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The effect of nasal staphylococcal carriage on the incidence of prosthesis infection in orthopedic surgery patients: A cohort study

Ortopedik protez cerrahisi hastalarında nazal stafilokok taşıyıcılığının protez enfeksiyonları üzerine etkisi: Bir kohort çalışması

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ABSTRACT

Objective: Prosthetic infections are commonly caused by coagulase-negative staphylococci (CoNS) and *Staphylococcus aureus* (*S. aureus*). Despite recommendations for preoperative *S. aureus* screening, data on screening for staphylococcal carriage, including CoNS, remains limited. Our study aimed to explore the relationship between nasal carriage of *S. aureus* and other staphylococci and prosthesis infections.

Methods: This prospective cohort study, conducted from January to September 2019, included 151 patients undergoing prosthetic surgery. Nasal cultures for staphylococcal carriage were collected 24 hours before surgery. Patients were monitored and blood tests were conducted at 1, 2, and 3 months postoperatively to assess prosthesis infection development. Infection rates were compared between patients with and without nasal carriage.

Results: In the postoperative three-month period, 5 patients (3.3%) developed prosthetic infections. Preoperative nasal swabs revealed methicillin-

ÖZET

Amaç: *Staphylococcus aureus* (*S.aureus*) ve koagülaz negatif stafilokoklar (KNS) protez enfeksiyonlarının en sık etkenleridir. Diz ya da kalça protezi ameliyatlarından önce nazal *S.aureus* taşıyıcılığının taranmasını öneren yayınlar olmasına karşın, başta KNS olmak üzere diğer stafilokok türlerinin taranmasına dair veriler sınırlıdır. Çalışmamız, *S.aureus* ve diğer stafilokokların nazal taşıyıcılığı ile protez enfeksiyonları arasındaki ilişkiyi araştırmayı amaçlamıştır.

Yöntem: Çalışmamız prospektif bir kohort çalışması olup, çalışmaya Ocak-Eylül 2019 tarihleri arasında protez cerrahisi geçiren 151 hasta dahil edilmiştir. Nazal stafilokok taşıyıcılığı taraması için preoperatif 24 saat önce burun sürüntü kültürleri alınmış ve değerlendirilmiştir. Hastalar yakın izlenerek ameliyat sonrası 1., 2. ve 3. aylarda polikliniğe çağrılmış ve kan tetkikleri istenmiştir. Nazal taşıyıcılık saptanan ve saptanmayan hastalar arasında protez enfeksiyonu oranları karşılaştırılmıştır.

Bulgular: Postoperatif 3 aylık dönemde 5 (%3.3) hastada protez infeksiyonu gelişti. Enfeksiyon gelişen

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resistant coagulase-negative staphylococci (MR-CoNS) in four patients and methicillin-sensitive coagulase-negative staphylococci (MS-CoNS) in one patient. None of the patients had preoperative Staphylococcus aureus. The increased risk of prosthetic infection was significantly associated with nasal CoNS carriage (p=0.025). The infected group exhibited elevated leukocyte, neutrophil, and lymphocyte counts, as well as increased C-reactive protein (CRP) levels at 24 hours post-surgery.

Conclusion: This study found no evidence of an association between *S. aureus* carriage and prosthesis infections, but an association was found for CoNS carriage. However, it is not possible to establish a clear relationship between carrying CoNS and infection. The results of our study suggest that nasal carriage screening before prosthetic surgery may be unnecessary. Further studies are needed to clarify the relationship between nasal carriage and prosthetic infection. Monitoring leukocyte and CRP levels in the early postoperative period may indicate prosthesis infection.

Key Words: Nasal staphylococcal carriage, prosthesis infection, osteomyelitis, *S.aureus*, coagulase-negative staphylococci, C-reaktive protein

hastalardan dördünün preoperatif sürüntü kültüründe metisiline dirençli koagülaz negatif stafilokok (MRKNS), birinde metisiline duyarlı koagülaz negatif stafilokok (MSKNS) üremesi oldu. Enfekte hastaların hiçbirinde nazal *S. aureus* taşıyıcılığı saptanmadı. Protez enfeksiyonu gelişme riski preoperatif nazal KNS taşıyıcılarında anlamlı olarak yüksek bulundu (p=0.025). Enfeksiyon gelişen hastalarda postoperatif 24. saat lökosit, nötrofil, lenfosit ve CRP düzeyleri yüksekti.

Sonuç: Bu çalışmada *S. aureus* taşıyıcılığı ile protez enfeksiyonları arasında bir ilişki olduğuna dair kanıt bulunamamıştır, ancak KNS taşıyıcılığı için bir ilişki bulunmuştur. Bununla birlikte, mevcut literatür verileriyle KNS taşıyıcılığı ile enfeksiyon arasında net bir ilişki kurmak mümkün değildir. Çalışmamızın sonuçları, protez cerrahisi öncesinde nazal taşıyıcılık taramasının gereksiz olabileceğini düşündürmektedir. Nazal taşıyıcılık ve protez enfeksiyonu arasındaki ilişkiyi netleştirmek için daha fazla çalışmaya ihtiyaç vardır. Ameliyat sonrası erken dönemde lökosit ve CRP düzeylerinin izlenmesi protez enfeksiyonuna işaret edebilir, hastaların yakın takibi önerilir.

Anahtar Kelimeler: Nazal stafilokok taşıyıcılığı, protez infeksiyonu, osteomyelit, *S.aureus*, koagülaz negatif stafilokok, C-reaktif protein, lökositoz

INTRODUCTION

Hip and knee arthroplasties are highly successful elective surgeries, with a 10-year survivorship rate exceeding 95%. In the United Kingdom (UK) and United State of America (USA) , around 800,000 such procedures are performed annually, with projections indicating this could rise to over 4 million by 2030. The rate of periprosthetic infection stands at approximately 1% for hip replacements and varies between 1% and 2% for knee replacements each year (1). Numerous bacteria have been linked to prosthetic joint infections (PJI), the microbiological profile can be influenced by several factors, including the timing of the surgical intervention, post-surgical soft tissue complications like poor wound healing, hematoma, and wound dehiscence, previous infections, known colonization with drug-resistant organisms like *Staphylococcus* spp, and the patient's underlying comorbidities (2).

Early prosthetic joint infections (PJIs) typically occur within the first three months following surgery, primarily involving bacteria introduced during the surgical procedure. These infections often involve

organisms with significant virulence or a large bacterial load, including *Staphylococcus aureus*, CoNS, as well as a higher proportion of anaerobic and aerobic gram-negative bacilli, and polymicrobial infections. Conversely, delayed infections usually manifest between three months and one year post-surgery, often involving less virulent bacteria that were also likely introduced during or shortly after the initial surgery. In these later cases, the prevalence of polymicrobial and aerobic gram-negative bacterial infections decreases as these are more typical of earlier presentations (2).

Various patient-specific comorbidities and demographic factors significantly elevate the risk of developing periprosthetic joint infections (PJI). Critical risk factors encompass previous joint infections, septicemia, active cutaneous or deep tissue infections, and blood transfusions. Furthermore, individual patient factors such as uncontrolled diabetes, malnutrition, morbid obesity, smoking habits, alcohol consumption, immunocompromising diseases, drug use, and nasal carriage of *S. aureus* also contribute to the increased vulnerability to PJIs (1). The community prevalence of MRSA has been increasing over the course of the last decade, and patient colonization with *S. aureus* has been shown to be an independent risk factor for the development of a surgical site infection after total hip or knee arthroplasty (3).

S. aureus colonisation and infection have a complex and multifactorial relationship, which is not yet fully understood. The mucosal surfaces that harbor *S. aureus* include the nose, throat, vaginal wall, and GI tract. Nasal carriage is probably most important because nose-picking could effectively disseminate the bacterium to other body surfaces and other hosts (4). However, various immunological mechanisms may also play a role in the pathogenesis of infection. There are studies indicating that *S. aureus* nasal colonisation may play a role in the pathogenesis of autoimmune disease due to its effects on the innate and adaptive immune response (5). Transient or persistent *S. aureus* colonization induces specific systemic immune responses. Humoral responses are the most studied of these and little is known of cellular responses induced by colonization. Nasal *S. aureus* carriage screening/decolonization procedures are heterogeneous and the evaluation of their clinical impact remains complex. On the other hand, there are studies that recommend screening and decolonisation of *S. aureus* carriage before cardiovascular surgeries, hip or knee replacement surgeries and in neonatal intensive care units (6).

CoNS are the most abundant micro-organisms colonizing human skin and mucous membranes. Among healthy individuals this commensal flora of CoNS remains relatively stable over time. However, hospital admissions, antibiotic treatment, and chemotherapy have all been shown to alter the flora, reduce the variety of strains, and result in accumulation of multi-drug-resistant CoNS. The role of CoNS as a significant contributor to bloodstream infections has been increasingly acknowledged, particularly in the context of immunocompromised individuals and those with indwelling medical devices. (7). There are studies indicating that CoNS carriage increases the risk of bacteraemia and sepsis in neonates and patients with malignancy (8,9).

The aim of this study was to screen for preoperative nasal staphylococcal carriage in patients who underwent knee or hip prosthesis surgery in the orthopedic clinic of our hospital and to compare the prosthetic infection rates in the first 3 months postoperatively in patients with and without staphylococcal carriage.

MATERIAL and METHOD

Study Population and Design

This study was designed as a prospective observational cohort study. A total of 151 patients older than 18 years of age who underwent knee or hip prosthesis implantation between January and September 2019 at the Istanbul University Medical

Faculty Orthopedics Clinic were included in the study. Preoperative nasal staphylococcal carriage was analyzed in these patients and the rates of prosthesis infection in the first 3 months postoperatively were evaluated.

A total of 151 patients older than 18 years of age who underwent knee or hip prosthesis implantation between January and September 2019 at the Istanbul University Medical Faculty Orthopedics Clinic were included in the study. Pregnant, pediatric patients and patients scheduled for revision surgery due to infected prostheses were not included in the study. Preoperative nasal staphylococcal carriage was analyzed in these patients and the rates of prosthesis infection in the first 3 months postoperatively were evaluated.

Data collection

Epidemiological and clinical information was recorded on a form. Demographic data, surgery indications, duration of surgery, preoperative, and postoperative hemogram data, sedimentation, CRP and procalcitonin levels were obtained from anamnesis and patient records. The patients and/or their families were informed that data from the research would be submitted for publication and gave their consent. Nasal swabs were taken from patients undergoing knee or hip replacement surgery 24 hours before surgery and cultured for the presence of bacteria. After incubation in 5% sheep blood agar at 37°C for 24 hours, the formation of round, smooth-surfaced yellow-white colonies represented growth. The colonies with positive catalase test were considered as staphylococci and DNAase test was performed. DNAase test positive strains were identified as *S. aureus* and negative strains were identified as CoNS. Antibiograms were performed on Mueller-Hinton medium and susceptibility to cefoxitin, cefazolin, penicillin, rifampicin, fusidic acid, trimethoprim-sulfomethoxazole, doxycycline, ciprofloxacin, erythromycin, clindamycin, gentamicin, and linezolid were determined using the disk diffusion method. Since our study was not an interventional study, no decolonisation treatment was given to patients with growth in nasal swab cultures, and routine prophylaxis schemes were applied peroperatively.

Definitions

Antibiotic susceptibilities were evaluated according to antibiotic zone diameters determined by European Committee on Antimicrobial Susceptibility Testing 2019 data. Patients were examined in the first, second and third post-operative months. Data such as swelling, redness, temperature rise, pain and movement restrictions, if any, were recorded in the patient form. Infection findings were evaluated according to the prosthetic joint infections guide published by the Infectious Diseases Society of America in 2013.

IBM SPSS Statistics for Windows Version 21.0 (Statistical Package for the Social Sciences, IBM Corp., Armonk, NY, USA) was used for statistical analysis of the study data. Data are expressed as mean, standard deviation and percentage (%)". Student's t-test was used to analyze normally distributed numerically measured variables and the Mann-Whitney U test was used to analyze non-normally distributed numerically measured variables. x2 test or Fisher's exact test was used to analyze categorical variables. And $p < 0.05$ was considered statistically significant in all analyses

The study was approved by the Istanbul University Faculty of Medicine Clinical Research Ethics Committee (Date: 09.07.2018 and Number: 993).

RESULTS

Demographic Characteristics

Thirty-four (22.5%) patients were male and 117 (77.5%) were female; The mean age of the patients was 63.1 years; the mean height and weight were 161.1 cm and 78.3 kg, respectively, and the mean body mass index (BMI) was 30.3 kg/m^2. Thirty-four (22.5%) patients were smokers and 117 (77.5%) were non-smokers.

Comorbid Conditions

71 (47%) patients had hypertension, 40 (26.5%) had diabetes, 18 (11.9%) had hypothyroidism, and 7 (4.6%) had rheumatoid arthritis; 30 patients had no comorbidities. Sixteen patients overall and one patient who developed infection were immunosuppressed.

Surgical Characteristics

76 (50.4%) and 75 (49.6%) patients underwent hip and knee prosthesis surgery, respectively. The indication was gonarthrosis in 76 (100%) patients who underwent knee prosthesis surgery. Indications for hip prosthesis surgery were coxarthosis in 30 (19.8%) patients, congenital hip dislocation in 20 (13.2%) patients, avascular femoral head necrosis in 9 (5.9%) patients, and avascular femoral head necrosis in 15 (9.9%) patients. The mean operation time was 120.5 minutes overall and 132 minutes for those who developed infection.

Preoperative Nasal Swab Culture Results

Figure 1 shows the distribution of preoperative nasal swap culture results.

Characteristics of Patients Developing Prosthesis Infection

Prosthesis infection developed in 5 (3.3%) patients in the postoperative 3-month period. Only one in five patients who developed infection was a smoker. The characteristics of the patients are shown in Table 1.

Preoperative and Postoperative Hemogram, CRP, and Sedimentation Values

Preoperative and postoperative 24th hour hemogram, CRP and sedimentation results of infected and uninfected patients are shown in Table 2.

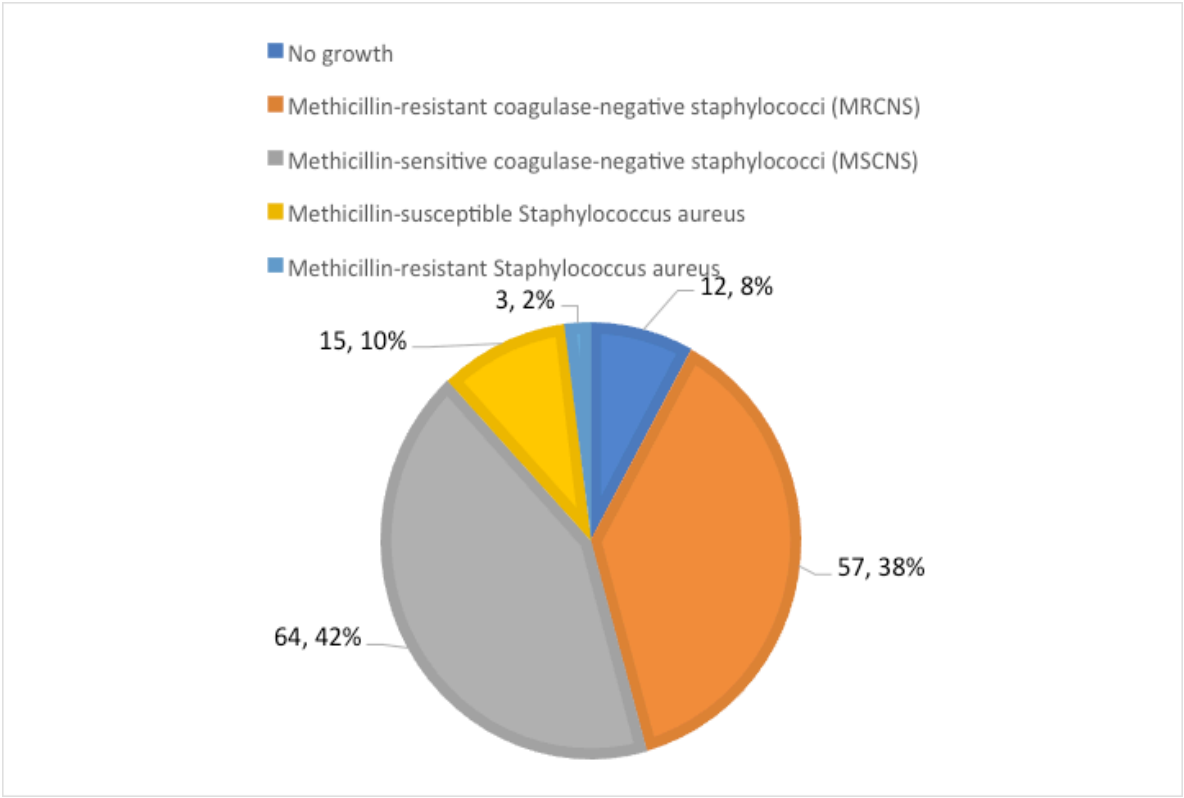

Figure 1. Distribution of preoperative nasal swab culture results according to factors

Table 1. Characteristics of Patients Developing Prosthesis Infection

Patient number	Age	Sex	Comorbidity	Surgery type	Surgery indication	Nasal swab culture	Infection development time (post operative/day)	Tissue culture
Patient 1	73	Female	Rheumatoid arthritis	Hip replacement surgery	Femoral neck fracture	MRCoNS	11 days	*Proteus mirabilis*
Patient 2	71	Female	Hypertension	Hip replacement surgery	Femoral neck fracture	MRCoNS	30 days	*Corynebacterium* spp.
Patient 3	71	Female	Hypertension	Knee replacemant surgery	Osteoarthritis	MSCoNS	45 days	No growth
Patient 4	49	Female	No comorbidity	Hip replacement surgery	Congenital hip dislocation	MRCoNS	49 days	C/G group streptococci
Patient 5	43	Male	Cerebrovascular disease	Hip replacement surgery	Heterotrophic ossification	MRCoNS	2 days	*Klebsiella pneumoniae*

MRCoNS: Methicillin-Resistant Coagulase Negative Staphylococci

MSCoNS: Methicillin-Sensitive Coagulase Negative Staphylococci

Table 2. Demographic characteristics of patients with and without postoperative prosthesis infection; preoperative and postoperative 24th hour laboratory values

Characteristics	**Patients without prosthesis infection (n = 146)**	**Patients with prosthesis infection (n = 5)**	***p***
Age, mean ± SD	63.17 ± 11.46	61.80 ± 14.09	0.793
Height (cm)	161.18 ± 8.90	158.60 ± 9.47	0.525
Weight (kg)	78.64 ± 14.55	68.80 ± 8.87	0.136
BMI (kg/m^2)	30.37 ± 0.48	27.69 ± 5.24	0.312
Operation time (min)	120.068 ± 25.723	132 ± 27.522	0.310
Preoperative leukocyte count (mm^3)	7495,83 ± 2376,86	8740 ± 4383.39	0.561
Preoperative neutrophil count (mm^3)	5002.08 ± 2315.39	6460 ± 4388.39	0.500
Preoperative lymphocyte count (mm^3)	1827.08 ± 594.16	1620 ± 216.79	0.439
Preoperative CRP level (mg/dL)	9.74 ± 17.65	9.60 ± 7.40	0.985
Preoperative sedimentation rate (mm/hour)	28.65 ±20.09	43.60 ±34.55	0.113
Postoperative leukocyte count (mm^3)	9413.47 ± 2619.41	14680 ± 3778.49	**< 0.01**
Postoperative neutrophil count (mm^3)	7308.65 ± 2403	11680 ± 3824.52	**< 0.01**
Postoperative lymphocyte count (mm^3)	1331.91 ± 545.14	1940 ± 733.48	**0.017**
Postoperative CRP level (mg/dL)	92.80 ± 82.97	139 ± 102.596	0.230
Postoperative sedimentation rate (mm/hour)	60.32 ±28.26	68.40 ±27.92	0.534

In the univariate analysis, leukocyte and neutrophil levels at the 24-hour postoperative mark were notably elevated in patients presenting with infections ($p < 0.01$). Additionally, lymphocyte counts measured 24 hours after surgery were significantly greater in these patients ($p = 0.017$).

There was no statistically significant difference in pre- and post-operative erythrocyte sedimentation rate and procalcitonin levels between patients with and without infection.

The study assessed the risk of developing an infection associated with preoperative nasal carriage of *S. aureus* using univariate analysis. The results showed no significant difference ($p = 0.256$). However, patients colonized with CoNS had a significantly increased likelihood of infection on univariate analysis ($p = 0.025$).

The mean BMI of patients with preoperative nasal *S. aureus* carriage was 32.71 compared to a mean BMI of 29.96 in non-carriers.

In our investigation, our findings indicate a lack of substantial relationship between smoking and immunosuppression in elevating the likelihood of post-operative prosthesis infection development ($p = 0.890$, $p = 0.528$). Furthermore, no notable variance was observed in the duration of surgery between patients who experienced infection and those who did not ($p=0.275$).

DISCUSSION

Our study suggests that carrying CoNS in the nasal passage increases the risk of prosthesis infection. No other studies in the literature have shown a link between nasal carriage of CoNS and an increased risk of prosthesis infection. Although our study adds value to the literature with this finding, further research will be needed to establish a clear association due to the small number of cases.

Furthermore, in five patients who developed an infection, the pathogens were different from CoNS found in nasal carriers. Although this finding is statistically significant, it is challenging to argue that there is an increased risk of prosthesis infection in CoNS carriers.

The prevalence of CoNS carriage in the community is high, but the intricacies of this phenomenon have been little studied. Nasal carriage of methicillin-resistant coagulase-negative staphylococci (MR-CoNS) is highly prevalent in community subjects, but its dynamic has been little investigated (10).

Studies have shown that CoNS weaken host defences and promote infection by damaging the natural barriers of the skin and mucous membranes (11). In addition, some factors, such as bacterial interactions in the human nose, may influence *S. aureus* colonisation and sometimes prevent colonisation. (12). Studies have demonstrated that nasal carriage of CoNS triggers various immunological mechanisms.Although CoNS have a much lower pathological potential than *S. aureus*, antigens of *S. haemolyticus* and *S. epidermidis* can induce dysfunctional immune responses. In vitro studies have shown that *S. epidermidis* may antagonise or cooperate with *S. aureus* in biofilm formation. These studies on the interactions of CoNS in mixed biofilms with *S. aureus* have primarily included healthy individuals (13). Indeed, it has been shown in various studies that there is a relationship between nasal CoNS carriage and the frequency and severity of atopic dermatitis in children (14). Considering the relationship of CoNS with other bacteria and their immunological effects, we hypothesise that nasal CNS carriage facilitates the development of infection by various mechanisms, although the infectious agents were non-CNS pathogens in 5 patients who developed infection. Our conclusion that the presence of CoNS in the nasal region increases the likelihood of prosthesis infection is supported by the results of studies investigating the relationship between CoNS and the development of infection.

If the results of our study are confirmed by further studies, it will be possible to clearly demonstrate the effect of nasal CoNS

on the development of prosthesis infections.

While the literature reports that nasal carriage of *S. aureus* is a risk factor for developing prosthetic infections, our study did not find such an association. The relationship between nasal *S. aureus* carriage and infection development has been evaluated in the literature and screening is recommended especially before cardiothoracic and orthopedic implant placement. In the current investigation, there was no development of prosthesis infection in any of the 18 patients with preoperative *S. aureus* carriage within the initial 3 months post-surgery (p = 0.256). In some studies, preoperative *S. aureus* carriage was found to be associated with infection, but there are also studies that did not find such a relationship. A landmark randomized-controlled trial evaluating the impact of S aureus decolonization reported a significant reduction in health care–associated S aureus infection, but could not find a significant reduction in PJIs in an underpowered subgroup analysis in orthopedic patients (15).

Prosthesis infection developed in five patients in our study. Of these, four patients were female and one was male. One study reported male sex as a risk factor for developing knee prosthesis infection (16). In another study investigating the risk factors for the development of hip prosthesis infection, female sex was reported as a protective factor against infection. (17) Since the number of female patients was significantly higher in the present study, the incidence of prosthesis infection was naturally higher in female patients.

In various publications, advanced age has been shown as a risk factor for the development of infections (18,19). In this study, the average age of women participating was 64.0 years, with those who developed an infection having an average age of 66.3 years.This finding is important in terms of demonstrating the increased risk of infection with age and is consistent with the literature.

A previous study reported that higher BMI was associated with a higher risk of infection and a BMI > 30 kg/m^2 is considered as a risk factor for the development of prosthesis infection (19).

In the present study, mean the BMI was 30.37 kg/m^2 among all patients compared to 27.69 kg/m^2 among patients who developed infection. There was no statistically significant difference between patients with and without infection in terms of BMI (p = 0.312). This may be attributed to the small number of patients who developed postoperative prosthesis infection.

The mean BMI of patients with preoperative nasal *S. aureus* carriage was 32.71 compared to a mean BMI of 29.96 in non-carriers. Although there was no statistically significant difference due to the small sample size (p = 0.059), BMI could be considered a risk factor for *S. aureus* carriage. In a study in which risk factors for staphylococcal carriage were evaluated, it was shown that every 2.5 kg/m^2 increase in BMI increased the risk of nasal staphylococcal carriage by 7%, which is consistent with our results (20).

One of the infected patients was diagnosed with rheumatoid arthritis, one with hypertension and one with diabetes. Diabetes is a known risk factor for the development of prosthesis infection.

In a cohort study conducted in patients with knee and hip prosthesis, it was found that the presence of diabetes increased the risk of infection 1.55 times (21). In the present study, no significant relationship was found between diabetes and infection risk (p = 0.187). This may also be attributed to the small number of patients. In the literature, rheumatoid arthritis is considered a risk factor for prosthesis infection. In a study comparing patients who underwent hip or knee replacement due to osteoarthrosis or rheumatoid arthritis, the risk of developing infection in the rheumatoid arthritis group was found to be 4.08 times higher than the osteoarthrosis group (22). However, no significant increase in infection risk was found in patients with rheumatoid arthritis in the present study (p = 0.204). Although a statistically significant increase could not be shown in our study due to the fact that

only six patients had rheumatoid arthritis, it is also interesting that one of the five patients who developed infection was diagnosed with rheumatoid arthritis.

There was no significant association between immunosuppression and development of prosthesis infection ($p = 0.528$). However, immunosuppression is considered a risk factor for the development of prosthesis infection (23). In a study evaluating the development of bone joint infection in patients who underwent hematopoietic stem cell transplantation, it was reported that immunosuppression constituted a serious risk factor and treatment response and prognosis were worse in immunosuppressed patients (23). In a case-control study conducted to evaluate the development of prosthesis infection in solid organ transplant patients, immunosuppression was determined as a risk factor for the development of infection (24).

Similarly, no significant relationship was found between smoking and development of infection. However, smoking is considered a risk factor for the development of infection. In another study, it was reported that the risk of developing prosthesis infection increased 1.8-fold in patients who had been smoking for more than one year (25). In the literature also reported that smoking increased MRSA colonization (26).

The lack of such a significant relationship in the present study may be due to the low number of smokers and patients who developed infection.

Leukocyte, neutrophil and lymphocyte counts were significantly increased in the infection group 24 hours after surgery ($p < 0.01$). In the literature, the sensitivity (79%) and specificity (46%) of leukocytosis in predicting prosthesis infection were found to be low and it was stated that it should not be used as a predictor unless there are additional abnormal findings (27). When comparing the CRP and erythrocyte sedimentation rates at 24 hours after surgery, no significant difference was observed. Although not statistically significant, postoperative CRP was found to be higher in the infection group than in the non-infection group. Similarly, a study in the literature reported that a CRP value > 10 mg/dL on postoperative day 4 was predictive of infection development in patients undergoing lumbar instrumentation (28). Early postoperative CRP elevation may be indicate developing of infection.

This study has several strengths. Firstly, the results of the study are valuable as it is a prospective cohort study. Secondly, patients underwent monthly postoperative evaluations for three months, during which they received comprehensive examinations and close monitoring for signs of prosthesis infection through blood tests. Thirdly, this is a rare study to evaluate CoNS carriage in relation to prosthesis infection development and may provide an idea for further studies. Our study has also several limitations. Firstly, our sample size was small and the number of patients who developed infection was 5 patients. The multivariate analysis was not performed due to the low number of patients who developed infection. Secondly, patients could be followed up for the first three months postoperatively. Finally, subtyping of CoNS grown in preoperative nasal swab cultures could not be performed due to inadequate laboratory facilities.

In conclusion; our study found no association between nasal *S. aureus* carriage and prosthesis infection. While nasal carriage of *S. aureus* is considered a significant risk for prosthetic infections, it is also likely that CoNS contribute to the pathogenesis of prosthetic infections. As the pathogens in patients with prosthesis infection differ from those causing CoNS, and the number of patients who went on to develop infection was 5, it is impossible to establish a clear link between carrying CoNS and infection. Considering the results of our study and the available literature data, it is not possible to make a clear recommendation regarding nasal staphylococcal carriage screening. Further studies are needed to clearly demonstrate the relationship between carriage and the pathogenesis of infection development. An understanding

of the pathogenic mechanisms of CoNS would facilitate the development of therapeutic approaches aimed at preventing prosthetic infections and combating their complications.

Finally, monitoring of leukocyte and CRP levels in the early postoperative period can be an indicator of prosthesis infection.

ETHICS COMMITTEE APPROVAL

* The study was approved by the Istanbul University Faculty of Medicine Clinical Research Ethics Committee (Date: 09.07.2018 and Number: 993).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

REFERENCES

1. Kapadia BH, Berg RA, Daley JA, Fritz J, Bhave A, Mont MA. Periprosthetic joint infection. The Lancet, 2016;387(10016):386-94.
2. Beam E, Osmon D. Prosthetic Joint Infection Update. Infect Dis Clin North Am,2018;32(4):843-59.
3. Weiser MC, Moucha CS. The Current State of Screening and Decolonization for the Prevention of *Staphylococcus aureus* Surgical Site Infection After Total Hip and Knee Arthroplasty: J Bone Jt Surg-Am Vol, 2015;97(17):1449-58.
4. Liu GY. Molecular Pathogenesis of *Staphylococcus aureus* Infection. Pediatr Res, 2009;65(5 Part 2):71R-77R.

5. Ceccarelli F, Perricone C, Olivieri G, Cipriano E, Spinelli F, Valesini G, et al. *Staphylococcus aureus* Nasal Carriage and Autoimmune Diseases: From Pathogenic Mechanisms to Disease Susceptibility and Phenotype. Int J Mol Sci, 2019;20(22):5624.

6. Brown AF, Leech JM, Rogers TR, McLoughlin RM. *Staphylococcus aureus* Colonization: Modulation of Host Immune Response and Impact on Human Vaccine Design.Front Immunol, 2014;4:507.

7. Ahlstrand E, Persson L, Tidefelt U, Söderquist B. Alteration of the colonization pattern of coagulase-negative staphylococci in patients undergoing treatment for hematological malignancy. Eur J Clin Microbiol Infect Dis, 2012;31(7):1679-87.

8. Boo N, Suhaida A, Rohana J. Frequent nasopharyngeal suctioning as a risk factor associated with neonatal coagulase-negative staphylococcal colonisation and sepsis. Singapore Med J, 2015;56(03):164-8.

9. Costa SF, Barone AA, Miceli MH, Van Der Heijden IM, Soares RE, Levin AS, et al. Colonization and molecular epidemiology of coagulase-negative Staphylococcal bacteremia in cancer patients: A pilot study. Am J Infect Control, 2006;34(1):36-40.

10. Lebeaux D, Barbier F, Angebault C, Benmahdi L, Ruppé E, Felix B, et al. Evolution of Nasal Carriage of Methicillin-Resistant Coagulase-Negative Staphylococci in a Remote Population. Antimicrob Agents Chemother, 2012;56(1):315-23.

11. Heilmann C, Ziebuhr W, Becker K. Are coagulase-negative staphylococci virulent? Clin Microbiol Infect, 2019;25(9):1071-80.

12. Iwase T, Uehara Y, Shinji H, Tajima A, Seo H, Takada K, et al. *Staphylococcus epidermidis* Esp inhibits *Staphylococcus aureus* biofilm formation and nasal colonization. Nature, 2010;465(7296):346-9.

13. Cau L, Williams MR, Butcher AM, Nakatsuji T, Kavanaugh JS, Cheng JY, et al. *Staphylococcus epidermidis* protease EcpA can be a deleterious component of the skin microbiome in atopic dermatitis. J Allergy Clin Immunol,2021;147(3):955-966.e16.

14. Ndhlovu GON, Dube FS, Moonsamy RT, Mankahla A, Hlela C, Levin ME, et al. Skin and nasal colonization of coagulase-negative staphylococci are associated with atopic dermatitis among South African toddlers. Kaliyadan F, editör. PLOS ONE, 2022;17(3):e0265326.

15. Romero-Palacios A, Petruccelli D, Main C, Winemaker M, de Beer J, Mertz D. Screening for and decolonization of *Staphylococcus aureus* carriers before total joint replacement is associated with lower S aureus prosthetic joint infection rates. Am J Infect Control, 2020;48(5):534-7.

16. Lenguerrand E, Whitehouse MR, Beswick AD, Kunutsor SK, Foguet P, Porter M, et al. Risk factors associated with revision for prosthetic joint infection following knee replacement: an observational cohort study from England and Wales. Lancet Infect Dis, 2019;19(6):589-600.

17. Resende VAC, Neto AC, Nunes C, Andrade R, Espregueira-Mendes J, Lopes S. Higher age, female gender, osteoarthritis and blood transfusion protect against periprosthetic joint infection in total hip or knee arthroplasties: a systematic review and meta-analysis. Knee Surg Sports Traumatol Arthrosc, 2021;29(1):8-43.

18. Berbari EF, Hanssen AD, Duffy MC, Steckelberg JM, Ilstrup DM, Harmsen WS, et al. Risk Factors for Prosthetic Joint Infection: Case-Control Study. Clin Infect Dis,1998;27(5):1247-54.

19. Kunutsor SK, Whitehouse MR, Blom AW, Beswick AD, INFORM Team. Patient-Related Risk Factors for Periprosthetic Joint Infection after Total Joint Arthroplasty: A Systematic Review and Meta-Analysis. Virdi AS, editör. PLOS ONE, 2016;11(3):e0150866.

20. Olsen K, Danielsen K, Wilsgaard T, Sangvik M, Sollid JUE, Thune I, et al. Obesity and *Staphylococcus aureus* Nasal Colonization among Women and Men in a General Population. Wertheim HFL, editör. PLoS ONE, 2013;8(5):e63716.

21. Maradit Kremers H, Lewallen LW, Mabry TM, Berry DJ, Berbari EF, Osmon DR. Diabetes Mellitus, Hyperglycemia, Hemoglobin A1C and the Risk of Prosthetic Joint Infections in Total Hip and Knee Arthroplasty. J Arthroplasty, 2015;30(3):439-43.

22. Bongartz T, Halligan CS, Osmon DR, Reinalda MS, Bamlet WR, Crowson CS, et al. Incidence and risk factors of prosthetic joint infection after total hip or knee replacement in patients with rheumatoid arthritis. Arthritis Care Res, 2008;59(12):1713-20.

23. Abad CL, Phuoc V, Kapoor P, Tosh PK, Sia IG, Osmon DR, et al. Bone and Joint Infections among Hematopoietic Stem Cell Transplant Recipients. J Bone Jt Infect, 2019;4(5):209-15.

24. Vergidis P, Lesnick TG, Kremers WK, Razonable RR. Prosthetic joint infection in solid organ transplant recipients: a retrospective case-control study. Transpl Infect Dis, 2012;14(4):380-6.

25. Gonzalez AI, Luime JJ, Uçkay I, Hannouche D, Hoffmeyer P, Lübbeke A. Is There an Association Between Smoking Status and Prosthetic Joint Infection After Primary Total Joint Arthroplasty? J Arthroplasty, 2018;33(7):2218-24.

26. Kulkarni R, Caskey J, Singh SK, Paudel S, Baral P, Schexnayder M, et al. Cigarette Smoke Extract-Exposed Methicillin-Resistant *Staphylococcus aureus* Regulates Leukocyte Function for Pulmonary Persistence. Am J Respir Cell Mol Biol, 2016;55(4):586-601.

27. Deirmengian GK, Zmistowski B, Jacovides C, O'Neil J, Parvizi J. Leukocytosis Is Common After Total Hip and Knee Arthroplasty. Clin Orthop, 2011;469(11):3031-6.

28. Iwata E, Shigematsu H, Koizumi M, Nakajima H, Okuda A, Morimoto Y, et al. Lymphopenia and Elevated Blood C-Reactive Protein Levels at Four Days Postoperatively Are Useful Markers for Early Detection of Surgical Site Infection Following Posterior Lumbar Instrumentation Surgery. Asian Spine J, 2016;10(2):220.