***Research Article / Araştırma Makalesi***

# The Effect of the Covid 19 Pandemic on the Antibiotic Resistance Levels of *Staphylococcus aureus* Strains

## Covid 19 Pandemisinin *Staphylococcus aureus* Suşlarının Antibiyotik Direnç Düzeylerine Etkisi

Ayşe Hümeyra TAŞKIN KAFA [1], Fatih ÇUBUK [2], Gonca ŞİMŞEK [1], Rukiye ASLAN [3]
Resul Ekrem AKBULUT [1], Mürşit HASBEK [1]

[1]Department of Medical Microbiology, Sivas Cumhuriyet University, Faculty of Medicine, Sivas, TÜRKİYE
[2]General Directorate of Public Health, Department of Microbiology Reference Laboratories and Biological Products, Ankara, TÜRKİYE
[3]Sivas Cumhuriyet University, Vocational School of Health Services, Department of Medical Services and Techniques, Sivas, TÜRKİYE

**Abstract**

**Background:** *Staphylococcus aureus* is a significant human pathogen that can cause a diverse range of diseases, from mild skin and soft tissue infections sepsis. The aim of this study was to retrospectively compare the antibiotic resistance status of *S. aureus* strains and the change in the prevalence of methicillin-resistant *S. aureus* (MRSA) before, during and after the Coronavirus Disease 2019 (COVID-19) pandemic in our hospital.
**Materials and Methods:** The present study was designed to encompass three cross-sectional phases before COVID-19 pandemic (1 January 2018 to 31 December 2019, two years), the pandemic period (11 March 2020 to 10 March 2022, two years), and the post-pandemic phase (5 May 2023 to 31 December 2023, seven months). In the study, the incidence and antibiotic resistance status of *S. aureus* strains cultured and identified from various clinical samples were retrospectively analyzed using data from the hospital laboratory information system.
**Results:** As a result of the study, when the antibiotic resistance status of *S. aureus* strains was examined, it was determined that gentamicin resistance had a resistance rate of 4% in the pre-pandemic period and 6.9% in the pandemic period. A downward trend was observed in MRSA rates during the pandemic. A higher MRSA prevalence was observed before the pandemic compared to the following two periods ($p$=0.093). In addition, a higher MRSA prevalence was observed in the intensive care unit in the pre-pandemic period compared to other wards ($p$=0.075).
**Conclusions:** The decrease in MRSA prevalence during the pandemic period may be due to a number of factors, such as the implementation of quarantine measures, improved hand hygiene practices and meticulous attention to contact precautions. The increase in gentamicin resistance rates observed during the pandemic period may be due to excessive intensive use of antibiotics.

**Keywords:** MRSA, Antibiotic resistance, COVID-19 Pandemic, *Staphylococcus aureus*

**Öz**

**Amaç**: *Staphylococcus aureus*, hafif seyirli deri ve yumuşak doku enfeksiyonlarından sepsise kadar çok çeşitli hastalıklara neden olabilen önemli bir insan patojenidir. Bu çalışmada, hastanemizde Koronavirüs Hastalığı 2019 (COVID-19) pandemisi öncesinde, sırasında ve sonrasında *S. aureus* suşlarının antibiyotik direnç durumu ile metisilin dirençli *S. aureus* (MRSA) prevalansındaki değişimin retrospektif olarak karşılaştırılması amaçlanmıştır.
**Materyal ve Metod:** Bu çalışma, COVID-19 pandemisi öncesi (1 Ocak 2018- 31 Aralık 2019, 2 yıl), pandemi dönemi (11 Mart 2020- 10 Mart 2022, 2 yıl) ve pandemi sonrası (5 Mayıs 2023- 31 Aralık 2023, 7 ay) olmak üzere üç kesitsel evreyi kapsayacak şekilde tasarlanmıştır. Çeşitli klinik örneklerden kültürlenen ve tanımlanan *S. aureus* suşlarının insidansı ve antibiyotik direnç durumu, hastane laboratuvar bilgi sistemindeki veriler kullanılarak retrospektif olarak analiz edilmiştir.
**Bulgular:** Çalışma sonucu olarak *S. aureus* suşlarının antibiyotik direnç durumu incelendiğinde gentamisin direncinin, pandemi öncesi dönemde %4, pandemi döneminde ise %6.9 direnç oranına sahip olduğu tespit edilmiştir. Pandemi süresince MRSA oranlarında bir düşüş eğilimi görülmüştür. Pandemi öncesinde, sonraki iki döneme kıyasla daha yüksek bir MRSA prevalansı gözlenmiştir ($p$=0,093). Ek olarak pandemi öncesi dönemde yoğun bakım ünitesinde diğer servislere kıyasla daha yüksek bir MRSA prevalansı gözlenmiştir ($p$=0,075).
**Sonuç:** Pandemi döneminde MRSA prevalansındaki azalmanın, karantina önlemlerinin uygulanması, gelişmiş el hijyeni uygulamaları ve temas önlemlerine titizlik gösterilmesi gibi bir dizi faktörden kaynaklanabilir. Pandemi döneminde gentamisin direnç oranlarında gözlenen artış, aşırı yoğun antibiyotik kullanımına bağlı olabilir.

**Anahtar Kelimeler:** MRSA, Antibiyotik direnci, COVID-19 Pandemisi, *Staphylococcus aureus*

**Corresponding Author / Sorumlu Yazar**

**Dr. Ayşe Hümeyra TAŞKIN KAFA**
Department of Medical Microbiology, Sivas Cumhuriyet University, Faculty of Medicine, Sivas, TÜRKİYE

**E-mail:** ahtaskin@cumhuriyet.edu.tr

**Received / Geliş tarihi:** 22.11.2024

**Accepted / Kabul tarihi:** 16.01.2025

**DOI:** 10.35440/hutfd.1588823

*This study was previously presented orally at the 15th Antimicrobial Chemoterapy Days Congress of the Turkish Society of Microbiology (9-11 May 2024, Marmara University Pendik Training and Research Hospital, Istanbul)*

## Introduction

*Staphylococcus aureus* is an important human pathogen that can cause a wide spectrum of diseases ranging from mild skin and soft tissue infections to sepsis. The emergence of methicillin-resistant strains has led to a higher risk of morbidity and mortality as well as limited treatment options (1). Methicillin resistance is caused by the acquisition of mecA/mecC genes located in a mobile genetic element that can be integrated into chromosome (2). In methicillin-resistant *S. aureus* (MRSA) isolates, penicillin-binding proteins (PBPs) 2a and 2c, encoded by these genes, cause the bacteria to show a lower affinity for beta-lactam antibiotics (3-4).

In an institution providing healthcare services, the prevalence of Hospital acquired MRSA (HA-MRSA) is accepted as an indicator of the general infection rate. It is stated that one of the main transmission sources of MRSA in hospitals is the hands of healthcare workers (1).

Antimicrobial resistance (AMR) was among the biggest public health problems in the twenty-first century before the COVID-19 outbreak. During the pandemic, increased hand hygiene, decreased international travel and elective hospital procedures were expected to reduce the development and spread of antimicrobial resistance in the short term, but the disruption of standard healthcare services resulted in more widespread and uncontrolled antibiotic use (5). The pandemic process has further increased the burden of infection control and prevention strategies used in the management of AMR. Due to the contagious nature of the pathogen, many different measures have been taken to prevent its spread, which have not been seen before (6). These measures, which were applied only in high-risk units before the pandemic period, ensured that the pandemic was controlled at various levels, while other areas where patient care was provided and control programmes for other hospital-acquired infections were damaged (7). This situation led to a change in priority and disruption of infection control measures during the pandemic, and it was determined that inappropriate use of antimicrobial agents before and during the pandemic contributed negatively to the formation and spread of resistance (8-10).

Continuous monitoring of microorganisms and regular updating antibiotic resistance patterns are required to maintain infection control practices in hospitals. During the Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV) epidemic, it was reported that MRSA rates increased in healthcare settings (11). Considering this information, this study was designed as a single-centre and retrospective study to obtain information about the antibiotic resistance status of *S. aureus* and MRSA strains isolated before and after the COVID-19 pandemic in our hospital and to make comparisons.

## Materials and Methods

### *Period of the research*

The World Health Organization (WHO) declared that the global health emergency announced on 30 January 2020 for the COVID-19 pandemic caused by SARS-CoV-2 ended on 5 May 2023. On the other hand, WHO emphasises that COVID-19 is still a global health threat (12). With the detection of the first COVID-19 case in Turkey on 10 March 2020, the pandemic has shown its effect very rapidly in our country (13). In this study, the results of various clinical specimens in which *S. aureus* strains were found to grow after culture and identification tests in three cross-sectional periods: before the COVID-19 pandemic (1 January 2018-31 December 2019, two years), during the pandemic period (11 March 2020-10 March 2022, two years) and after the declaration of the end of the global health emergency; after the pandemic (5 May 2023-31 December 2023, 7 months) were compiled retrospectively from the hospital laboratory information system as a single center.

### *Inclusion criteria*

In this study, among various clinical samples sent to of Sivas Cumhuriyet University Medical Faculty Application and Research Hospital Microbiology Laboratory, if more than one bacterial agent grew from the same type of sample belonging to a patient, only the antimicrobial susceptibility result of the first bacterial strain was evaluated.

### *Laboratory*

Various clinical samples sent to of Sivas Cumhuriyet University Medical Faculty Application and Research Hospital Microbiology Laboratory for culture procedures were routinely cultured on 5% sheep blood agar and Eosine Methylene Blue (EMB) agar media and incubated in an oven at 35-37°C for 24-48 hours. Sterile body fluids were inoculated into BD BACTEC Peds Plus/F (Becton Dickinson, USA) culture bottles by the manufacturer's recommendations and incubated in BD BACTEC 9120 (Becton Dickinson, USA) blood culture device. Blood agar was passage from the bottles with a positive signal and incubated in an oven at 35-37°C for 24-48 hours. After incubation, the isolated agents were identified by MALDI Biotyper Microflex LT (Bruker Daltonics, Germany) automated system based on matrix-mediated laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS) and antimicrobial susceptibility profiles were analyzed by BD Phoenix 100 (Becton Dickinson, USA). Antimicrobial susceptibilities of the strains were evaluated in accordance with the criteria of the European Committee on Antimicrobial Susceptibility Testing (EUCAST, v.13.1). The presence of methicillin resistance in *S. aureus* isolates was accepted as Minimum Inhibition Concentration (MIC) value '>4 mg/L' for cefoxitin.

For erythromycin-resistant and clindamycin-susceptible *S. aureus* isolates, the presence of inducible clindamycin resistance was investigated in accordance with EUCAST recommendations (the D phenomenon). In the presence of inducible clindamycin resistance, the isolate was considered resistant except for short-term treatment of less serious skin and soft tissue infections (14).

### *Statistical Analysis*

Statistical Package for the Social Sciences (SPSS) v.23.0, (IBM Co., USA) package program was used to evaluate the data obtained from this study. Numerical variables were given as frequency (n) and percentage (%). Antimicrobial susceptibility test results were categorised as 'susceptible' and 'resistant'. Chi-square ($x^2$) and Fisher's exact $x^2$ tests were used to evaluate the antimicrobial resistance data. $p<0.05$ was considered statistically significant.

## Results

In the pre-pandemic period, *S. aureus* was grown in 1027 of the clinical samples sent to the hospital Microbiology Laboratory and MRSA was detected in 104 (10.1%) of these samples. During the pandemic period, 582 *S. aureus* were grown and MRSA was detected in 41 of them (7%), while in the post-pandemic period, 135 *S. aureus* were grown and MRSA was detected in 10 of them (7.4%). No statistically significant difference was found between the periods. ($p>0.05$). The rate of MRSA was 10.9% in the intensive care unit (ICU) and 8.1% in other wards ($p>0.05$) (Table 1).

**Table 1.** Frequency of MRSA in clinical samples before, during and after the COVID-19 pandemic

| | Total | | MRSA | | *p* |
|---|---|---|---|---|---|
| | n | % | n | % | |
| **Period** | | | | | |
| Pre-Pandemic * | 1027 | 58.9 | 104 | 10.1 | |
| Pandemic ** | 582 | 33.4 | 41 | 7.0 | 0.093 |
| Post-Pandemic *** | 135 | 7.7 | 10 | 7.4 | |
| **Hospital unit** | | | | | |
| Intensive Care Unit | 479 | 27.5 | 52 | 10.9 | 0.075 |
| Service | 1265 | 72.5 | 103 | 8.1 | |
| **Sample** | | | | | |
| Blood | 354 | 20.3 | 36 | 10.2 | |
| Respiratory samples | 491 | 28.2 | 43 | 8.8 | |
| Wound site | 306 | 17.5 | 27 | 8.8 | |
| Tissue biopsy | 117 | 6.7 | 9 | 7.7 | |
| Nasal swab | 70 | 4.0 | 8 | 11.4 | |
| BOS | 6 | 0.3 | 1 | 16.7 | 0.898 |
| Joint fluid | 37 | 2.1 | 1 | 2.7 | |
| Pleural fluid | 10 | 0.6 | 1 | 10.0 | |
| Abscess | 62 | 3.6 | 4 | 6.5 | |
| Urine | 125 | 7.2 | 13 | 10.4 | |
| Other *(aspiration materials, catheter, peritoneal fluid, ear and other swab)* | 166 | 9.5 | 12 | 7.2 | |
| **Total** | **1744** | **100.0** | **155** | **8.9** | |

**1 January 2018- 31 December 2019, **11 March 2020- 10 March 2022, ***5 May 2023- 31 December 2023.*

When the antibiotic resistance rates of the isolated *S. aureus* strains were analyzed, it was found that the resistance rate of gentamicin resistance higher during the pandemic period. It was found that the resistance rate was 4% in the pre-pandemic period and 6.9% in the pandemic period. The difference between these periods was statistically significant ($p$=0.006). No significant difference was detected in terms of resistance to levofloxacin, erythromycin, clindamycin, tetracycline and TMP-SMX antibiotics used before and after the pandemic ($p>0.05$). No resistance to vancomycin, teicoplanin and linezolid antibiotics was detected in the samples (Table 2).

The resistance rates of gentamicin antibiotic, whose resistance rates increased during the pandemic period, were statistically analyzed by comparing the resistance rates in the wards and ICUs, but no significant difference was found ($p>0.05$) (Table 2).

Compared to the wards, resistance rates for gentamicin, erythromycin, clindamycin and tetracycline antibiotics were statistically significantly higher in ICUs (Figure 1).

When MRSA and MSSA isolates were evaluated in terms of resistance to the antibiotics used, a much higher rate of resistance was found in MRSA isolates (Figure 2).

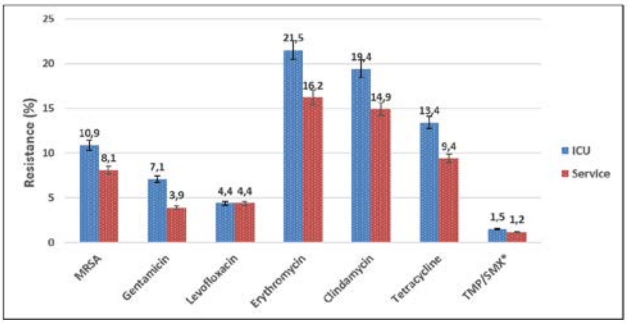


**Figure 1.** Comparison of resistance rates detected in *S. aureus* isolates from intensive care units (ICU) and other services [%] *Trimethoprim/sulfamethoxazole

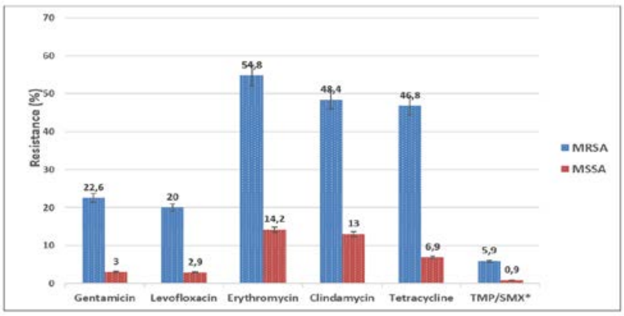


**Figure 2.** Distribution of resistance rates detected in *S. aureus* isolates according to methicillin susceptibility (%). *Trimethoprim/sulfamethoxazole

**Table 2.** Resistance rates of *S. aureus* isolates from intensive care units and other wards before, during and after the COVID-19 pandemic [n (%)]

| | n | A | B | C | Total | *p* |
|---|---|---|---|---|---|---|
| **Gentamicin** | **1744** | **41 (4.0)** | **40 (6.9)** | **2 (1.5)** | **83 (4.8)** | **0.006** |
| ICU | 479 | 15 (6.7) | 18 (8.7) | 1 (2.2) | 34 (7.1) | 0.286 |
| Service | 1265 | 26 (3.3) | 22 (5.9) | 1 (1.1) | 49 (3.9) | **0.036** |
| **Levofloxacin** | **1744** | **46 (4.5)** | **23 (4.0)** | **8 (5.9)** | **77 (4.4)** | 0.596 |
| ICU | 479 | 9 (4.0) | 9 (4.3) | 3 (6.5) | 21 (4.4) | 0.747 |
| Service | 1265 | 37 (4.6) | 14 (3.7) | 5 (5.6) | 56 (4.4) | 0.678 |
| **Erythromycin** | **1712** | **174 (17.0)** | **97 (17.6)** | **31 (23.0)** | **302 (17.6)** | 0.228 |
| ICU | 469 | 51 (22.8) | 39 (19.6) | 11 (23.9) | 101 (21.5) | 0.671 |
| Service | 1243 | 123 (15.3) | 58 (16.5) | 20 (22.5) | 201 (16.2) | 0.218 |
| **Clindamycin** | **1712** | **161 (15.7)** | **90 (15.8)** | **29 (21.5)** | **280 (16.2)** | 0.217 |
| ICU | 469 | 49 (21.8) | 33 (16.3) | 10 (21.7) | 92 (19.4) | 0.324 |
| Service | 1243 | 112 (14.0) | 57 (15.5) | 19 (21.3) | 188 (14.9) | 0.167 |
| **Vancomycin** | **1744** | **0 (0.0)** | **0 (0.0)** | **0 (0.0)** | **0 (0.0)** | - |
| ICU | 479 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | - |
| Service | 1265 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | - |
| **Teicoplanin** | **1744** | **0 (0.0)** | **0 (0.0)** | **0 (0.0)** | **0 (0.0)** | - |
| ICU | 479 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | - |
| Service | 1265 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | - |
| **Linezolid** | **1744** | **0 (0.0)** | **0 (0.0)** | **0 (0.0)** | **0 (0.0)** | - |
| ICU | 479 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | - |
| Service | 1265 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | - |
| **Tetracycline** | **1740** | **108 (10.6)** | **63 (10.8)** | **11 (8.1)** | **182 (10.5)** | 0.649 |
| ICU | 478 | 36 (16.1) | 23 (11.1) | 5 (10.9) | 64 (13.4) | 0.270 |
| Service | 1262 | 72 (9.0) | 40 (10.7) | 6 (6.7) | 118 (9.4) | 0.445 |
| **TMP/SMX*** | **1707** | **10 (1.0)** | **9 (1.5)** | **3 (2.2)** | **22 (1.3)** | 0.400 |
| ICU | 473 | 3 (1.4) | 3 (1.4) | 1 (2.2) | 7 (1.5) | 0.918 |
| Service | 1234 | 7 (0.9) | 6 (1.6) | 2 (2.2) | 15 (1.2) | 0.393 |

*A: Before the pandemic, B: During the pandemic, C: After the pandemic, *Trimethoprim/sulfamethoxazole, ICU: Intensive Care Unit*

## Discussion

Since *S. aureus* strains cause both nosocomial and community-acquired infections, antibiotic resistance data of the bacteria are of critical importance for public health. In particular, the presence and prevalence of MRSA strains with methicillin resistance necessitates the implementation of a special antimicrobial resistance management program against the bacteria (3).

It is a known fact that the COVID-19 pandemic has caused an increase in antimicrobial resistance. This is supported by several published reports (15-16). The cause is multifaceted. During the COVID-19 pandemic, prolonged hospital stays in inpatients, intensive use of antibiotics and steroids, and interventional procedures such as mechanical ventilation and catheter use have led to an increase in AMR rates (17).

The COVID-19 pandemic resulted in high rates of morbidity and mortality during the first periods when it was first observed. The presence of co-infection has been reported in a large proportion of patients in this process (16-20). Tabah and Laupland reported in their study that *S. aureus* was the most common pathogen causing super-infection and co-infection during COVID-19 and that MRSA infections increased intensely in this process (21). However, unlike the result of this study, a decreasing trend in MRSA rates during the pandemic period was found in our study. Similarly, some studies in the literature reported a decrease in *S. aureus* and MRSA rates during the pandemic period (20-22-23). This is thought to be related to the intensive control measures taken to prevent infection transmission. Quarantine practices, widespread hand hygiene awareness in the community and social distancing rules played an active role in this decrease (24).

In our study, no significant difference was found in the MRSA strain rates between periods. Similar to our study, Kahraman et al. reported that no significant difference was observed between the pre-pandemic period and the pandemic period in terms of MRSA strain rates. In our study, the increase in gentamicin resistance rates of *S. aureus* strains during the pandemic period is remarkable. In contrast to this result, Kahraman et al. found a significant decrease in gentamicin resistance rates during the pandemic period, but in parallel with our study, they reported that resistance rates did not differ between wards and ICUs (25). Aytaç et al. reported increased methicillin resistance during the pandemic period compared to the pre-pandemic period (26). In their study, Yılmaz et al. found an increased gentamicin resistance during the pandemic period compared to the pre-pandemic period, as in our study, and similarly, they did not report resistance to vancomycin, teicoplanin and linezolid antibiotics (27).

In our study, resistance rates of MRSA strains to most antibiotics did not change significantly during the pandemic. An exception was the significant decrease in cefoxitin resistance observed during the pandemic period. Different rates of drug resistance of MRSA strains have been reported during the COVID-19 pandemic, possibly due to the diverse sample sources, populations and time periods studied (28-29).

In our study, resistance rates in MRSA isolates were higher than in MSSA isolates for all antibiotics except vancomycin, teicoplanin and linezolid, as expected. Bahçeci et al. reported higher resistance rates for MRSA compared to MSSA for all antibiotics except vancomycin, teicoplanin, linezolid, daptomycin and tigecycline (30).

In our study, it was determined that the MRSA rates in the pre-pandemic (10.1%), pandemic (7%) and post-pandemic (7.4%) periods were similar, and there was no significant difference between the periods in terms of MRSA isolation. These results are not completely consistent with previous studies. These differences in MRSA rates between centres can be attributed to many factors such as the density and functioning of hospitals during the pandemic period, ICU rates, antibiotic use profiles, and study populations.

Furthermore, the highest MRSA distribution was found in the intensive care unit (10.9%) in this study. This result indicates that equipment-associated infections represent the highest risk for MRSA transmission (31).

Implementation of infection control measures, review of antimicrobial resistance control programs, and appropriate and rational use of broad-spectrum antibiotics are of critical importance to prevent the increasing resistance rates of bacterial infection agents such as MRSA, which are difficult to treat and have high mortality.

More comprehensive and multicenter studies are needed to see the long-term impact of the COVID-19 pandemic on the prevalence of multi-resistant bacteria, including MRSA, and the change in AMR rates. We hope that our study will contribute to the rational use of antibiotics in patients with MRSA isolation.

## Limitation

In this study, not knowing whether the patients had COVID-19 or not was considered as a limitation of the study. Secondly, since it was a retrospective study, sufficient information could not be obtained about the patients (such as treatments applied, having chronic diseases). In addition, the fact that it is a single-centre study affects generalisation.

***Ethical Approval:*** *This study was conducted with the approval of Sivas Cumhuriyet University Non-Interventional Clinical Research Ethics Committee (dated 2024-01/05 and numbered 18.01.2024).*

***Author Contributions:***
*Concept: A.H.T.K., F.Ç.*
*Literature Review: A.H.T.K., F.Ç., G.Ş., R.A.*
*Design : A.H.T.K., F.Ç.*
*Data acquisition: F.Ç., R.E.A., M.H.*
*Analysis and interpretation: A.H.T.K., F.Ç.*
*Writing manuscript: A.H.T.K., G.Ş., R.A.*
*Critical revision of manuscript: A.H.T.K., F.Ç., M.H.*
***Conflict of Interest:*** *The authors have no conflicts of interest to declare.*
***Financial Disclosure:*** *Authors declared no financial support.*

## References

1. Roohı S, Ahmed T, Altaf I, Fomda B. Isolation of Methicillin-Resistant *Staphylococcus aureus* from Wound Samples during the COVID-19 Pandemic: A Retrospective Study. Journal of Clinical & Diagnostic Research. 2023;17(3): p1.
2. Idrees MM, Saeed K, Shahid MA, Akhtar M, Qammar K, Hassan J, et al. Prevalence of mecA-and mecC-Associated Methicillin-Resistant *Staphylococcus aureus* in Clinical Specimens, Punjab, Pakistan. Biomedicines. 2023;11(3): 878.
3. Hou Z, Xu B, Liu L, Yan R, Zhang J, Yin J, et al. Prevalence, drug resistance, molecular typing and comparative genomics analysis of MRSA strains from a tertiary A hospital in Shanxi Province, China. Frontiers in Microbiology. 2023; 14:1273397.
4. Tang KWK, Millar BC, Moore JE. Antimicrobial resistance (AMR). British Journal of Biomedical Science. 2023; 80, 11387.
5. Knight GM, Glover RE, McQuaid CF, Olaru ID, Gallandat K, Leclerc QJ, et al. Antimicrobial resistance and COVID-19: Intersections and implications. Elife. 2021;10, e64139.
6. Wang X, Ferro EG, Zhou G, Hashimoto D, Bhatt DL. Association between universal masking in a health care system and SARS-CoV-2 positivity among health care workers. Jama. 2020; 324(7): 703-4.
7. McMullen KM, Smith BA, Rebmann T. Impact of SARS-CoV-2 on hospital acquired infection rates in the United States: predictions and early results. Am. J. Infect. Control. 2020; 48(11):1409-11.
8. Abubakar U. Antibiotic use among hospitalized patients in northern Nigeria: a multicenter point-prevalence survey. BMC Infect. Dis. 2020; 20(1):1-9.
9. Langford BJ, So M, Raybardhan S, Leung V, Soucy JPR, Westwood D, et al. Antibiotic prescribing in patients with COVID-19: rapid review and meta-analysis. Clin Microbiol Infect. 2021; 27(4): 520-31.
10. Abubakar U, Al-Anazi M, Rodríguez-Baño J. Impact of COVID-19 pandemic on multidrug resistant gram positive and gram negative pathogens: A systematic review. J. Infect. Public Health. 2022; 16(3); 320-31
11. Yap FH, Gomersall CD, Fung KS, Ho PL, Ho OM, Lam PK, et al. Increase in methicillin-resistant *Staphylococcus aureus* acquisition rate and change in pathogen pattern associated with an outbreak of severe acute respiratory syndrome. Clin. Infect. Dis. 2004; 39(4); 511-6.
12. Wise J. COVID-19: WHO declares end of global health emergency. BMJ. 2023; 381:1041.
13. Cakir B. COVID-19 in Turkey: Lessons learned. J Epidemiol Glob Health. 2020:10(2):115-7.
14. EUCAST, The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters; Version 13.1. 2023.
15. Adebisi YA, Alaran AJ, Okereke M, Oke GI, Amos OA, Olaoye OC, et al. COVID-19 and antimicrobial resistance: a review. Infectious Diseases. 2021; 14:11786337211033870.
16. Lai CC, Chen SY, Ko WC, Hsueh PR. Increased antimicrobial resistance during the COVID-19 pandemic. Int J Antimicrob Agents. 2021;57(4):106324.
17. Tiri B, Sensi E, Marsiliani V, Cantarini M, Priante G, Vernelli C, et al. Antimicrobial stewardship program, COVID-19, and infection control: Spread of carbapenem-resistant Klebsiella pneumoniae colonization in ICU COVID-19 patients. What did not work? J. Clin. Med. 2020;9:2744.
18. Altınbaş R, Yağmuroğlu A, Çetin E, Çaprak S, Türkay S, Karkaç E, ve ark. COVID-19 Tanılı Hastalarda Koenfeksiyonlar ve Antimikrobiyal Direnç. Eskisehir Med J. 2023;4(2): 95-101.
19. Salar-Gül S, Çiftçi N, Türk-Dağı H, Arslan U. Investigation of respiratory pathogens responsible for coinfection in COVID-19

patients. Klimik Derg. 2024;37(2):91-6.
20. Avan Mutlu T, Bozok T. COVID-19 hastalarının alt solunum yolu örneklerinden izole edilen bakteriyel etkenlerin identifikasyonu ve antibakteriyel direnç paternlerinin incelenmesi. Turk Mikrobiyol Cemiy Derg. 2022;52(1):48-55.
21. Tabah A, Laupland KB. Update on Staphylococcus aureus bacteremia. Curr Opin Crit Care. 2022;28(5):495-504.
22. Hirabayashi A, Kajihara T, Yahara K, Shibayama K, Sugai M. Impact of the COVID-19 pandemic on the surveillance of antimicrobial resistance. J Hosp Infect. 2021;117:147-56.
23. Wee LEI, Conceicao EP, Tan JY, Magesparan KD, Amin IBM, Ismail BBS et al. Unintended consequences of infection prevention and control measures during COVID-19 pandemic. Am J Infect Control. 2021;49(4):469- 77.
24. Güner R, Hasanoğlu I, Aktaş F. COVID-19: Prevention and control measures in community. Turk J Med Sci. 2020;50(SI-1):571-7. doi: 10.3906/sag-2004-146.
25. Kahraman G, Duran PK, Kayabaşı E, Öksüz Ş, Çalışkan E. Staphylococcus aureus suşlarının antibiyotik direnç oranlarını COVID-19 pandemisi etkiledi mi? Turk Mikrobiyol Cemiy Derg. 2024;54(2):118-25.
26. Aytaç Ö, Şenol FF, Şenol A, Öner P, Aşçı-Toraman Z. COVID-19 pandemisi öncesi ve sırasında yoğun bakım ünitesi hastalarından alınan kan kültürü izolatlarının tür dağılımı ve antibiyotik duyarlılık profillerinin karşılaştırılması. Turk Mikrobiyol Cemiy Derg. 2022;52(1):39-47.
27. Yılmaz N, Altınkanat-Gelmez G, Söyletir G. Türkiye'de COVID-19 pandemi döneminde antimikrobiyal direnç değişimi. Mikrobiyoloji Bülteni. 2023;57(4):507-34.
28. Ai L, Fang L, Zhou C, Liu B, Yang Q, Gong F. The impact of the COVID-19 pandemic on Staphylococcus aureus infections in pediatric patients admitted with community acquired pneumonia. Sci Rep. 2024;14(1):15737.
29. Okobi OE, Evbayekha EO, Shittu HO, Arinze IE, Nnaji CG, Umeh NJ, et al. Antibiogram at a Rural Hospital Against the Background of COVID-19: A Five-Year Retrospective Review. Cureus. 2022;14(7):e27221.
30. Bahçeci İ, Aksoy D, Karaca E, Yıldız S, Alpdoğan YE, Duran ÖF, ve ark. Kan kültürlerinden izole edilen Staphylococcus aureus suşlarında antimikrobiyal direnç: üç yıllık çalışma S. aureus bakteriyemisi ve antimikrobiyal direnç. Rize Medical Journal. 2023;4(1):6-19.
31. Lan T, Zhang B, Liu JL, Jia Q, Gao J, Cao L, et al. Prevalence and Antibiotic Resistance Patterns of Methicillin-Resistant Staphylococcus aureus (MRSA) in a Hospital Setting: A Retrospective Study from 2018 to 2022. Indian J Microbiol. 2024;64(3):1035-43.