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## Antibiotic resistance of pathogens causing hospital–acquired infections after surgical interventions in the hospital of Lithuanian University of Health Sciences Kaunas Clinics

Gintarė Lukoševičiūtė<sup>1</sup>, Tautvydas Skripkauskas<sup>1</sup>, Valdemar Loiba<sup>2</sup>

<sup>1</sup>Faculty of Medicine, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

<sup>2</sup>Department of Orthopaedics and Traumatology, Faculty of Medicine, Medical Academy, Lithuanian University of Health Sciences, Kaunas, Lithuania

### Abstract

**Background.** The global community is facing a significant and concerning rise in antibiotic–resistant infections. In Lithuania, drug resistant pathogens are ranked as the fifth leading cause of death, underscoring the critical nature of this issue. This is particularly relevant in the field of orthopaedics and traumatology, where the presence of foreign bodies amplifies the risk of infection, necessitating strict interventions to combat antibiotic resistance.

**Aim.** The purpose of this study was to evaluate antibiotic resistance and infection risk factors in postoperative infections in the department of orthopedics and traumatology of Kaunas Clinics.

**Methods.** The data of 104 patients from 2017 to 2021 were selected as the research object. All data were obtained from hospital information database.

**Results.** This study, involving 104 patients, revealed a male predominance (66.3 %) with an average age of  $53.43 \pm 2.029$ , statistically differing from females. Stratification into age groups showed middle–aged individuals (62.5%) more prone to infections. *S. aureus* was the primary pathogen (48.1 %). While penicillin G resistance for this pathogen was 66 %, sensitivity to gentamicin, rifampicin, trimethoprim/sulfamethoxazole, and vancomycin was 100 %. Significant age and gender differences were found in *S. aureus* infections. Lower extremity surgeries were more common (76 %) with *S. aureus*. Gender–dependent ciprofloxacin resistance distribution was observed. Sensitive causative agents were more frequently found in males.

**Conclusions.** *S. Aureus* was the dominant gram–positive pathogen in this study. Its drug resistance pattern showed that antibiotic resistance is a serious concern.

**Keywords:** drug resistance, nosocomial infections, orthopaedics, traumatology

## 1. Background

Every year, microorganisms resistant to antibiotics cause numerous infections, often complicated by death. It has been estimated that in 2019 alone, antibiotic-resistant pathogens worldwide caused approximately 1.27 million deaths [1]. In the same year, infections caused by methicillin-resistant *S. aureus* killed more United States (US) citizens than emphysema, HIV, Parkinson's disease, and suicide combined [2]. Additionally, the Centers for Disease Control and Prevention (CDC) in the US has calculated that infections caused by antibiotic-resistant pathogens cost the US healthcare system an additional \$20 billion annually [3]. In Europe, these infections incur an additional cost of about €9 billion [4]. It is projected that these numbers will continue to rise, and without urgent actions to curb the spread of antibiotic-resistant microorganisms, it is estimated that by 2050, around 10 million people worldwide will die from infections caused by antibiotic-resistant pathogens [5]. In Lithuania, resistant pathogens annually cause the death of 1900 people, ranking as the fifth most common cause of death [6].

This issue is particularly relevant in orthopaedics and traumatology, where various foreign bodies such as endoprostheses or plates are often used during surgeries. They increase the frequency of postoperative infections by at least 10000 times, as foreign bodies provide an excellent environment for pathogens to multiply, requiring very few of them to cause an infection [7]. Microorganisms that adhere to the foreign body form biofilms, which are more resistant to the immune response and antimicrobial drugs. These infections are challenging to treat because the causative agents are often of nosocomial origin, making them significantly resistant to antibiotics. It has been found that in endemic

areas, more than half of staphylococcus-related postoperative infections were caused by methicillin-resistant strains [8]. This poses additional challenges in treating these patients, as more potent antibiotics and even revision surgeries are often required.

## 2. Methods

During the study, a retrospective analysis of the medical documents of infected patients treated between 2017–2021 in the department of orthopedics and traumatology of Kaunas Clinics was performed. 133 patients were selected based on ICD codes M00 and T84.7 and after excluding duplicates, 104 cases were used. Subjects were divided into groups according to infectious agents. Antibiotic resistance of pathogens was evaluated, as well as the dependence of the most causative agent – *S. aureus* – and those infected with it on gender, age, time of year, type of operation and operated area. Subjects are divided into male and female groups according to gender. According to the World Health Organization (WHO), the subjects were divided into three groups by age: patients under 18, from 18 to 65 years. age and 65 years age and older patients.

All clinical specimens, including wound secretions (skin and tissue that were already injured pre-surgery), incisional secretions (skin and tissue intact pre-surgery), urine, blood, and joint fluids, obtained from the orthopedics department between January 2017 and December 2021 were included in the analysis if they tested positive for pathogens.

Statistical data analysis was performed using the IBM SPSS Statistics 23.0 software. Research data were processed using Chi-square ( $X^2$ ), non-parametric – Mano Whitney was used to compare two independent samples. The Kruskal

Wallis non-parametric test was applied when there were more than two study groups. Differences were considered statistically significant when the obtained p-value was lower than the chosen significance level  $\alpha=0.05$ .

### 3. Results

In the study, there were 104 infections after surgical interventions in the orthopedics and traumatology department, with 69 being male patients (66.3 %) and 35 female patients (33.7 %). The average age for females was  $70.46 \pm 2.427$ , and for males –  $53.43 \pm 2.029$ . According to the Mann-Whitney criterion, the age of onset of infection statistically differed between males and females ( $p < 0.05$ ) – males were prone to a higher infection risk at a younger age than females.

The subjects were also divided into age groups: up to 18 years (Group 1 – boys, girls), 18–65 (Group 2 – men, women), and 65+ (Group 3 – seniors). The group of middle-aged individuals consisted of 65 persons (62.5 %), while seniors were 39 (37.5 %). In the middle-aged group of 65 patients, microorganisms did not grow in 14 samples (21.5 %), and in the senior group of 39, 8 samples (20.5 %). For a fifth of patients in each age group, an infection diagnosis was recorded without a positive culture result.

Out of 104 patients, microorganisms did not grow for 22 individuals (21.2 %), and for the remaining 82 (78.8 %), the most common causative agents were *Staphylococcus aureus* (60.9 %, 50/82), *Staphylococcus epidermidis* (7.3 %, 6/82), *Cutibacterium acnes* (4.88 %, 4/82), *Streptococcus agalactiae* (6.09 %, 5/82), and *Enterobacter* (6.09 %, 5/82).

It was observed in the study that the Gram-positive bacterium *S. aureus* was the most common causative agent of infections in the

orthopedics and traumatology department (48.1 %, 50/104). The majority, 66 % (33/50), were resistant to at least one of the tested antibiotics (oxacillin, penicillin G, ciprofloxacin, clindamycin, erythromycin, tetracycline, gentamicin, rifampicin, trimethoprim/sulfamethoxazole, vancomycin), and 34 % (17/50) were susceptible.

In 28 cases, *S. aureus* strains were identified from joint fluid, 24 through biopsy, and 15 from pus cultures. A statistically significant difference between age and gender was found ( $p < 0.05$ ). In joint fluid samples, the average age for females was  $69.70 \pm 17.3$ , for males –  $50.78 \pm 16.4$ . In biopsy samples, the average age for females was  $74.83 \pm 15.2$ , for males –  $56.44 \pm 15.3$ . In pus culture samples, it was  $76.00 \pm 14.0$  for females, and  $59.91 \pm 11.9$  for males.

Out of 50 individuals with *S. aureus* caused infections, the majority were males (70.0 %, 35/50), and the rest females (30%, 15/50). Most individuals belonged to age group 2 (64.0 %, 32/50), while the older age group comprised 36 % (18/50). A statistically significant difference was found between the age of *S. aureus* infected males and females ( $p < 0.05$ ) – females more frequently fell into the 65+ age group, with an average age of  $72.27 \pm 15.9$ , while males were under 65, with an average age of  $54.66 \pm 14.9$  years.

Both middle-aged and older individuals more frequently underwent lower extremities (76 %, 38/50) rather than upper extremities (24 %, 12/50) surgeries in the presence of *S. aureus* as the causative agent ( $p < 0.05$ ).

In cases of *S. aureus* caused infections, the most frequently performed surgeries were debridement (28.0 %, 14/50), osteotomy (22.0 %, 11/50), osteosynthesis (22.0 %, 11/50), and revision surgeries for endoprosthesis (14.0 %, 7/50).

7/50). During debridement surgeries, it was found that in half of the cases (50 %), *S. aureus* strains were sensitive, and in the other half (50 %), resistant to at least one of the tested antibiotics. For osteotomy surgeries, 81.8% were resistant to at least one of the tested antibiotics, and 22.2 % were sensitive. Similarly, for revision and osteosynthesis surgeries, the majority (71.4 % and 60 %, respectively) of *S. aureus* strains were resistant to at least one of the tested antibiotics. No statistically significant difference was found between *S. aureus* sensitivity/resistance and the type of intervention performed ( $p < 0.05$ ). *S. aureus* and other pathogen

*S. aureus* showed the highest resistance to penicillin G (66 %, 33/50) and the lowest resistance to gentamicin, rifampicin, trimethoprim/sulfamethoxazole, and vancomycin (100%, 50/50 sensitive). Analyzing the selected antibiotics: oxacillin, penicillin G, ciprofloxacin, clindamycin, erythromycin, gentamicin, rifampicin, vancomycin, trimethoprim/sulfamethoxazole – no statistically significant dependence of *S. aureus* sensitivity/resistance on time, age, gender, or area was found ( $p < 0.05$ ). There was a statistically significant difference in the distribution of ciprofloxacin resistance/sensitivity based on gender. Sensitive causative agents were more frequently found in males, while resistant ones in females ( $p < 0.05$ ).

## 4. Discussion

### 4.1 Demographic insights

The observed increased susceptibility of men to infections at younger ages is consistent with previous studies showing sex differences in infection risk. Gender-specific immunological differences and hormonal influences contribute to this discrepancy. After puberty, women are

initially less susceptible to infectious diseases because of their increased ability to mobilize and activate immune responses comparing to men. Furthermore, testosterone in men has immunosuppressive properties, which could lead to the discrepancies [9].

The stratification of subjects into age groups highlighted distinct infection patterns. Notably, a significant proportion of infections occurred in the middle-aged group rather than senior group. Previous studies showed similar results. Biscoff et al. found increasing age predicted increased surgical site infection risk until age 65 years. After 65 years of age, increasing age predicts lower infection risk. The decreased susceptibility to infection of senior population may be influenced by a combination of factors, including less frequent surgeries and “hardly survivor“ effect [10]. Although these factors remain controversial and further research is needed.

### 4.2 Microbiological landscape and antibiotic resistance

In our study, like several previous findings, the most common pathogen causing nosocomial infections was *S. aureus* (60.9 %) [11–14]. These microorganisms are part of the natural skin microflora, however, when introduced into a surgical wound, they can cause opportunistic wound infections. This is particularly relevant in orthopedics and traumatology, as foreign bodies used in surgeries create an excellent environment for pathogens to multiply [15].

Our study identified *S. aureus* as the predominant Gram-positive bacterium, aligning with its well-established role as a major pathogen in orthopedic infections [16]. Of particular concern is the high resistance observed to penicillin G, reaching 66 % (33/50) in our study. In contrast, a comprehensive study

conducted by Latha et al. revealed a resistance prevalence of only 57.3 % among *Staphylococcus aureus* strains to penicillin. [17]. Currently, numerous medical practitioners administer empirical antibiotics without awaiting sensitivity reports [18,19]. Our findings demonstrated a major problem with antimicrobial resistance and necessitates a cautious approach in selecting empirical antibiotic therapies in the study hospital. Therefore, we strongly advise against the empiric use of penicillin in orthopaedics and traumatology department. In contrast, *S. aureus* showed least resistance to gentamicin, rifampicin, trimethoprim/sulfamethoxazole, and vancomycin, suggesting that they can be safely used in the clinic. However, in 2002, a report emerged regarding the presence of a vancomycin-resistant *S. aureus* isolate [20]. Thus, this antibiotic should be exclusively administered in cases of severe infections that are unresponsive to other antibiotics.

The intricate resistance patterns observed in *S. aureus* strains underscore the challenges in antibiotic management. The gender-dependent distribution of ciprofloxacin resistance highlights the need for nuanced considerations in antibiotic selection, considering patient-specific factors.

#### 4.3 Clinical correlations

The type of surgery played a crucial role in *S. aureus* infections, with lower extremity surgeries being more frequently associated with the bacterium. A study conducted by Onyekwelu et al. demonstrated a significantly elevated risk of surgical site infections in lower extremities compared to upper extremity surgeries [21,22]. Various factors such as vascularity and susceptibility to contamination may contribute to

this phenomenon, however, additional research is needed to further study these mechanisms.

#### 5. Conclusion

In this study, we found that *S. aureus* was the dominant gram-positive pathogen responsible for nosocomial infections in the department of orthopaedics and traumatology of Kaunas Clinics. Drug resistance pattern of this pathogen showed that antibiotic resistance is a serious concern. Based on our results, we highly recommend the implementation of thorough and dynamic surveillance of antibiotic-resistant bacteria, in addition to cautious utilization of antibiotics, as an effective approach to controlling the development of antimicrobial resistance in pathogens.

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