatment is limited by the emergence of vancomycin-resistant *S. aureus* (VRSA), vancomycin-intermediate *S. aureus* (VISA), and heterogeneous VISA (hVISA). A meta-analysis conducted in 2020 revealed a significant increase in the prevalence of VRSA, VISA, and hVISA after 2010, with rates rising by 2.0, 3.6, and 1.3 times, respectively, compared to previous years [15]. Although these drugs are still effective in treating MRSA, the wiggle resistance rate should be closely monitored to prevent further limitations of effective treatment options for MRSA. Infection control measures should be meticulous, and antibiotic use should be cautious to prevent new resistance developments. MRSA antibiotic susceptibility data from different studies conducted in Turkey are shown in Table 5.

Table 4: Some previous MRSA and MSSA studies.

MRSA	MSSA	Source
63 (%36.4)	110 (%63.6)	[10]
101 (%50.2)	100 (%49.8)	[11]
115 (%45.3)	139 (%54.7)	[16]
12 (%17.9)	55 (%82.1)	[17]
781(12.4)	5536 (%87.5)	[19]
205 (%23.3)	674 (%76.7)	[8]
172 (%28.9)	423 (%71.1)	[5]
59 (%25.77)	170 (%74.23)	Bu çalışma (2023)

Table 5: Antibiotic susceptibilities of MRSA isolates that have been reported in some previous studies.

Antibiotics	[10]	[11]	[9]	[8]	[5]	Bu Çalışma (2024)
Chloramphenicol	-	11 (%11)	-	3 (%1,8)	-	-
Clindamycin	23 (%36,5)	40 (%39,6)	352 (45%)	87 (%43,5)	60 (%34,9)	4 (6.78%)
Erythromycin	37 (%58,7)	54 (%53,4)	447 (57,4%)	89 (%45,1)	66 (%38,4)	30 (50.85%)
Levofloxacin	-	53 (%52,5)	398 (50,9%)	34 (%26,3)	-	11 (18.64%)
Trimethoprim-sulfamethoxazole	13 (%20,6)	10 (%10)	163 (20,9%)	25 (%14,6)	18 (%10,5)	10 (16.95%)
Ciprofloxacin	42 (%66,6)	-	347 (44,4%)	69 (%37,5)	49 (%28,5)	11 (18.64%)
Linezolid	-	-	6 (0,8%)	0(%0)	0 (%0)	1 (1.69%)
Vancomycin	0 (%0)	-	-	0(%0)	0 (%0)	1 (1.69%)
Penicillin	63 (%100)	-	781 (100%)	147 (%98)	172 (%100)	59 (100%)
Tetracycline	-	-	424 (54,3%)	54 (%38,2)	-	29 (49.15%)
Gentamicin	26 (%41,3)	-	391 (50%)	53 (%33)	55 (%31,9)	5 (8.47%)
Rifampin	39 (61,9)	-	440 (56,3%)	44 (%25)	-	7 (11.86%)

Antibiotic resistance rates of MSSA strains were generally lower. Low resistance rates to antibiotics such as amikacin (1.18%), oxacillin (0%), daptomycin (0%), linezolid (0.59%), and vancomycin (0%) suggest that a broader range of antibiotics can be used to treat MSSA infections.

Limitations in our study include the fact that it was a single-center study and the clinical conditions of the patients were not included in the study. Obtaining more meaningful data through studies conducted in more centers and including patients' clinical data will contribute to the scientific world in terms of controlling antibiotic resistance in *S. aureus* infections.

Conclusion

In conclusion, this study provides essential data on the antibiotic resistance rates of MSSA and MRSA strains and the distribution of isolated samples. Multi-drug resistance in MRSA limits treatment options and increases the importance of infection control measures. In particular, the presence of

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isolates resistant to alternative drugs such as glycopeptides, even at low rates, is alarming. In contrast, MSSA strains were generally found to have lower resistance rates, and it appears that a broader range of antibiotics can be used to treat these strains. These data will be used to guide infection control measures and treatment strategies. In addition, regular monitoring and updating of antimicrobial resistance rates is critical for infection control and treatment success, as well as preventing new resistance developments. Compared to studies conducted worldwide and in Turkey, the results of this study are consistent with the literature and provide up-to-date information on the antibiotic resistance rates of MRSA and MSSA strains. In light of the data we obtained, it seems that aminoglycosides, quinolones, rifampicin, and trimethoprim sulfamethoxazole group antibiotics can be used in the empirical treatment of *S. aureus* infections. However, the fact that low-level resistance has begun to be observed for glycopeptide and linezolid has once again demonstrated the need to be careful not to use these antibiotics in empirical treatment and the importance of a limited reporting policy.

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