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## Research Article

# Prevalence and Antimicrobial-Resistance of *Staphylococcus aureus* Isolated from Blood Culture in University Hospital, Turkey

### Abstract

**Introduction:** In this study, our aim was to detect the prevalence and antibiotic resistance of *Staphylococcus aureus*, isolated from blood culture in Kafkas University Hospital, Kars, Turkey retrospectively and to present the first data from this university hospital.

**Materials and Methods:** Total 1456 blood culture bottles were sent to Microbiology Laboratory of between January-2013 and December-2014. All bottles were placed into Automated Blood Culture System. After the positive bottles were detected by machine, the bacteria were identified and antibiotic susceptibility tests were performed by using both Microorganism Identification System and Kirby-Bauer Disk Diffusion method.

**Results:** Total 63 *Staphylococcus aureus* positive samples were detected. Interestingly, 32 (50.8%) of total *Staphylococcus aureus* positive samples were Methicillin-Resistant *Staphylococcus aureus* and 31 (49.2%) of them were Methicillin-Sensitive *Staphylococcus aureus*. When the antibiotic resistance profiles were checked, it was seen that 29 *Staphylococcus aureus* strains were only resistant to Erythromycin and 18 strains were only resistant to Clindamycin whereas 10 strains were resistant both to Erythromycin and Clindamycin.

**Conclusions:** The antibiotic resistance is getting increased by uncontrolled antibiotic usage and wrong choices in empiric therapy day by day. Each hospital has to detect its own antibiotic resistance profiles and apply empiric therapy according to these profiles.

## Introduction

Nosocomial bloodstream infections (BSIs) are associated with major morbidity and mortality all over the world. Additionally, the incidence of nosocomial BSIs and the prevalence of antibiotic resistance among the microorganisms that cause these infections are getting increased day by day [1,2]. *Staphylococcus* species are one of the most frequent isolated pathogens from blood cultures in clinical microbiology laboratories [3].

*Staphylococcus aureus* (*S.aureus*) is a facultative anaerobe, gram-positive, spherical bacterium which produces catalase and coagulase. This microorganism is often found on skin, skin glands and mucous membranes particularly in the nose of healthy individuals. It is associated with skin and soft-tissue infections, infective endocarditis, osteomyelitis, pneumonia, brain abscesses, and meningitis and bloodstream infection [4-6]. Furthermore, *S.aureus* is a common cause of bacteremia due to gram-positive pathogens [7]. The ratio of infections caused by penicillin-resistant *S.aureus* increased in hospitals in the mid-1940s [8]. On the other hand, Methicillin-Resistant *Staphylococcus aureus* (MRSA) were first reported in the early 1960's and are now regarded as a major hospital acquired pathogen worldwide. Additionally, the prevalence of MRSA infections is increasing in the community [9,10]. Non- $\beta$  lactam antimicrobial

agents have recently come to the fore in the treatment of infections caused by MRSA strains. So that, it is important to determine the effectiveness of these antibiotics with antimicrobial susceptibility tests. MRSA strains are a reservoir for multiple drug resistant genes. Therefore, the limitation of treatment options is a serious health problem [10,11].

Erythromycin and clindamycin belong to the macrolide, lincosamide and streptogramin (MLS) antibiotic families. Macrolides are major alternative antimicrobial agents for the treatment of infections caused by gram-positive bacteria. Clindamycin can be administered orally, good tissue penetration and is tolerable, therefore it is usually used to treat skin and bone infections. Macrolides and lincosamides resistant gram-positive bacteria are increasingly reported in clinical isolates. Both antimicrobial agents inhibit protein synthesis by binding to the 50S ribosomal subunits of bacterial cells [12-15].

Regular monitoring of antimicrobial drug resistance is important for determination of prescription and choice of drug for empirical therapy. The aim of this study was to investigate retrospectively the prevalence and antibiotic resistance of *S.aureus*, isolated from blood culture in Kafkas University Health Research and Application Hospital, Kars, Turkey and to present the first data from this university hospital.

## Material and Methods

### Study design

A total of 1456 blood culture bottles were sent to Microbiology Laboratory of Kafkas University Health Research and Application Hospital between January 2013 and December 2014. In this study, the prevalence and antibiotic resistance of *S.aureus* isolated from blood culture were investigated retrospectively.

If only one of at least three blood cultures was positive, it was evaluated as contamination. It was considered as microbial pathogen when same microorganism was detected at more than one blood cultures. Only one blood culture from when the same patient was included in the study.

### Bacteria identification and susceptibility tests

All culture bottles were placed into Automated BACTEC 9050 Blood Culture System. Media were followed for seven days. After the positive signal of machine, bloods were removed from the machine and cultured in 5% Sheep Blood Agar and Eosin-Methylene Blue (EMB) agar to obtain bacterial colonies.

At first, the bacterial colonies were identified by conventional methods such as gram staining, catalase test, coagulase test. Then a bacterial suspension (McFarland 0.5) was prepared and placed into the microorganism identification machine, Phoenix 100 BD Microorganism Identification System (Becton Dickinson, Diagnostic Instrument Systems, Sparks, USA), to confirm the data obtained by the conventional methods.

Antibiotic susceptibility tests also were first performed by using Kirby-Bauer Disk Diffusion method conventionally, then to confirm the data they were tested by using BD Phoenix Microorganism Identification System. The results were evaluated according to the standards of Clinical and Laboratory Standards Institute (CLSI). Methicillin resistance was evaluated by using cefoxitin disc when conventional method was performed. *S.aureus* ATCC 25923 strain was used as control strain.

### Statistical analysis

The statistical analysis was performed using IBM SPSS for Windows Version 19.0 (IBM, Armonk, NY, EUA).

## Results

During the 24-month period started at January 2013 till December 2014, a total of 1456 blood culture bottle were sent to Microbiology Laboratory of Kafkas University Health Research and Application Hospital.

During this period, total 63 *S.aureus* positive samples were detected. *S.aureus* strains were isolated from the blood culture which came from different clinics such as; Internal Intensive Care Unit (n:31, 49.5%), Cardiovascular Surgery Intensive Care Unit (n:7, 11.1%), Surgery Intensive Care Unit (n:6, 9.5%), Infectious Disease Clinic (n:6, 9.5%), Internal Medicine (n:4, 6.3%), Neurology, Pediatrics and Chest Diseases Clinics (n:3, 4.7%) as seen in **Table 1**. On the other hand, 34 (53.9%) of total *S.aureus* positive samples were belonged to male whereas 29 (46.1%) of them were belonged to female patients.

**Table 1:** Distribution of *S.aureus* strains in terms of isolated clinics.

Clinics	Total Blood Culture number (n)	Positive Blood Culture number (n)	%
Internal Intensive Care Unit	328	31	49.5
Cardiovascular Surgery Intensive Care Unit	220	7	11.1
Surgery Intensive Care Unit	186	6	9.5
Infectious Disease Clinic	227	6	9.5
Internal Medicine	195	4	6.3
Neurology Clinics	58	3	4.7
Pediatrics Clinics	173	3	4.7
Chest Diseases Clinics	69	3	4.7
Total	1456	63	100

Interestingly, 32 (50.8%) of total *S.aureus* positive samples were MRSA and 31 (49.2%) of them were Methicillin-Sensitive *Staphylococcus aureus* (MSSA). When the antibiotic resistance profiles were checked, it was seen that 29 *S.aureus* strains were only resistant to Erythromycin and 18 *S.aureus* strains were only resistant to Clindamycin whereas 10 *S.aureus* strains were resistant both to Erythromycin and Clindamycin. 21 of 32 (%65.6) MRSA strains were only resistant to Erythromycin, 13 of 32 (%40.6) MRSA strains were only resistant to Clindamycin and 7 of 32 (%21.9) MRSA strains were resistant both to Erythromycin and Clindamycin. Furthermore, 8 of 31 (%25.8) MSSA strains were only resistant to Erythromycin, 5 of 31 (%16.1) MSSA strains were only resistant to Clindamycin and 3 of 31 (%9.7) MSSA strains were resistant both to Erythromycin and Clindamycin (**Table 2**).

When the other antibiotics resistance profiles were examined, there was no resistant to vancomycin and linezolid in both MRSA and MSSA strains. In MRSA strains, the resistant rates to ciprofloxacin, gentamicin and trimethoprim sulfamethoxazole were 71.9%, 31.2% and 65.6% respectively. Additionally in MSSA strains, the resistance rates to the same antibiotics, were 35.5%, 6.4% and 32.2% respectively. Resistance of antimicrobial agents for MRSA and MSSA were shown in **Table 3**.

## Discussion

Bloodstream infections (BSIs) are one of the major cause of morbidity and mortality all over the world and *Staphylococcus aureus* is one of the most common causative pathogens of bloodstream infections [16,17]. MRSA is currently recognized as a major problem in hospitals and the broader community throughout the world. Both in the world and our country, 40-60% of *Staphylococcus aureus* strains are resistant to methicillin and these ratios are higher especially in intensive care units [18,19]. Penicillin was introduced in the early 1940s. Shortly after, penicillin resistant *S.aureus* was first reported in 1944. Methicillin was introduced in Europe in 1959 and in the United States in 1961. The first cases of MRSA were reported in the United Kingdom in 1961, followed soon thereafter by reports in other European countries, Japan, and Australia [19].

The European Antimicrobial Resistance Surveillance System

**Table 2:** Erythromycin and Clindamycin resistance of *S.aureus* strains (n, %).

Antibiotics	MSSA (n:31)		MRSA (n:32)	
Erythromycin	8	25,8%	21	65,6%
Clindamycin	5	16,1%	13	40,6%
Erythromycin and Clindamycin	3	9,7%	7	21,9%

**Table 3:** Antimicrobial resistance of *S.aureus* strains (n, %).

Antibiotics	MSSA (n:31)		MRSA (n:32)	
Erythromycin	12	38.7%	27	84.3%
Clindamycin	8	25.8%	20	62.5%
Linezolid	0	0.0%	0	0.0%
Vancomycin	0	0.0%	0	0.0%
Ciprofloxacin	11	35.5%	23	71.9%
Gentamicin	2	6.4%	10	31.2%
Trimethoprim sulfamethoxazole	10	32.2%	21	65.6%

(EARSS) is used in most European countries to record the incidence of bloodstream and cerebrospinal MRSA infections [20]. Referring to the literature, the ratio of MRSA in *S.aureus* blood culture isolates was less than 5% in Denmark, the Netherlands, Finland, Sweden, Iceland, Norway and Estonia. Proportion of MRSA less than 10% was found in Slovenia, Austria and Luxembourg. Additionally; Germany France, Hungary, Belgium, Czech Republic, Poland, Latvia and Switzerland reported the proportion was between 10-24%. In Republic of Ireland, Bulgaria, Greece, Croatia, Romania, Cyprus, Italy, Israel, Spain, United Kingdom and Turkey, the proportion equal to or above 25%. In Malta and Portugal, this ratio was reported as above 50% [19]. Furthermore, the ratio of MRSA was determined between 25-50% in China and African countries. Methicillin resistance is seen at high rates in East Asia countries [21].

In a different study, Antibiotic Resistance Surveillance and Control in the Mediterranean Region (ARMed) Project has documented the prevalence of antibiotic resistance in several important pathogens isolated in the eastern and southern Mediterranean countries. In this study, the proportion of MRSA was found 45%, 55%, 52%, 56%, 12%, 50%, 19%, 18% and 39% in Algeria, Cyprus, Egypt, Jordan, Lebanon, Malta, Morocco, Tunisia and Turkey respectively [22]. In another study, The SENTRY Antimicrobial Surveillance Program the proportion of MRSA was detected 32.4% in North and Latin America and 27.7% in Europe [23]. In conclusion, these different results between countries show once again the importance of local surveillance study.

MRSA has been increasing in Turkey as well as all over the world. In a study, 93 of 136 *S.aureus* strains (68%) were MSSA and 43 (32%) were MRSA. In MRSA strains the resistance rates to linezolid and vancomycin were 0%, to rifampin 23% and to other antibiotics 70-95% [24]. In another study, Aytar et al. isolated 173 (65.5%) MRSA from 264 *S.aureus* strains. All MRSA were susceptible to vancomycin and linezolid. Additionally MRSA strains were resistant to trimethoprim-

sulfamethoxazole and erythromycin, 35% and 78%, respectively [11]. Celik et al. examined 257 *S.aureus* strains isolated from nosocomial bloodstream infection and methicillin resistance was found to be 8.9%. In MRSA strains, the resistance rates to erythromycin, clindamycin and gentamicin were 56.5%, 52.2% and 39.1% while these rates were 10.3%, 4.7% and 0.9% respectively in MSSA strains [25]. When these results were compared with our data, it was seen that the results were parallel.

Macrolide antibiotics (erythromycin, azithromycin and spiramycin) are commonly used in treatment of staphylococcal infections. The macrolide antibiotic resistance is usually caused either by ribosomal modification mediated by 23S rRNA methylases or by active efflux of the antimicrobial agent by an ATP-dependent pump encoded by *msrA* gene in *S.aureus* [26]. Referring to the literature, erythromycin resistance of MSSA strains were the range of 13% and %19 while it was 71% and %84 for MRSA strains [7,24,27-29]. In our study, erythromycin resistance of MSSA and MRSA strains were detected as 38.7% and 84.3% respectively and proportion of erythromycin resistance was higher than other studies.

Clindamycin has long been an option for treating both MSSA and MRSA infections, particularly for skin and soft-tissue infections. This antibiotic is an alternative for the penicillin-allergic patients. On the other hand expression of inducible resistant to clindamycin could limit the effectiveness of this drug [26,30]. In our study, clindamycin resistance of MSSA and MRSA strains were detected as 25.8% and 62.5% respectively. In other studies, the resistance rate for MRSA was between 50% and 70% while it was between 2% and 5.9% for MSSA strains [24,25,29-31]. In our study, rates of clindamycin resistance in MRSA strains were consistent with other studies. However rate of clindamycin resistance in MSSA strains were detected higher than other studies. As a result there might be clindamycin resistant strains during empiric treatment of MSSA infection.

## Conclusion

In conclusion, nosocomial bloodstream infections (BSIs) are associated with major morbidity and mortality worldwide, and *S.aureus* is one of the most frequent isolated pathogens from blood cultures in clinical microbiology laboratories. Prevalence of community associated and healthcare associated MRSA infections are increasing both in our country and world. Additionally, MRSA with multidrug resistant could lead to treatment failure. Proportion of MRSA and antibiotic resistance of these strains are different in various countries and hospitals. These different results between countries and hospitals show once again the importance of local surveillance study. All centers should determine their resistance profiles, the appropriate antibiotic policy and current information should be followed for empiric therapy and prophylactic treatment. Furthermore specific antimicrobial therapy should be initiated according to the culture results.

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