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ORIGINAL ARTICLE

Orthopedic surgery related infections; study of antibiotic resistance and associated comorbidities

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Abstract

Interventions in the field of orthopedics and traumatology involve more and more the frequent use of osteosynthesis materials and prostheses. Therefore, an increasing number of patients live with these implants, having an increased risk in comparison to the general population to develop complications. Although technological developments have brought this change for the better, it must not be forgotten that these foreign materials come with certain risks, the most feared being the associated infections.

For this article, we conducted an epidemiological study on infections identified in patients treated in the Orthopedics and Traumatology Department of University Emergency Hospital in Bucharest, from 01.01.2016 to 01.06.2019. We were able to extract data about patients without neglecting their confidentiality.

The information sought, primarily involved the pathogen causing the infection and its antibiogram, but at the same time we tried to build a more accurate history of each patient in order to determine the cause of infection and the risks posed by various associated pathologies. During these 4 years we were able to identify 139 patients who suffered an infection in the musculoskeletal system. In most cases we identified unimicrobial infections, but there were 7 cases in which two pathogens were identified.

Keywords: orthopedics and traumatology, infections, antibiogram

Introduction

Infectious pathology related to surgery was an important problem for all surgical specialties. Until the middle of the 19th century, the risk of postoperative infection rose to 70-80%. After the discovery of pathogens that could cause infections in 1876 by Robert Koch, microbiologists began to

isolate various microorganisms, which represented the time when surgery began to become feasible. During the Second World War, the importance of debridement of contaminated tissues was understood and the use of iodine-based tinctures was implemented, thus developing the concept of aseptic surgery, leading to a significant decrease in surgical infections [1].

Within the Discipline of Orthopedics and Traumatology, a major complication that is found in both degenerative and traumatic pathology is represented by implant infection. Despite the use of preoperative antibiotic prophylaxis combined with management at high standards, infections related to surgery continue to occur. The incidence of infectious pathologies must be divided into two categories, because when we talk about traumatology, the rate can start from 1% in the case of closed fractures that are treated by minimally invasive methods and can reach up to 30% in high energy trauma, with significant tissue damage and opening of the fracture site [2,3]. In the case of elective interventions, the incidence rate starts from 0.7% and can reach up to 4.2% [4]. Due to the increasing number of pathogens with antibiotic resistance and the association in some cases of extensive interventions, socio-economic costs are increasing and the risks of an unfavorable evolution with functional impotence is increasing [3].

One of the challenges related to infections in this field is the emergence and increase in number of pathogens that are resistant to antibiotics, most of which make a biofilm with significant protective capacity. Among these pathogens we must mention *gram-negative bacilli* resistant to ciprofloxacin and *staphylococci* resistant to rifampicin and methicillin [1,2]. Unfortunately, MRSA (Methicillin-resistant *Staphylococcus aureus*) is not only an identified pathogen in medical units, it has become common among the general population. A study by Kock R et al. described the involvement of more than 150,000 patients in Europe [5], and the study by Torbert JT described the presence of this pathogen in 25%-32% of the cases of infections after osteosynthesis in the USA [6].

Materials and methods

We conducted an epidemiological study on infections identified in patients treated in the

Orthopedics and Traumatology Department of University Emergency Hospital in Bucharest, from 01.01.2016 to 01.06.2019. Using the hospital's patient management software, we were able to extract data about patients without neglecting their confidentiality.

The information sought, primarily involved the pathogen causing the infection and its antibiogram, but at the same time we tried to build a more accurate history of each patient in order to determine the cause of infection and the risks posed by various associated pathologies.

Patients under the age of 18 were removed from the study, and, when one patient had several hospitalizations with the same pathology treated sequentially, the data were corroborated so that there was no artificially increased number of patients.

After accumulating data for their interpretation, the software R (v 3.2.1) and RStudio (v 1.0.136) were used.

Results

During these 4 years, we were able to identify 139 patients who suffered from an infection in the musculoskeletal system. In most cases, we identified unimicrobial infections, but there were 7 cases in which two pathogens were identified. The graphics show the susceptibility and resistance of pathogens to antibiotics currently used in the microbiology laboratory of University Emergency Hospital in Bucharest. Consistent to literature, the most commonly identified bacteria were those of the *Staphylococcus* species followed by *Enterobacteria* and nonfermentative pathogens. Also, two infections were caused by *Enterococci* (Fig. 1).

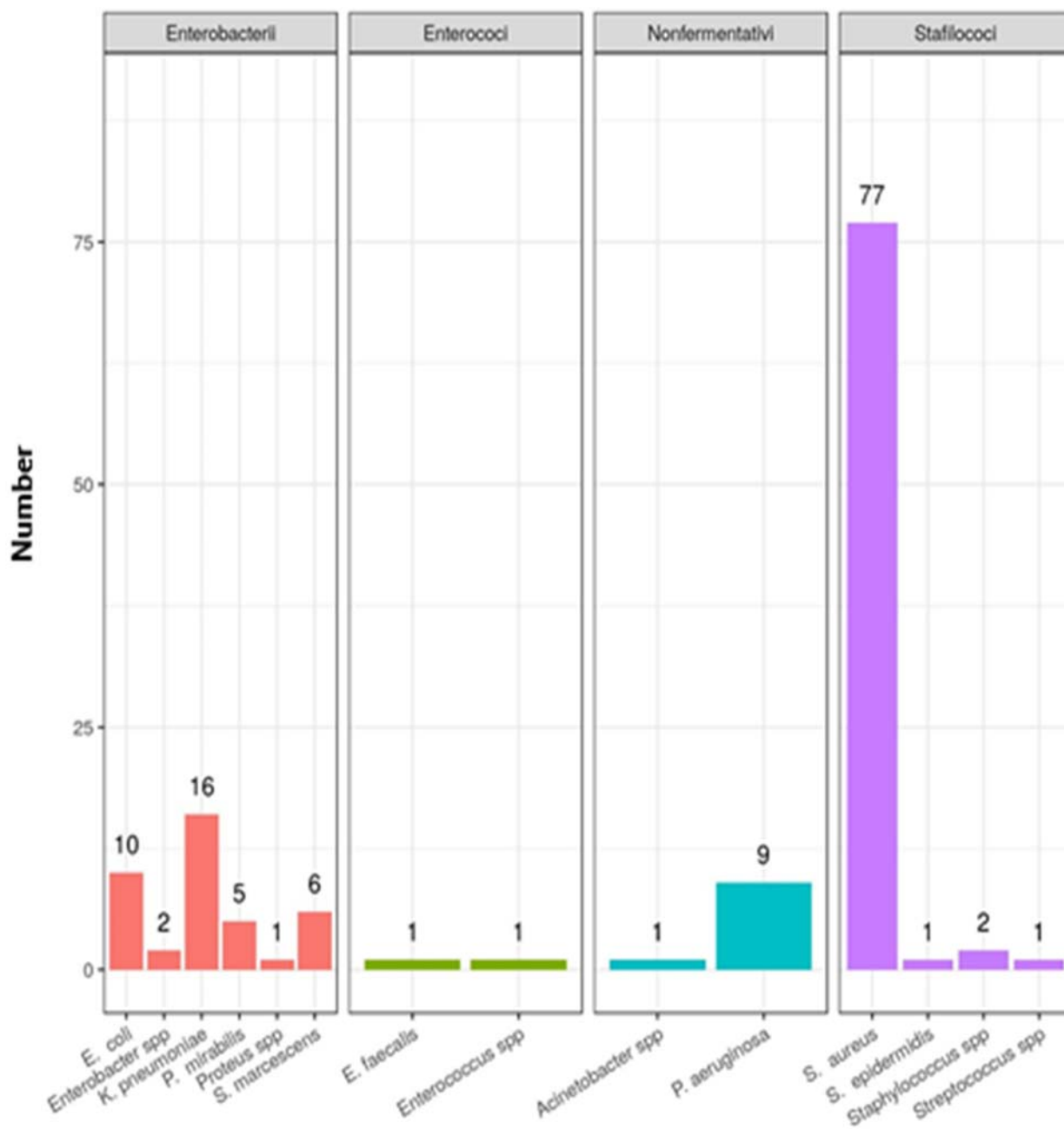


Fig. 1 Graphic representation of isolated bacterial strains

If we look at the statistical data, we will notice that there is no significant difference when we relate to the sex of the patients, both women and men being affected to almost the same extent. The mean age of the patients was 63 years, with the patient group having a standard deviation of 15 years. Most infections occurred in people aged between 30 and 80

years, most cases being identified in people over 50 years. Patients between the ages of 30 and 50 are active people at high risk of engaging in various activities that can cause fractures. In patients aged between 50 and 80 years, comorbidities may increase the risk of infection (Fig. 2).

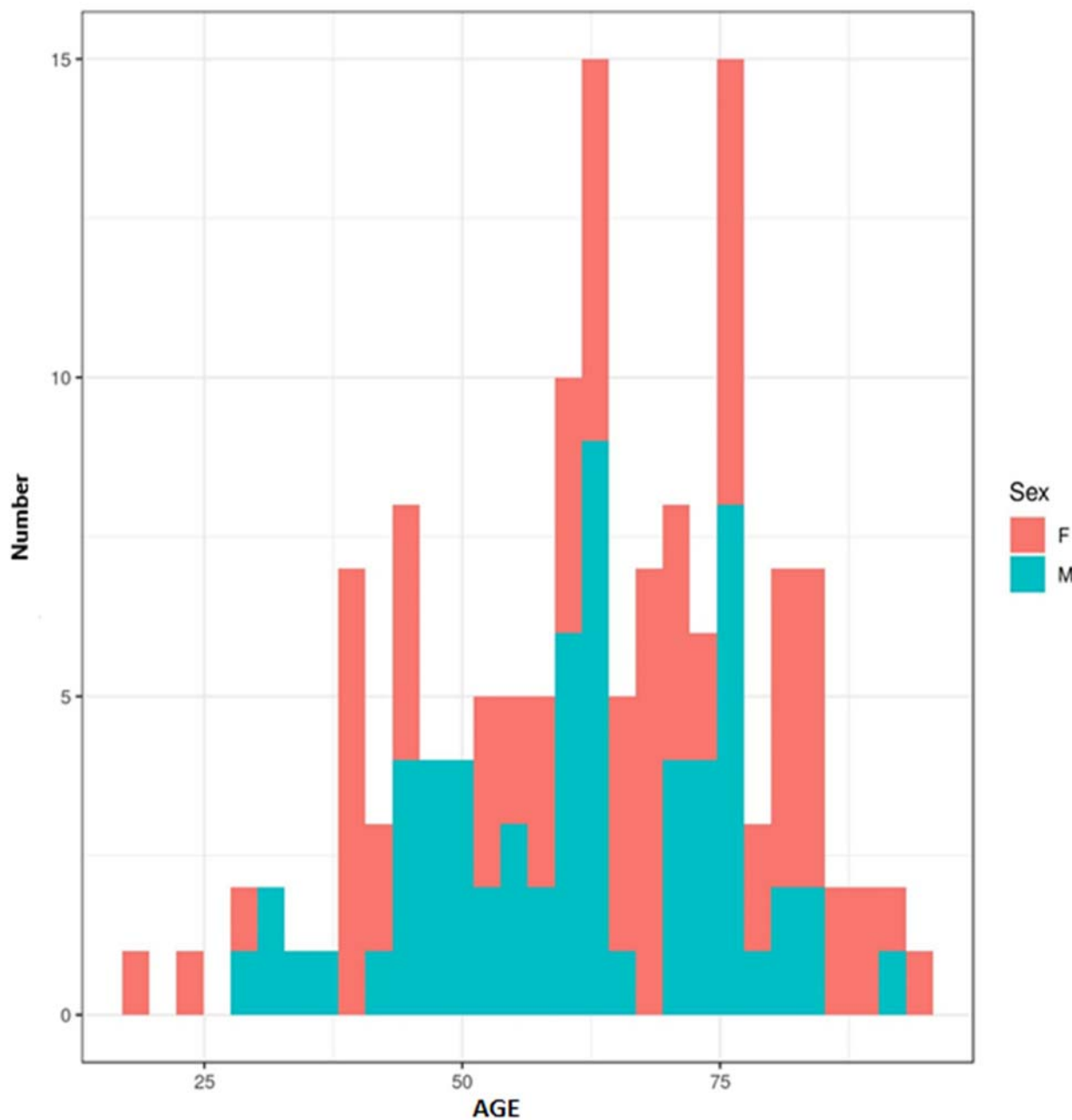


Fig. 2 Distribution of patients by age and sex

We divided the cases into 4 categories, depending on the reason of hospitalization, therefore making it easier to identify the causes that increase the risk of infections in the field of orthopedics and traumatology. Most of the young patients underwent surgery following a fracture, and in the case of the elderly, reintervention was performed due to a septic arthroplasty. We were able to identify

11 septic arthritis caused by punctures or intra-articular infiltrations in patients without significant comorbidities. At the same time, we described 23 cases of septic arthritis without surgery in immunocompromised patients with poor hygiene, superficial infections near the joint or patients with diabetes and Charcot's foot (Fig. 3).

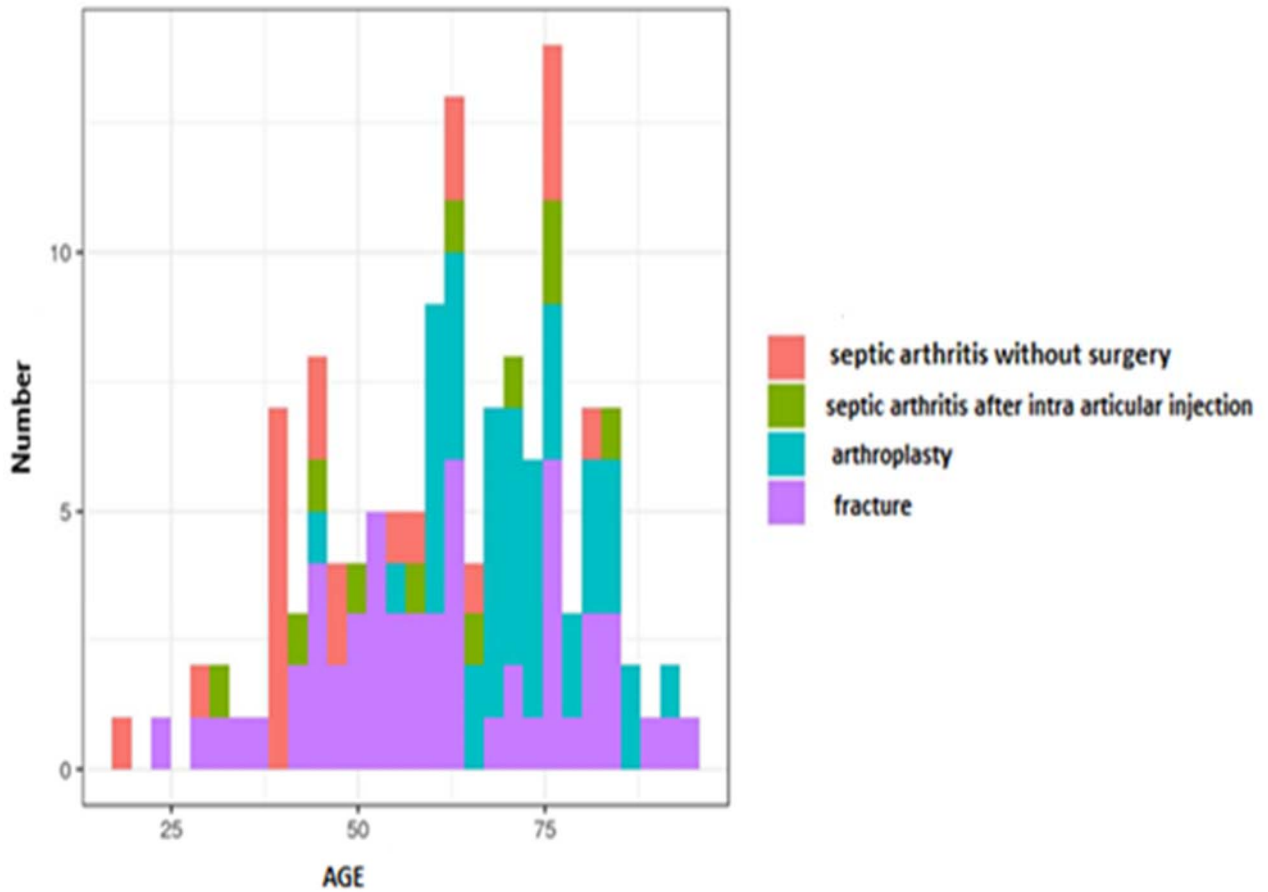


Fig. 3 Distribution of patients according to the reason for hospitalization

Staphylococcus aureus

Most of the pathogens identified in the study were 77 strains of *Staphylococcus aureus*. An important step in the research was to determine the number of strains resistant to common antibiotics. Consulting the guidelines developed by CLSI (Clinical and Laboratory Standards Institute) and EUCAST (European Committee on Antimicrobial Susceptibility Testing), we established that currently, the differentiation between sensitive and methicillin-resistant strains (MSSA/ MRSA) is not achieved by identifying a resistance to oxacillin but to cefoxitin [7]. In the study, we were able to identify a significant difference

between the resistance of the bacterium to oxacillin below 50% and that to cefoxitin above 50%. Resistance to cefoxitin leads to resistance to all beta lactams. Erythromycin and Clindamycin were tested on most strains in which a significant resistance was observed, with approximately equal values between resistance and sensitivity. Only a few cases of bacterial resistance have been reported with Chloramphenicol, Rifampicin, Ciprofloxacin, Moxifloxacin, Levofloxacin, Moxifloxacin, Amikacin, Gentamicin and Bisepitol. No resistance was identified to Vancomycin, Linezolid and Teicoplanin (Fig. 4).

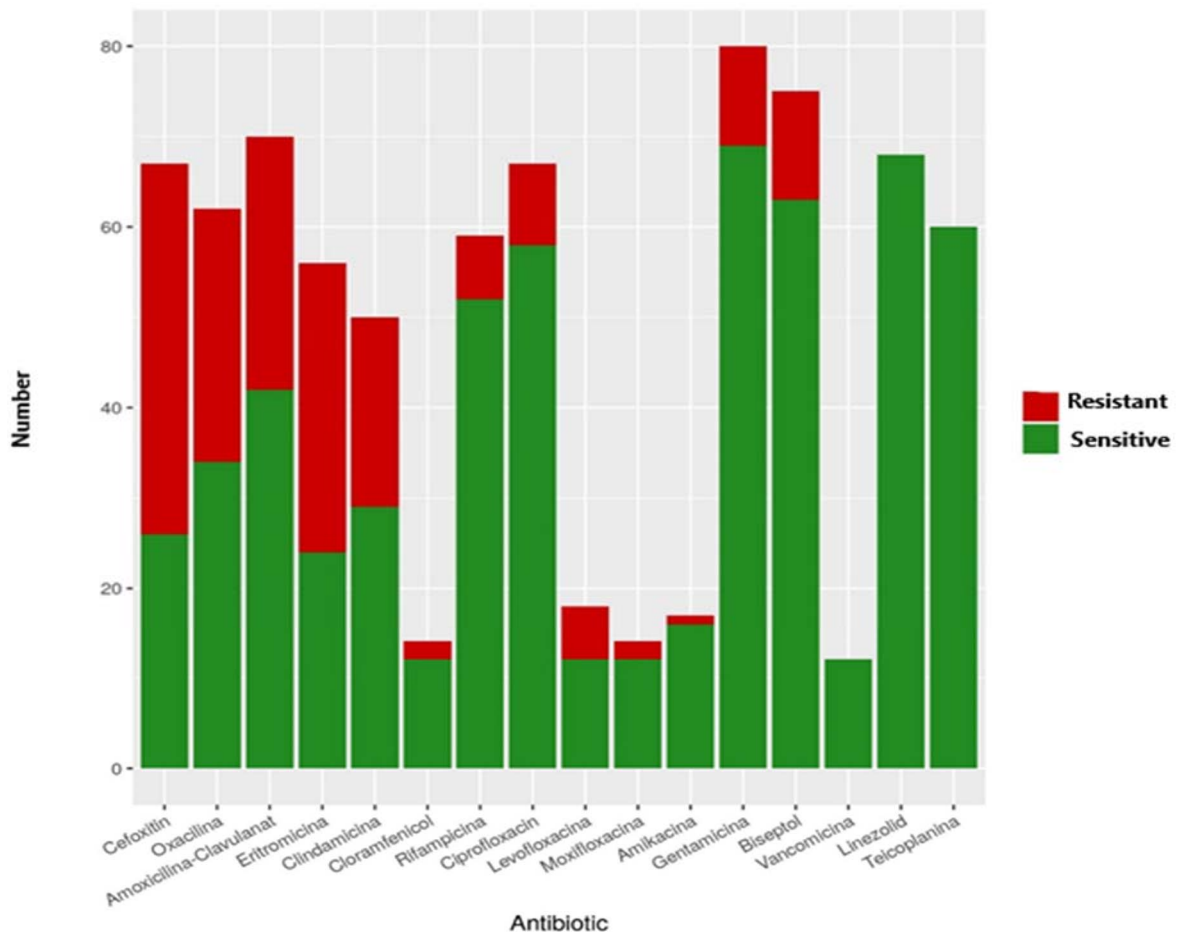


Fig. 4 Graphical representation of the number of staphylococci sensitive to the antibiotics tested. An uneven test of different antibiotics is noted

Enterobacteriaceae

Consistent to literature, pathogens following staphylococcus as incidence are *enterobacteriaceae*. In our study, the most common were 16 microorganisms of the genus *Klebsiella pneumoniae*, followed by 10 strains of *Escherichia coli*, 7 strains of *Proteus mirabilis* and 5 strains of *Serratia marcescens*.

E. coli is part of the enterobacteria with natural resistance group 1 - naturally susceptible to all antibiotics active on enterobacteria due to very poorly phenotypically expressed chromosomal cephalosporinase (e.g. natural resistance to Penicillin and Vancomycin, which does not cross the outer membrane).

In the case of isolates obtained from the patients included in the study, resistance to

the combination aminopenicillin-beta-lactamase inhibitor (amoxicillin-clavulanate) could be observed in one strain. In 4 other isolates, resistance to 2nd generation cephalosporins (cefuroxime) was identified. Preservation of susceptibility to 3rd-generation cephalosporins and the lack of synergy imaging between them and clavulanic acid showed that the strains were not producing extended-spectrum beta-lactamases (ESBL). All strains tested were susceptible to carbapenems. One isolate was resistant to fluoroquinolones (ciprofloxacin, levofloxacin). Resistance to trimetoprim-sulfometoxazole (Biseptol) was found in 5 cases (50% of the tested cases).

Proteus mirabilis is also part of natural resistance group 1. The isolates are

multisensitive, 4 strains being resistant to gentamicin. An isolate of *Proteus* that could not be identified up to the species level was only susceptible to meropenem, amikacin and piperacillin-tazobactam.

K. pneumoniae is an enterobacterium belonging to natural resistance group 2, being naturally resistant to aminopenicillins, due to a chromosomal penicillinase (90% of the isolates carrying the blaSHV gene), which is inhibited by clavulanic acid. Thus, in most cases, resistance to second-generation amoxicillin-clavulanate and cephalosporins is due to acquired resistance mechanisms. The presence of resistance to 3rd generation cephalosporins (ceftazidime) and the presence of an image of synergy between them and clavulanic acid, diagnoses strains producing ESBL. The presence of susceptibility to piperacillin-tazobactam combination as well as to imipenem with a single ertapenem-resistant isolate suggests either the presence of an impermeability mechanism associated

with overproduction of ESBL or acquired cephalosporinase (AmpC) or the presence of an isolated carbapenemase producer with low lytic activity type bla_{OXA-48-LIKE}, bla_{GES}, etc. Multiple strains show a first mechanism of resistance to fluoroquinolones being resistant to ciprofloxacin, only one strain to levofloxacin. Most strains were resistant to Bisepitol and Gentamicin. Amikacin retains bactericidal activity on 13 strains tested.

Serratia marcescens is part of group 3 of natural resistance, having an inducible chromosomal cephalosporinase and resistance to colistin. Practically, as we tested different molecules, we identified susceptibility maintained only to carbapenems (meropenem) and levofloxacin.

Enterobacter spp. is also part of group 3 of natural resistance. The isolates preserve susceptibility to the combination of ureidopenicillin-clavulanic acid inhibitor (piperacillin-tazobactam) and carbapenems. One isolate was resistant to Bisepitol.

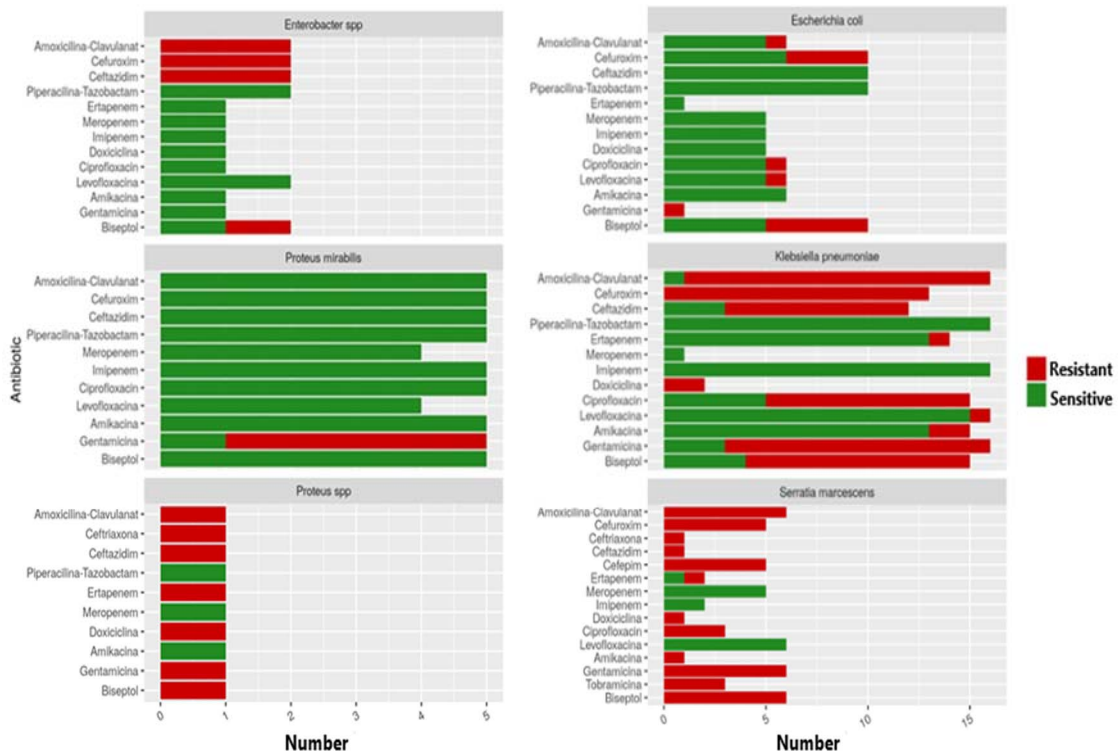


Fig. 5 Graphical representation of antibiotic resistance by species

Discussions

Curative surgeries for chronic or acute musculoskeletal disorders show a significant increase in accordance with technological developments and social status. As a result, two trends could be observed, which will most likely intensify in the near future. Traumatic pathology has two peaks of incidence. The first is represented by the young population, especially the male population, which is more frequently exposed to trauma by involvement in various risky actions, and the second peak is observed in very elderly patients who, due to osteoporosis or other associated pathologies, suffer fractures due to minimal trauma [8]. The other trend is determined by the evolution of stents that offer, by improving the surgical technique and the manufacturing method, an important benefit to elderly patients with locomotor deficit and chronic pain syndrome. Due to the increase in the number of surgeries and the number of implanted materials, the complications increase in direct proportion. Of these, peri-implant infections are among the most problematic, presenting a difficult and long-lasting treatment [9].

At present, the increasing number of antibiotic-resistant pathogens is a general problem of the medical system, for which a definitive solution has not been developed. In order to raise awareness of the problem, the World Health Organization (WHO) has proposed the acronym ESKAPE in reference to multidrug-resistant pathogens which, if left unchecked, could reach a stage that current treatments are ineffective [10].

Conclusions

Infections in the field of orthopedics and traumatology are a side of this specialty that, without a rapid diagnosis and the establishment of a targeted treatment, can produce disastrous effects, with implications

for both patients and health systems. This type of pathology is not very well documented, the number of publications on this topic is relatively limited in both Romanian and international literature.

The information presented in this study is consistent with that in literature both in terms of identified pathogens, their resistance and comorbidities and risk factors of patients who are most commonly identified with such a pathology.

Conflict of Interest statements

Authors state no conflict of interest.

Informed Consent and Human and Animal Rights statements

Informed consent has been obtained from all individuals included in this study.

Authorization for the use of human subjects

Ethical approval: The research related to human use complies with all the relevant national regulations, institutional policies, is in accordance with the tenets of the Helsinki Declaration, and has been approved by the authors' institutional review board or equivalent committee.

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