Osteoarticular infections (OAI) are very common in children living in low- and middle-income countries, yet the bacterial aetiology and antibiotic susceptibility of OAI in children are not well described.

Methods.

The study included all patients who underwent surgery for OAI over a 3-year period, and those with organisms identified from tissue, pus, or blood. Duplicate cultures from the same patient were excluded if the organism and antibiotic susceptibility profiles were the same. Patients were categorised by age and class of infection (septic arthritis, acute osteomyelitis, fracture-related infection, postoperative sepsis and chronic osteomyelitis) and organisms were stratified accordingly.

Results.

We identified 132 organisms from 123 samples collected from 96 patients. Most cultured organisms were from children older than 3 years with acute haematogenous septic arthritis, osteomyelitis or both. Methicillin-sensitive *Staphylococcus aureus* accounted for 56% (n=74/132) of organisms cultured. The Enterobacteriales accounted for 17% (n=22/132) of organisms cultured, mostly in the fracture-related and postoperative infection groups. Of these, six each were extended-spectrum β-lactamase producers and AmpC producers, respectively. There were no carbapenemase-producing Enterobacteriales.

Conclusion.

Methicillin-sensitive *S. aureus* is the most common infecting organism in paediatric OAI and anti-staphylococcal penicillin is the most appropriate empiric treatment for haematogenous OAI in our environment. In fracture-related or postoperative infections, Enterobacteriales were more frequently cultured, and treatment should be guided by culture and susceptibility results.
testing. Identification and susceptibility testing of organisms were performed using the VITEK 2 automated system (bioMérieux, France), biochemical or antigen-detection methods and disc or gradient diffusion antibiotic susceptibility testing methods where appropriate. Results of antibiotic susceptibility tests were interpreted using the Clinical Laboratory and Standards Institute (CLSI) guidelines for the relevant year. In this review, antibiotic susceptibility was classified as either susceptible or non-susceptible, with the non-susceptible category including both the ‘intermediate’ and ‘resistant’ categories as defined by the CLSI guidelines.

For the analysis, OAs were divided into six categories: acute haematogenous septic arthritis, acute haematogenous osteomyelitis, acute haematogenous osteomyelitis and septic arthritis, chronic osteomyelitis, fracture-related infection and postoperative infection. Acute haematogenous infections were defined as infections that arose de novo with no predisposing injury or insult such as trauma or surgery. Fracture-related infection was defined as per the international consensus criteria. Postoperative infection was defined as infection arising at a previously sterile site following elective surgery. Patients were categorised into three age groups: those younger than 3 months, those between 3 months and 3 years and those who were 3 years and older. The age categorisation was based on published trends observed on the aetiology of OAs based on age in children.

Descriptive analysis was performed using Stata version 14.2 (StataCorp., USA) and Microsoft Excel (Microsoft Corp., USA). Categorical variables were described using absolute values and percentages.

Results

A total of 123 samples collected from 96 patients were included in the analysis. Patient ages ranged from 1 month to 15 years (mean=6.5 years) old. A total of 132 organisms were isolated from these samples (Table 1). The distribution of organisms based on infection and age categories is summarised in Tables 2 and 3, respectively. Most organisms were cultured from patients older than 3 years (81%; age categories is summarised in Tables 2 and 3, respectively. Most organisms were cultured from patients older than 3 years (81%; n=107/132) and those presenting with acute haematogenous septic arthritis, osteomyelitis, or both (83%; n=109/132), as defined by the CLSI guidelines.

Table 1. Summary of presenting characteristics of patients in whom organisms were identified

<table>
<thead>
<tr>
<th>Variables</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organisms identified</td>
<td>132</td>
</tr>
<tr>
<td>Age category</td>
<td></td>
</tr>
<tr>
<td>&lt;3 months</td>
<td>7</td>
</tr>
<tr>
<td>3 months - 3 years</td>
<td>18</td>
</tr>
<tr>
<td>&gt;3 years</td>
<td>107</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>79</td>
</tr>
<tr>
<td>Female</td>
<td>53</td>
</tr>
<tr>
<td>Type of infection</td>
<td></td>
</tr>
<tr>
<td>Acute haematogenous septic arthritis</td>
<td>50</td>
</tr>
<tr>
<td>Acute haematogenous osteomyelitis</td>
<td>43</td>
</tr>
<tr>
<td>Acute haematogenous osteomyelitis and septic arthritis</td>
<td>16</td>
</tr>
<tr>
<td>Fracture-related infection</td>
<td>13</td>
</tr>
<tr>
<td>Chronic osteomyelitis</td>
<td>6</td>
</tr>
<tr>
<td>Postoperative sepsis</td>
<td>4</td>
</tr>
</tbody>
</table>

Bacterial aetiology and antibiotic susceptibility of commonly isolated or clinically relevant organisms

*Staphylococcus aureus* (*S. aureus*) accounted for 56% (n=74/132) of isolates cultured across the whole cohort. During the study period, no methicillin-resistant *S. aureus* was isolated. All *S. aureus* isolates were also susceptible to the following non-β-lactam antibiotics: clindamycin, vancomycin, linezolid and ciprofloxacin. Forty percent of *S. aureus* isolates were resistant to trimethoprim-sulfamethoxazole.

Enterobacteriaceae were the second-most frequent cause of osteoarticular infection in our cohort, particularly in fracture-related infections (48%) and postoperative infections (50%), while only accounting for 17% (n=22/132) of all isolates. *Escherichia coli* (n=5) and *Enterobacter cloacae* (n=5) were the most frequently identified. Resistance to the β-lactam antibiotics due to AmpC-producing β-lactamases was identified in 6/22 (27%) isolates. Of these, all were susceptible to piperacillin-tazobactam, cefepime and trimethoprim-sulfamethoxazole, and five were susceptible to ciprofloxacin. Extended-spectrum β-lactamase (ESBL) producing Enterobacteriaceae accounted for 6/22 (27%) isolates. Of these isolates, only three were susceptible to ciprofloxacin and one to trimethoprim-sulfamethoxazole. Carbapenem-resistant Enterobacteriaceae (CRE) were not isolated in this cohort.

Bacterial aetiology and antibiotic susceptibility of infrequently isolated but clinically relevant organisms

Only 7/132 (5%) β-haemolytic streptococci were isolated. Of those, one was identified as *Streptococcus agalactiae* (Group B streptococcus) and, unsurprisingly, was isolated from an infant <3 months old. The rest were identified as *Streptococcus pyogenes* (Group A streptococcus). Three of these β-haemolytic streptococci were tested against and found to be susceptible to penicillin.

*Streptococcus pneumoniae* and *Haemophilus influenzae*, both of which have vaccines included in the childhood vaccination programme, were only isolated on one occasion each and both were tested against and found to be susceptible to penicillin and amoxicillin, respectively.

*Pseudomonas aeruginosa* was isolated in 2% of isolates (n=3/132), two were from fracture-related infections and one from chronic osteomyelitis. All were susceptible to the anti-pseudomonal β-lactam antibiotics piperacillin-tazobactam, cefazadime, cefepime, imipenem and meropenem and two were susceptible to ciprofloxacin.

![Fig. 1. Selection of patients eligible for inclusion in the analysis.](image-url)
Mixed cultures
Infections where more than one organism was identified were present in 13 patients, of whom seven had haematogenous septic arthritis. Six patients had underlying conditions predisposing to infection or poor healing, such as spina bifida, open fractures, postoperative infections, and despite relatively low numbers of these types of infection, this allowed a better understanding of the bacterial aetiology of these infrequent conditions.

In accordance with published data from high- and low-income countries, S. aureus was the most frequently isolated organism in our patients, regardless of age. Interestingly, no cases of methicillin-resistant S. aureus (MRSA) were identified. The incidence of MRSA osteoarticular infections in children has been reported to be as high as 40% in the USA and Australia,[12,14] and rates of 29% and 17% have been reported in Japan and Thailand, respectively.[15] India, in particular, has classified MRSA as an endemic infection, with studies reporting an incidence as high as 55%. In Africa, the reported incidence of MRSA is low, with many series also reporting no MRSA.[16] However, incidences of 9% and 15% have been reported in Tanzania and Tunisia, respectively.[17,18]

Kingella kingae (K. kingae) is considered the most frequent cause of osteoarticular infections in children between 3 months and 3 years of age.[18] Kingella is a fastidious, slow-growing Gram-negative bacillus that is difficult to culture using standard techniques. Positive cultures are more often obtained when inculcating samples into blood culture bottles. However, the gold standard for diagnosis is molecular methods, including PCR using specific gene targets from the K. kingae RTX toxin locus.[19] PCR testing for K. Kingae is not performed at our institution, which may explain why we had no cases of K. kingae in our cohort.

Enterobacteriales, which include Gram-negative enteric bacteria such as E. coli, E. cloacae, Salmonella species and Klebsiella pneumoniae, are known to be frequent causes of bone and joint infections in neonates and young children.[6,7] In our cohort, Enterobacteriales accounted for 17% of overall infections, but in patients older than 3 months. These children in our cohort tended to have infections secondary to fractures and trauma or prior surgery. However, the small number of cases precludes the identification of any definitive associations. Salmonella species was responsible for only three cases of osteoarticular infections in our cohort. This is in stark contrast to the published series by Lavy et al.[6] from Malawi, where Salmonella species accounted for more than 50% of culture-positive septic arthritis cases in their larger cohort of 204 children.

Antibiotic susceptibility for the Enterobacteriales varied. There were no CRE isolated in our group, but six isolates were ESBL producers and another six were AmpC β-lactamase producers, conferring resistance to widely used and available β-lactam antibiotics.

There are several limitations to our study. The retrospective study design and our method of patient identification may have been inadequate to identify all cases of OAI during the study period. The subgroups 'fracture-related infection' and 'postoperative sepsis' included only a handful of patients, precluding any definitive antibiotic

### Table 2. Organism frequency categorised by type of infection

<table>
<thead>
<tr>
<th>Infection type</th>
<th>Organism class in order of frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASA (n=50)</td>
<td>Staphylococcus aureus</td>
<td>48</td>
</tr>
<tr>
<td></td>
<td>Enterobacterales</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>β-haemolytic streptococci</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Coagulase-negative staphylococcus</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Bacillus species</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Other†</td>
<td>14</td>
</tr>
<tr>
<td>AHO (n=43)</td>
<td>Staphylococcus aureus</td>
<td>81</td>
</tr>
<tr>
<td></td>
<td>Bacillus species</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Enterobacterales</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>β-haemolytic streptococci</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Coagulase-negative staphylococcus</td>
<td>3</td>
</tr>
<tr>
<td>AHO and ASA (n=16)</td>
<td>Staphylococcus aureus</td>
<td>62</td>
</tr>
<tr>
<td></td>
<td>Enterobacterales</td>
<td>19</td>
</tr>
<tr>
<td></td>
<td>Coagulase-negative staphylococcus</td>
<td>13</td>
</tr>
<tr>
<td></td>
<td>Other†</td>
<td>6</td>
</tr>
<tr>
<td>Chronic osteomyelitis (n=6)</td>
<td>Staphylococcus aureus</td>
<td>67</td>
</tr>
<tr>
<td></td>
<td>Pseudomonas aeruginosa</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>β-haemolytic streptococci</td>
<td>11</td>
</tr>
<tr>
<td>Fracture-related infection (n=13)</td>
<td>Enterobacterales</td>
<td>46</td>
</tr>
<tr>
<td></td>
<td>Enterococcus species</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>Pseudomonas aeruginosa</td>
<td>15</td>
</tr>
<tr>
<td></td>
<td>Staphylococcus aureus</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>β-haemolytic streptococci</td>
<td>8</td>
</tr>
<tr>
<td>Postoperative infection (n=4)</td>
<td>Enterobacter</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Other†</td>
<td>50</td>
</tr>
</tbody>
</table>

ASA = acute haematogenous septic arthritis; AHO = acute haematogenous osteomyelitis.
†Acinetobacter, Enterococcus, Haemophilus influenzae, Streptococcus pneumonia, anaerobes.
†Sphingomonas paucimobilis.
†Streptococcus mitis, coagulase-negative Staphylococcus.

### Table 3. Organism frequency categorised by age group

<table>
<thead>
<tr>
<th>Age category</th>
<th>Organism class in order of frequency</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3 months (n=7)</td>
<td>Staphylococcus aureus</td>
<td>43</td>
</tr>
<tr>
<td></td>
<td>Streptococcus agalactiae</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Streptococcus pneumoniae</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Enterococcus faecalis</td>
<td>14</td>
</tr>
<tr>
<td></td>
<td>Coagulase-negative staphylococcus</td>
<td>14</td>
</tr>
<tr>
<td>3 months – 3 years (n=18)</td>
<td>Staphylococcus aureus</td>
<td>44</td>
</tr>
<tr>
<td></td>
<td>Enterobacterales</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Streptococcus pyogenes</td>
<td>11</td>
</tr>
<tr>
<td></td>
<td>Other†</td>
<td>23</td>
</tr>
<tr>
<td>&gt;3 years (n=107)</td>
<td>Staphylococcus aureus</td>
<td>58</td>
</tr>
<tr>
<td></td>
<td>Enterobacterales</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>Coagulase-negative staphylococcus</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td>Streptococcus pyogenes</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Bacillus species</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Enterococcus species</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Pseudomonas aeruginosa</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Other†</td>
<td>6</td>
</tr>
</tbody>
</table>

*Haemophilus influenzae, Pseudomonas aeruginosa, Acinetobacter baumannii, Bacillus species.
†Clostridium perfringens, Pseudomonas species, Sphingomonas paucimobilis, Streptococcus mutans.
recommendations. As we do not have access to PCR testing for **K. kingae**, we were unable to provide any information regarding this common pathogen.

**Conclusion**

Methicillin-sensitive **S. aureus** was the most frequently isolated organism causing haematogenous osteoarticular infections in our population. This was followed by a wide spectrum of Enterobacterales causing mostly fracture-related or postoperative infections. Empiric treatment of haematogenous OAI’s consisting of an anti-staphylococcal penicillin such as cloxacillin is still recommended. For postoperative or fracture-related infections, the addition of a β-lactam with broad Gram-negative activity against AmpC-producing and ESBL Enterobacterales and **Pseudomonas aeruginosa** is recommended, due to the high incidence of Gram-negative organisms seen in these groups. Identification of the causative organisms in OAI remains essential and once established, antibiotic regimens should be adjusted accordingly.

**Declaration. None.**

**Acknowledgements. None.**

**Author contributions. AH: Conceptualisation, data capture, write-up. CC: Data analysis. ML: Protocol development HT: Data analysis and oversight.**

**Funding. None.**

**Conflicts of interest. None.**


Accepted 23 August 2023.