Methicillin Resistance and *Staphylococcus aureus* in Nasal Cultures Before and During the Covid-19 Pandemic: A Comparison of the Results

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ABSTRACT

Background: The COVID-19 pandemic remains a serious problem adversely affecting public health. The present study has been conducted in an attempt to evaluate the nasal carriage of *Staphylococcus aureus* before and during the pandemic.

Methods: In this study, the results of nasal cultures taken from patients who applied to our hospital for screening before and during the pandemic were retrospectively analyzed.

Results: In total, 2707 patients participated in the study. Out of these patients, 1602 were admitted to our hospital in 2019 and 1105 in 2020. According to the results of the study, the detection rates of *Staphylococcus aureus* were found to be 5.1% and 0.8% in 2019 and 2020, respectively. Such a decrease occurring during the time of the Covid-19 pandemic period was found to be statistically significant ($\chi^2 = 36.61$; $P = .000$). On the other hand, an increase was detected in the rate of methicillin-resistant *Staphylococcus aureus* during the pandemic. It was determined to be 17.3% in 2019 whereas it was 55.6% in 2020. This was found to be statistically significant ($\chi^2 = 7.12$; $P = .008$).

Conclusions: According to this study, there was a sharp decrease in *Staphylococcus aureus* carriage during the pandemic period compared to pre-pandemic, while methicillin-resistant *Staphylococcus aureus* rates increased more than 3 folds. This increase in methicillin-resistant *Staphylococcus aureus* rates may be due to the increasing trend of methicillin-resistant *Staphylococcus aureus* in recent years or may indicate that it depends on the measures associated with the pandemic. Further research in this area is essential.

Keywords: Covid-19, nasal culture, methicillin resistance, pandemic, Staphylococcus aureus

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INTRODUCTION

The SARS-CoV-2 virus that broke out during the last months of 2019 has turned into a global pandemic commonly referred to as the Covid-19 pandemic. It remains a serious problem for public health because of the rate of morbidity and mortality it causes. Analogous to other viral respiratory infections, bacterial co-infections during Covid-19 infections have a key role in the increment of morbidity and mortality rates. One of the most prominent microorganisms as a bacterial co-infection factor in Covid-19 cases is *Staphylococcus aureus*.[1]

Staphylococci are nonmotile, sporeless, catalase-positive, gram-positive cocci, which are common in nature. *Staphylococcus aureus* often leads to disease in humans and brings a wide range of infections, which are capable of colonizing in various regions including notably the nose, throat, skin, vagina, rectum, and perineum.[2,3] As a result of their developed resistance, methicillin-resistant *S. aureus* (MRSA) strains still remain a serious health problem that can cause nosocomial epidemics across the globe. In recent times, an increase has been observed in the MRSA rate in community-acquired infections, particularly in skin and soft tissue infections.[4,5] Nasal carriage is one of the most known risk factors for *S. aureus* infections.[6] Therefore, screening for nasal carriage in people with direct contact with food sector workers and the community has become a legal obligation due to the risks those individuals pose for both themselves and their environment.[7]

Because of its direct effects on individuals as well as social life and healthcare systems, the Covid-19 pandemic indirectly affects medical processes in many known and even unknown ways. Therefore, the present study has been conducted in an attempt to evaluate nasal carriage before and during the pandemic. Understanding the effects of the pandemic on the nasal *S. aureus* carriage will contribute to the management of *S. aureus* infections during and after this period.

METHODS

In this study, results of the nasal cultures of 2707 outpatients who were screened at the Serik State Hospital from May 1 to September 31, 2019, and from May 1 to September 31, 2020, were examined retrospectively. Ethics committee approval of the study was received from Akdeniz University Faculty of Medicine clinical research committee (December 9, 2020/936). The data usage permission has been obtained for informed consent.

Nasal swab samples of the patients were collected by inserting sterile cotton swabs moistened with sterile saline into each of the 2 nostrils at approximately 2.5 cm depth and then by sinking and turning the swabs in the nasal mucosa a few times. The samples were delivered to microbiology laboratories within 15 minutes of collection where they were cultivated in a blood agar growth medium of 5% and incubated at 37°C. After an initial test in which an 18-24-hour incubation was performed for plates, no reproduction was observed, and thus the incubation time for the plates was extended up to 48 hours. Possible Staphylococcus colonies reproduced in the blood agar after incubation were examined using conventional microbiological methods. A catalase test with 3% H_2O_2 was performed for colonies determined to be gram-positive in the process of gram staining and then a latex agglutination test (Staphylase test, Oxoid, UK) and an in-tube plasma coagulase test were performed for colonies detected catalase-positive. The methicillin-susceptibility of the isolates that were found to be positive in the coagulase test and defined as *S. aureus* was determined using the disk diffusion method in line with The European Committee on Antimicrobial Susceptibility Testing recommendations. Suspensions were prepared from reproduced colonies in sterile saline according to the 0.5 McFarland turbidity standard and cultivated in the Müeller Hinton Agar growth medium. After they were incubated at 37°C for 24 hours with an addition of a 30 µg cefoxitin (Becton, Dickinson and Company, New Jersey, USA) disk, the colonies having a zone diameter of cefoxitin ≥22 mm were evaluated as methicillin-susceptible while those with a zone diameter of cefoxitin <22 were found as methicillin-resistant. ATCC 29213 was preferred as a reference strain.

Data Evaluation and Analysis

The statistical evaluation of the data obtained in the study was conducted using the Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM SPSS Corp.; Armonk, NY, USA) pocket program. For quantitative variables of the study defined through measuring, the mean and standard deviations were represented in number and percentage as defining statistics while such defining statistics were given for its qualitative variables defined through counting. A chi-square test was performed to examine the correlation between 2 qualitative variables. The overall significance level of the study was accepted at .05.

RESULTS

In total, 2707 patients (1602 screened in 2019 and 1105 screened in 2020) participated in the present study. The age and sex distribution of the patients partaking in the study in each month are given in Table 1.

Table 1. Distribution by Age, Gender, and Months

Variable	2019 (Pre-pandemic Period)		2020 (Pandemic Period)		General	
Age	Mean ± SD 26.88 ± 9.47		Mean ± SD 29.43 ± 11.17		Mean ± SD 27.92 ± 10.27	
Months	**n**	**%**	**n**	**%**	**n**	**%**
May	442	27.6	7	0.6	449	16.6
Jun	450	28.1	44	4.0	494	18.2
July	340	21.2	262	23.7	602	22.2
August	166	10.4	689	62.4	855	31.6
September	204	12.7	103	9.3	307	11.3
Gender						
Female	440	27.5	349	31.6	789	29.1
Male	1162	72.5	756	68.4	1918	70.9

SD, standard deviation.

The detection rate of *S. aureus* and MRSA before and during the pandemic is compared in Table 2. When examining this table, the decrease occurring in the detection rate of *S. aureus* during the pandemic was found to be statistically significant ($\chi^2 = 36.61$; $P = .000$).

However, an increase was detected in the rate of MRSA during the pandemic. It was determined to be 17.3% in 2019 whereas it was 55.6% in 2020. This increase was also found to be statistically significant ($\chi^2 = 7.12$; $P = .008$).

DISCUSSION

A great number of factors affecting Covid-19 infection prognoses have been discovered since isolation of the novel coronavirus. Secondary bacterial infections are prominent among these.[8] Therefore, examining co-infection factors in the patients diagnosed with Covid-19 has now been a subject of research in numerous studies. In the studies conducted, *S. aureus* has been suggested as an important co-infection factor.

According to a meta-analysis comprised of 18 studies, bacterial, fungal, or viral agents (36.8%) were found in 3038 out of 8249 patients with Covid-19. This report points out that *S. aureus* was the origin of 39.2% of all co-infections. According to 5 of 18 studies conducted in the report, it was determined that MRSA was responsible for 25% of bacterial co-infections.[9] In a study conducted by De Santis et al on 248 patients severely affected with Covid-19 chosen from 8 intensive care units across Italy, *S. aureus* was isolated from bronchoalveolar lavage samples of 34 patients and blood culture samples of 8 patients.[10] In a study conducted by Mahmoudi, blood and endotracheal aspirate cultures taken from 340 patients who tested positive for Covid-19 were evaluated, and secondary bacterial infection was found in 43 patients (12.46%). It was determined that 9 (20.93%) of these patients were affected by methicillin-susceptible *S. aureus* (MSSA) and 6 (13.95%) by MRSA.[1] In a study carried out for 7 different adult intensive care units across the UK, the most common microorganism detected in patients hospitalized with a diagnosis of Covid-19 within the first 48 hours following their admission to the hospitals was determined to be *S. aureus*.[11] In their study, Houlihan et al compared bacterial bloodstream infections during the pandemic with those before the pandemic

Table 2. The Relationship Between Pre-pandemic and Pandemic Period *Staphylococus aureus* Positivity and Methicillin Resistance

Variable	2019 (Pre-pandemic Period)		2020 (Pandemic Period)		Test Statistic	
	n	%	n	%	χ^2	*P*
S. aureus						
–	1521	94.9	1096	99.2		
+	81	5.1	9	0.8	36.61	.000
Methicillin Resistance						
–	67	82.7	4	44.4		
+	14	17.3	5	55.6	7.12	.008

and discovered that despite a decrease in bloodstream infections during the pandemic, there was a statistically significant increase in community-acquired bloodstream infections resulting from *S. aureus*.[12]

The subject of nasal carriage of *S. aureus* is one of the most known risk factors of *S. aureus* infections[6] as the nostrils are an appropriate place for settlement of *S. aureus* due to their elevated levels of ventilation and moisture. Individuals carrying bacteria in their nostrils may both directly infect others and contaminate the environment as well. Thus, determining nasal carriers is of great importance. It is even a legal obligation for some sector workers.[7,13] It has been reported with various studies that in addition to MSSA, the existence of MRSA in nostrils leads to a greater susceptibility to infection development and contagiousness.[14,15]

Age, gender, alcohol use, underlying diseases, antibiotic use, and relationship with the hospital have an effect on nasal carriage of *S. aureus*.[14-18] Thus, the prevalence varies depending on the population where it is examined. In research carried out by Hidron et al in Georgia, MSSA carriage of 16.4% and MRSA carriage of 7.3% were detected in patient nasal cultures of.[19] Erdenizmenli et al found no MRSA carriage but detected nasal carriage of *S. aureus* of 9.4% in their study of 500 individuals, including adult and child patients of Dokuz Eylül University.[20] In the research conducted by Kantarcıoğlu et al. on a group comprising 140 companions and visitors at Cerrahpaşa Faculty of Medicine, nasal carriage of *S. aureus* was determined in 21.4 % and MRSA carriage in 2.1%.[21] In another study conducted by Shopsin et al on 500 healthy children and their parents visiting a New York City hospital, nasal carriage of *S. aureus* was found in 35% of the children tested and 28% of the adults, while MRSA was detected in only 1 child.[22]

As seen in these studies, the rates of *S. aureus* carriage and, in particular, MRSA carriage in healthy individuals or patients with community-acquired diseases vary greatly depending on the region, demographic characteristics of the people, co-morbidities, and relationships with the hospital. In the present study, the rates of nasal carriage, which were determined to be 5.1% in 2019 and 0.8% in 2020, are quite low compared to the previously mentioned studies. This may be attributed to the fact that the study group consisted of healthy young workers having relatively lower risks of carriage. In fact, in a study carried out with a similar group in the same region, the rate of *S. aureus* carriage was found to be 3.37%. Of the 526 strains detected, 28 (5.3%) were defined as MRSA.[13]

After the Covid-19 infection became a pandemic, various measures began to be implemented to reduce the effects of Covid-19 in Turkey as well as around the world. These measures include limiting the admittance of non-emergency patients to health institutions in addition to measures such as mask-wearing, physical distancing, reducing crowds, and ensuring hand hygiene. During this pandemic, the people's states of health have been affected by these measures as well as the Covid-19 infection. According to the present study, changes detected in the rates of nasal carriage and MRSA between 2019 and 2020 can also be evaluated in this context. It seems possible that the measures implemented during the pandemic may be effective in reducing the transmission of *S. aureus* as well as preventing the transmission of Covid-19. Although no other study has been conducted on the carriage of *S. aureus* during this pandemic, the effects of the pandemic process especially on the spread of viral infections have been discussed.

In the United States, it was reported that the circulation of influenza viruses decreased in the following 2 weeks after the declaration of a state of emergency due to Covid 19, and this decrease was attributed to the measures taken due to the pandemic.[23] In a meta-analysis consisting of 9 studies conducted by Alqahtani et al. it was reported that there was a 50% decrease in hospitalizations due to COPD exacerbation compared to the pre-Covid-19 period. The researchers noted that this decrease was most likely due to the reduction in viral infection-induced COPD exacerbations. They support the opinion that measures such as maintaining physical distance, wearing masks, and ensuring hand hygiene taken for Covid-19 during the pandemic period have reduced the spread of other viral infections in society.[24]

As a result of this study, a sharp decrease in the overall carriage of *S. aureus* from 5.1% to 0.8% during the pandemic (2020) compared to the pre-pandemic period (2019) was determined. In addition, the rate of MRSA in *S. aureus* reproductions was seen to increase by more than 3 times in 2020 (55.6%) compared to 2019. Such a relative increase in the rates of MRSA can be attributed to a recent trend of increase in the MRSA strains, or it may indicate that the nasal carriage of MSSA and MRSA have been differently affected by pandemic measures. The data obtained on this subject will contribute to proper management of the carriage and infections of *S. aureus* in the long term. Therefore, further detailed investigations of the subject are recommended.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Akdeniz University (Approval number: December 9, 2020/936).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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