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11-year Surveillance of the Epidemiological and Bacteriological Profile of Osteoarticular Infections in Children

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Abstract: Osteoarticular infections are an important cause of morbidity and mortality in the pediatric age group. *Staphylococcus aureus* is the most frequently identified. Early adequate and multidisciplinary care is required. Recently, an increasing incidence of OAI has been related to the improvement of identification methods of microorganism. The aim of this study was to describe, over a period of 11 years, the epidemiological and bacteriological profile of pediatric osteoarticular infections. This retrospective study conducted at the Microbiology Department of the University Hospital of Marrakech over a period of 11 years (2010-2020) including all strains isolated from synovial fluid or bone or joint samples obtained from the pediatric orthopedic surgery department. Six hundred thirty-nine samples were analyzed. The positivity rate to bacteria was at 56,5%. The mean age was 6,5 years. The male gender was predominant with a sex-ratio at 2,65. Arthritis represented 60%. The main etiological agent was *Staphylococcus aureus,* followed by *Streptococcus Beta hemolytic* group A (13,3%). Strains of *Enterobacteriaceae* (EB) were resistant to third-generation cephalosporins by production of Extended Spectrum Betalactamase in 45% of cases. An early diagnosis and start of antimicrobial treatment are crucial for good patient outcome, as well as the control of the infectious focus. Cytobacteriological examination is essential in order to isolate the germ, to study its susceptibility to antibiotics.

Keywords: Arthritis, Pediatric, Bacterial Arthritis, Osteoarticular Infection, *Staphylococcus aureus*

1. Introduction

Osteoarticular infections (OAI) in children remain a growing problem associated with significant morbidity and mortality considering their potential for systemic aftereffects, since they can progress to irreversible orthopedic damages or sepsis [1]. Early adequate and multidisciplinary care is required [2]. Recently, an increasing incidence of OAI has been related to the improvement of identification methods of microorganism [3]. OAI are a frequent cause of hospital admission in pediatric orthopedics [4]. They can be divided into three types according to the source of infection: hematogenous; secondary to contiguous infection; or secondary to direct inoculation. The hematogenous OAI are the most common. *Staphylococcus aureus* remains the main bacterial cause of OAI in every age group of children, but other microorganisms can be incriminated, which vary with the patient's age, infection location, and clinical conditions. Bacterial identification and antibiotic susceptibility testing play an essential role in patient care and the control of antibiotic resistance [5, 6]. Several treatment protocols have

been published over the past decade [7]. The aim of this study was to describe, over a period of 11 years, the epidemiological and bacteriological profile (bacteria and antibiotic susceptibility) of pediatric osteoarticular infections isolated at the University Hospital of Marrakech.

2. Material and Methods

This retrospective study was conducted at the Microbiology Department of the University Hospital of Marrakech over a period of 11 years (2010-2020) including all strains isolated from synovial fluid or bone or joint samples obtained from the pediatric orthopedic surgery department.

The cytobacteriological study was carried out according to conventional methods with qualitative and quantitative cytology, direct examination and culture on enriched and selective media (blood agar, chocolate agar, Brain Heart infusion ‘’BHI’’ broth, Mac Conkey agar, Colombia CNA agar…) incubated in aerobic and anaerobic atmospheres. Liquid samples were systematically inoculated into blood culture bottles and incubated in BD Bactec*(Biomérieux).

Bacterial identification was made according to standard morphological, cultural, biochemical and antigenic characters. In some cases, the BioFire FilmArray® (Pneumonia panel), the Maldi-TOF-MS or BD Phoenix were also used for identification.

The antibiotic susceptibility test was performed by using disc diffusion or microdilution method and was carried out according to the standards of the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

We recorded for each sample: age, sex, department, isolated germ and its susceptibility to antibiotics. Statistical analysis and data entry was carried out by Microsoft office Excel 2007. The frequency of standard descriptive statistics such as mean and standard deviation were used to summarize patient characteristics.

3. Results

Six hundred thirty-seven samples were sent to the Microbiology Laboratory for cytobacteriological study. Among these samples, 356 were confirmed to be positive for Bacteria (55,8%, n=637). The mean age was 6,5 years with extremes ranging from 01 month to 16 years. The male gender was predominant with a sex-ratio (M/F) at 2,65.

Arthritis represented 59% (n=356) of cases followed by abscess under periosteum (21%, n=356), osteomyelitis (11%, n=356) and osteoarthritis (9%, n=356). (Figure 1)

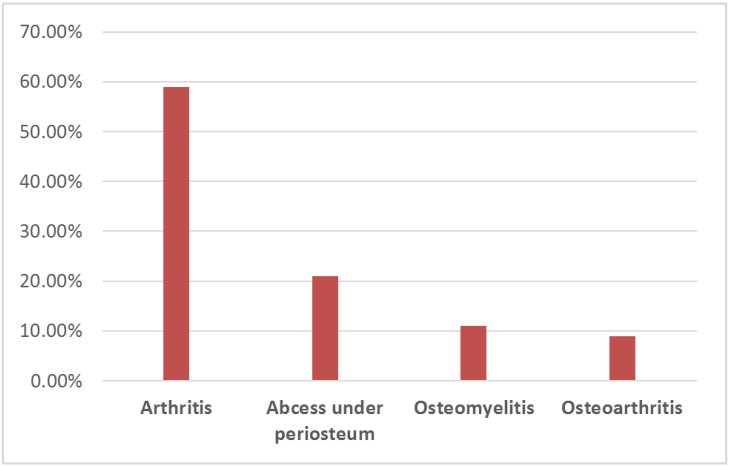

Figure 1. *Distribution of bone and joint samples according to the type of infection (n=356).*

The bacteriological profile was dominated by Gram positive bacteria in 75,5% of cases. While Gram negative bacteria were isolated in 24,5% of cases. (Figure 2)

The strains isolated were mainly represented by Staphylococcus aureus (52,2%), followed by Streptococcus Beta hemolytic group A (12,2%), Streptococcus pneumoniae (4,2%), non hemolytic Streptococcus (3%) and Enterococcus spp (2,2%).

Enterobacteriaceae represented 16,5% of isolates dominated by Enterobacter cloacae found in 6% of cases, followed by Klebsiella pneumoniae in 5% of cases, Escherichia Coli 3%, Salmonella spp 1,5%, Citrobacter spp 0,5% and Proteus mirabilis in 0.5%.

The non-fermentative gram-negative bacteria were isolated in 8% dominated by Pseudomonas aeuroginosa in 6% of cases. (Figure 3).

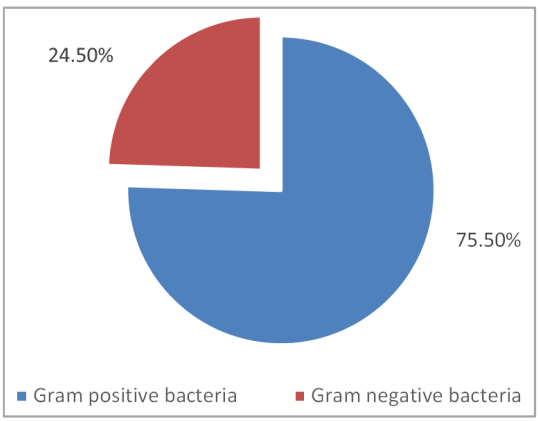

Figure 2. *Distribution of isolated bacterial species according to gram staining (n=361).*

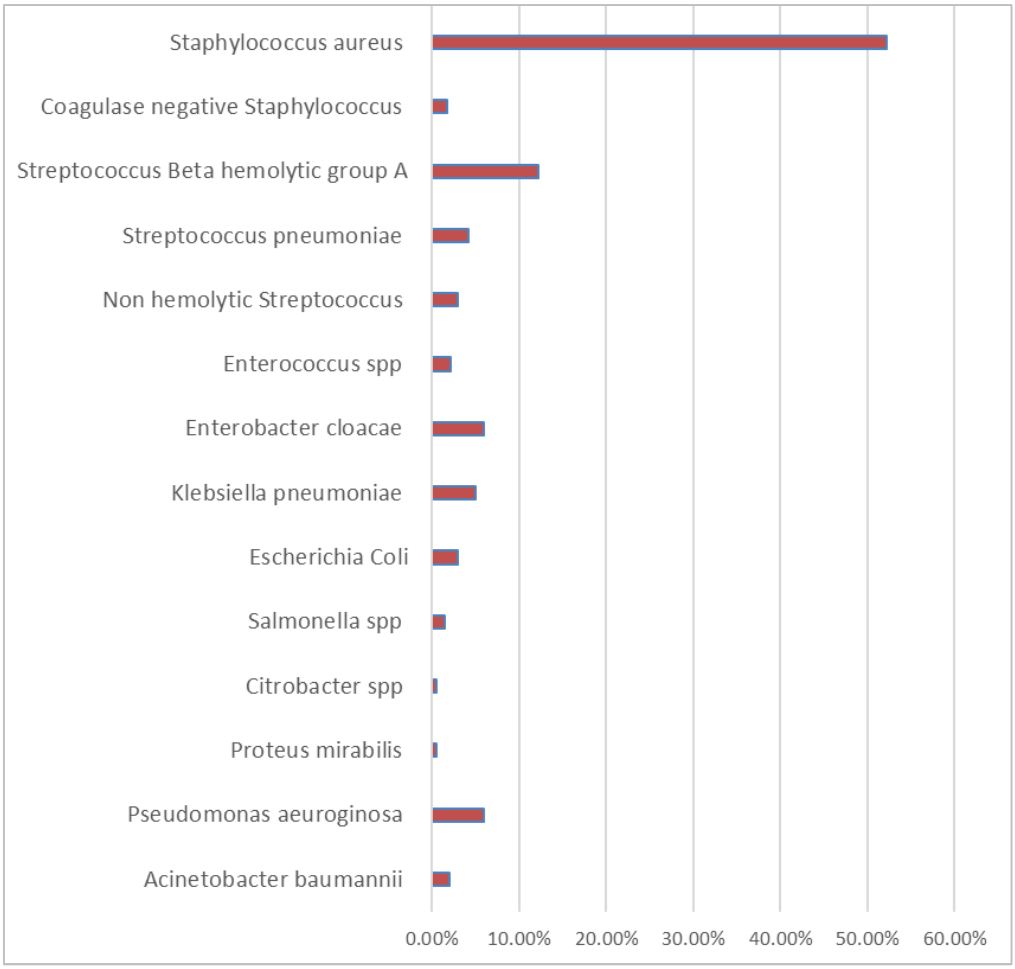

Figure 3. *Distribution of bacteria isolated from OAI in children at the University Hospital of Marrakech (n=361).*

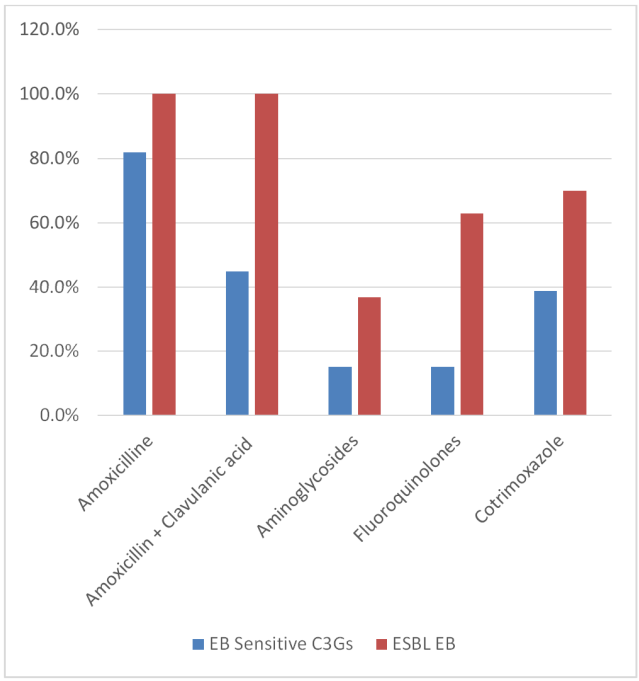

Figure 4. *Comparison of antibiotic resistance of EB species sensitive to C3Gs (n=33) and ESBL EB (n=27) isolated from OAI.*

Coagulase negative Staphylococcus (CNS) was found in 1,7% and acinetobacter baumannii (AB) in 2%. In Both cases, a nosocomial context and a multidrug-resistance have been described.

Strains of Enterobacteriaceae (EB) were resistant to third-generation cephalosporins (C3Gs) by production of Extended Spectrum Betalactamase (ESBL) in 27 isolates (45%, n=60) with high co-resistance to other antibiotics compared to strains sensitive to C3Gs. Within the antibiotics tested, all ESBL strains were resistant to Amoxicillin + Clavulanic acid, 37% of samples (n=27) were resistant to aminoglycosides, 63% to Fluoroquinolones, 70% to cotrimoxazole (Figure 4).

In our study, three molecules were used mainly: Penicillin M, amoxicillin associated to clavulanic acid and gentamycin. The combination of penicillin M and an aminoglycoside was the most used.

4. Discussion

Recognition of bone or joint infections in children is often difficult. The early initiation of appropriate medical and sometimes surgical therapy is necessary to minimize permanent damage [8]. The cornerstone of the diagnosis of

OAI is the identification of a microorganism from a bone, a contiguous anatomical structure or from a blood culture [9], but this is not always possible. Overall, cultures provide a microbiological diagnosis in only 30–80% of cases [10].

This study analyzed, over a period of 11 years, the epidemiological and bacteriological characteristics of OAI in children. The results showed male predominance which was also found in other series [4, 11, 12]. Similar data in relation to the mean age (6,5 years) was reported by other works [4, 13].

Bacteriology was positive in 55,8% of all samples, a result similar to those of Wang et al. [14] Trifaa et al. [4]. and Bonhoeffer et al. [12]. Other studies reported much lower percentage of positive cultures this may have been due to the large number of infections affected by prior antibiotherapy [15].

More than the half of the patients were diagnosed with arthritis (59%) in agreement with literature [4], followed by abscess under periosteum (21%), osteomyelitis (11%) and osteoarthritis (9%). The presence of septic arthritis did not differ between patients of different ages, peripheral osteomyelitis was predominant among patients under 50 years of age and vertebral osteomyelitis was more frequent in older patients. Overall, the pattern of OAI in younger patients reflected the predominance of native arthritis and peripheral osteomyelitis, whereas older patients had more prosthetic joint infections and vertebral osteomyelitis [3],

In our study, the main etiological agent of OAI in children was Staphylococcus aureus found in 52,9% of cases similar to most reports in litarature [4, 15-18]. No case of Haemophilus influenzae was detected unlike studies performed in the 1990's, where has been the most frequently isolated [19, 20]. This change in microbiological profile may be due to the spread of anti-Haemophilus b vaccination. Kingella kingae was not isolated in our study, unlike other works using specific real-time polymerase chain reaction (PCR) that found K. kingae occupying the first row [4, 21, 22]. This technique, by amplifying a gene specific to a bacterial cytotoxin, increases detection sensitivity.

Over the past years, the prevalence of nosocomial episodes of OAI significantly increased with a rise in multidrug-resistant bacteria. These trends should be considered when planning diagnostic and therapeutic guidelines for OAI [3]. In our work, multidrug-resistant Acinetobacter baumannii and Coagulase negative Staphylococcus were found respectively in 2% and 1,7% of all cases. AB and CNS infections are a significant proportion of nosocomial infections. Their sensitivity to currently used antibiotics is significantly decreasing, they are resistant against most antibiotics. Their Management is challenging issue with just a few remaining therapeutic options [23, 24].

In our study, 45% of Enterobacteriaceae were resistant to C3Gs by producing ESBL, which was higher than 22,09% reported in Telenchana-Chimbo P [25]. It has been associated to high co-resistance to other antibiotics compared to strains sensitive to C3Gs. That has serious consequences on infection control (use of broad-spectrum antibiotics) and hospital management of patients and hospital costs.

The basis of OAI treatment includes antimicrobial therapy and control of infectious foci. Generally, hospitalization is recommended for the start of parenteral antibiotic therapy and close monitoring of the case evolution. Empirical antimicrobial therapy should provide coverage for the main etiological agent according to the type of injury, clinical conditions, and patient age range [26]. In our study, the combination of penicillin M and an aminoglycoside was the most used, which covers the main etiological agent of OAI in our context: Staphylococcus aureus.

5. Conclusion

Osteoarticular infections are an important cause of morbidity in the pediatric age group and it is important to consider their diagnosis when appropriate. Staphylococcus aureus is the most frequently identified. Nosocomial infections remain a challenging problem, microbiological documentation is necessary to initiate adapted antibiotic therapy depending on the germ found. An early diagnosis and start of antimicrobial treatment are crucial for good patient outcome, as well as the control of the infectious focus.

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