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**RESEARCH**

# Clinical manifestations and outcomes of children with bone and joint infections

## Kemik ve eklem enfeksiyonları olan çocukların klinik bulguları ve sonuçları

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**Abstract**

**Purpose:** This study aimed to determine the clinical, laboratory, imaging, and bacteriological features of bone and joint infections in children and to identify their characteristic features for early diagnosis.

**Materials and Methods:** In this retrospective study patients diagnosed with osteomyelitis and septic arthritis, based on established guidelines, were included. We collected demographic, clinical, and imaging data, along with inflammatory markers and microbiological data, and any invasive procedures performed by orthopedic surgeons. We also reviewed the development of long-term sequelae, the duration of treatments, and the types of antibiotics used for both oral and parenteral therapy.

**Results:** The study group consisted of 25 patients with osteomyelitis, 10 with septic arthritis, and 5 with combined infection (osteomyelitis and septic arthritis). Inflammatory marker levels were abnormal in most children. The most commonly identified organism was the Staphylococcal species. Radiological findings compatible with bone and joint infections were detected in all patients whose magnetic resonance imaging results were available. Invasive procedures were performed in 44%, 90%, and 100% of the patients with osteomyelitis, septic arthritis, and combined infection, respectively.

**Conclusion:** Sensitivity increased when all the markers were used together. Magnetic resonance imaging considered the most informative imaging modality for bone and joint infections provided the highest sensitivity in our study. These sensitive indicators can be helpful for the early diagnosis and long-term follow-up of patients with unclear presentations.

**Keywords:** Children, osteomyelitis, septic arthritis

**Öz**

**Amaç:** Bu çalışmada çocuklarda kemik ve eklem enfeksiyonlarının klinik, laboratuvar, görüntüleme ve bakteriyolojik özelliklerinin saptanması ve erken tanı için karakteristik özelliklerinin belirlenmesi amaçlandı.

**Gereç ve Yöntem:** Retrospektif bu çalışmaya pediatrik osteomiyelit ve septik artritin tanı ve tedavisine ilişkin kılavuz kriterlerine göre osteomiyelit ve septik artrit tanısı alan hastalar çalışmaya dahil edildi. Hastaların demografik, klinik ve görüntüleme verilerinin yanı sıra inflamatuar belirteç düzeyleri ve mikrobiyolojik verileri, ortopedi uzmanlarının gerçekleştirdiği invaziv işlemler değerlendirilmiştir. Ayrıca uzun vadeli sekellerin gelişimi, oral ve parenteral tedavide kullanılan antibiyotik türleri ve tedavi sürelerini incelendi.

**Bulgular:** Çalışma grubunu 25 osteomiyelit, 10 septik artrit ve 5 kombine enfeksiyon (osteomiyelit ve septik artrit) hastası oluşturdu. Çoğu çocukta inflamatuar belirteçler anormal düzeylerdeydi. En sık tanımlanan organizma Stafilokok türleriydi. Manyetik rezonans görüntüleme sonuçları mevcut olan hastaların tamamında kemik ve eklem enfeksiyonları ile uyumlu radyolojik bulgular tespit edildi. Osteomiyelit, septik artrit ve kombine enfeksiyonu olan hastaların sırasıyla %44, %90 ve %100'üne invaziv işlemler uygulanmıştı.

**Sonuç:** Tüm belirteçlerin bir arada kullanılmasıyla tanıya yönelik sensitivitenin arttığı tespit edildi. Kemik ve eklem enfeksiyonlarında en bilgilendirici görüntüleme yöntemi olarak kabul edilen manyetik rezonans görüntüleme, çalışmamızda en yüksek duyarlılığı sağlamıştır. Bu hassas göstergeler, nonspesifik bulguları olan hastaların erken tanısında ve uzun süreli takibinde yardımcı olabilir.

**Anahtar kelimeler**: Çocuk, osteomiyelit, septik artrit

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## INTRODUCTION

Bone and joint infections (BJIs) in children are common causes of hospitalization and can lead to high morbidity and mortality. BJIs account for 1% of hospitalizations and frequently occur in children aged < 5 years[1]. BJIs can be classified into osteomyelitis (OM) and septic arthritis (SA). Children can be affected by both conditions. In both cases, prompt diagnosis and treatment are essential to achieve optimal results[2].

SA requires urgent treatment because delayed infection control can lead to long-term joint damage and, rarely, disseminated infection [3]. Pyogenic conditions of the joint space can be complicated by avascular necrosis and/or destruction of the articular cartilage. These potential complications include long-term sequelae, chronic arthritis, and joint replacement surgery[3,4]. Therefore, early SA diagnosis and effective treatment initiation are critical [3]. OM is a medical emergency with a risk of infection spread and rapid destruction of the bone [1]. It is caused by bacteria that can enter the bone hematogenous bone, direct inoculation by trauma or surgery, or local invasion due to concurrent infections [5]. In a recent study involving 23 pediatric patients with BJIs, it was observed that the presentation of ankle and foot BJIs often lacks specificity and has a subtle onset. Notably, complications in these cases included subperiosteal abscesses, underscoring the critical importance of early diagnosis[1].

*Staphylococcus aureus* is the most frequently cultured bacterium in children with osteoarticular diseases[3]. Nevertheless, routine cultures of blood and wound aspirates fail to identify any microorganism in up to 50% of cases[6]. In a retrospective analysis of children diagnosed with OM and SA, it was found that 42% of patients had no identified etiologic agent, while the most commonly detected pathogens in the other patients were *Staphylococcus aureus*, *Streptococcus pyogenes*, and *Streptococcus pneumoniae*[7]. In a recent pediatric study analyzing BJIs in children, 38% of patients had positive culture results, with synovial fluid and bone tissue showing the highest positivity rates[2].

BJIs of the knee, hip, and ankle are the most commonly affected [2], although any bone or joint can be affected[1]. A study involving nine pediatric patients found that those with SA in the shoulders experienced delayed diagnosis compared to those with hip infections. This delay in diagnosis can lead to complications and long-term effects[4].

There is a substantial knowledge gap in the current literature concerning the diagnosis of BJIs in pediatric patients with unclear clinical presentations. Distinguishing between BJIs and other conditions causing joint pain remains a challenging diagnostic dilemma. Delayed diagnosis can result in complicated infections, long-term complications, and prolonged antibiotic use[5].

The low positive culture rates observed in previous studies emphasize the significance of employing additional methods alongside microbiological analysis for early diagnosis of osteoarticular infections[6].

In light of these challenges, we hypothesized that inflammatory markers, microbiological analysis, and imaging methods collectively contribute to the diagnosis of BJIs in patients presenting with nonspecific joint pain. However, it is crucial to note that a single test may not be sufficient to reliably exclude bone or joint infections. The objectives of this study are as follows: 1) Identify methods that can aid in the early diagnosis and guide the diagnostic process of pediatric patients with BJIs presenting with nonspecific clinical findings 2) Investigate the clinical, laboratory, imaging, and bacteriological features of BJIs in children and identify distinctive characteristics for early diagnosis 3) Compare baseline characteristics, laboratory features, and durations of parenteral and oral treatments between SA and OM in pediatric patients 4) Evaluate treatment modalities for pediatric patients with BJIs by reviewing the current literature.

## MATERIALS AND METHODS

### Study population

We conducted a retrospective study using medical records and the hospital database of patients aged < 18 years diagnosed with OM and/or SA who were under the care of the pediatric infectious disease department at Sanlıurfa Training and Research Hospital between January 1, 2020, and January 1, 2023. Sanlıurfa Training and Research Hospital is the most comprehensive healthcare facility in Sanliurfa. The hospital has a dedicated capacity of 400 beds for pediatric patients, and the orthopedic department performs an average of 5,400 surgical procedures annually.

Patients with BJIs who were hospitalized and/or received follow-up care from the pediatric infection

department were included in this study. Inclusion criteria required the availability of electronic patient records, and patients needed to meet the following inclusion criteria.

Patients diagnosed with SA based on these criteria were included in this study [3]:

1. Clinical symptoms (fever, decreased ambulation, pain/sensitivity, erythema, swelling, and/or limited motion of the affected joint)
2. White blood cell (WBC) count of synovial fluid > 50 000/μL or positive culture of synovial fluid or blood

Patients diagnosed with the following diagnostic criteria of OM were included in this study [5].

1. History and physical examination findings suggesting bone infection, limited use of extremities, limping, refusal to walk, irritability, decreased appetite or activity with or without fever, localized pain, and swelling lasting a few days to a few weeks
2. Compatible laboratory results, compatible radiological imaging with a bone infection (bone marrow edema, abscesses, sequestrum formation, and cartilage destruction), and/or culture-confirmed histopathological examination and/or isolation of a pathogen from the blood, bone tissue, or abscess

Patients who did not meet the guidelines' diagnostic criteria were excluded from the study. This exclusion applied to patients who displayed clinical symptoms of SA but did not meet the synovial fluid WBC count criteria or did not test positive in cultures. Similarly, patients who exhibited clinical findings suggestive of OM but lacked supporting laboratory, microbiological, and/or culture-confirmed histopathological evidence were also excluded.

A retrospective analysis of medical files, imaging, and microbiological data was conducted by a pediatric infectious disease specialist to determine if the BJI criteria were met. Only cases that met these criteria were included in the study. Patients diagnosed with OM caused by *Brucella* spp were also excluded from this study. This decision was influenced by the high prevalence of brucellosis in the region, as well as the need for prolonged treatment for this unusual pathogen and management that could affect the study results. The flowchart displaying the selection process for patients is presented in Figure 1.

## Procedure

We gathered demographic data on the patients, recorded their clinical symptoms, and documented the affected bone and/or joint. Clinic information about the patients was extracted from medical notes authored by pediatric infectious disease specialists who were actively working at the hospital during the study period. These notes were electronically stored as patient records in the hospital database. Inflammatory markers, such as total WBC count, erythrocyte sedimentation rate (ESR) (normal range, 0–20 mm/h), and C-reactive protein (CRP) level (normal range, 0–5 mg/L), measured at admission were recorded.

Microbiological data from blood cultures, synovial and periosteal fluids, wounds, abscess aspirates, and bone tissues, including culture growth and antimicrobial susceptibility, were noted. In addition, the results of imaging modalities, such as magnetic resonance imaging (MRI), computed tomography (CT), and ultrasonography (USG), if performed, were summarized.

Invasive procedures performed by experienced orthopedic surgeons, needle aspiration, debridement or curettage, and implant removal were also recorded. We also reviewed the development of long-term sequelae, such as multifocal infections, pathological fractures, atypical bone growth, chronic OM, avascular necrosis, limited joint mobility, and the need for surgery at follow-up.

We also documented the duration of treatment and the specific antibiotics used for both oral and parenteral therapy. These treatment regimens were determined by the pediatric infectious disease specialist who was actively managing the patients during the study period.

The study was approved by the Harran University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (Approval date: 2023-02-20, number: HRÜ/23.03.23).

## Statistical analysis

All statistical analyses were performed using the SPSS version 25.0 software (IBM SPSS Statistics, Armonk, NY, IBM Corp.). Continuous variables are expressed as means ± standard deviations (SDs), medians ($25^{th}$–$75^{th}$ percentiles [interquartile ranges {IQRs}]), and categorical variables as numbers and percentages. The Shapiro–Wilk test was used to examine the

normal distribution. To analyze the data means with SDs were used for normally distributed variables, and medians with IQRs were used for non-normally distributed variables. If continuous variables were normally distributed, an independent sample t-test was used; for nonnormally distributed variables, the Mann–Whitney U test was used. Frequencies were used to summarize the categorical variables. Fisher's exact test was employed if any expected values were below 5. Statistical significance was set at $p < 0.05$.

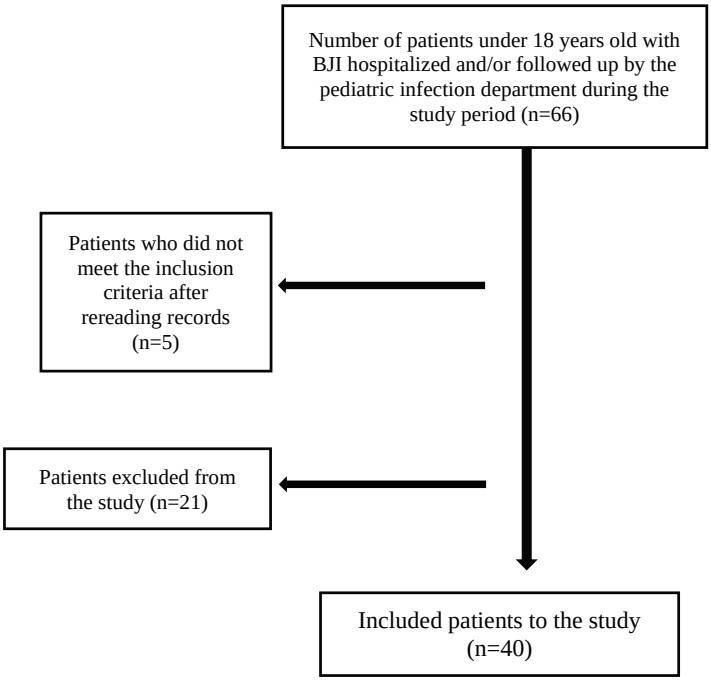


**Figure 1. Flowchart of the selection of the patients**

## RESULTS

Overall, 40 pediatric patients (12 girls, and 28 boys) were diagnosed with BJIs at our hospital between January 1, 2020, and January 1, 2023, were included in this study. The study group consisted of 25 patients with only OM, 10 with only SA, and 5 with both OM and SA. The children's ages ranged from 1 month to 17 years, with a mean of 7.5 ± 4.9 years. The median age of the patients with SA was 3 (IQR, 0.6–7.7) years, whereas that of the patients with OM was 9 (IQR, 6.5–13) years. There was a significant difference in favor of OM between the ages of patients with SA and OM ($p = 0.007$). The symptoms of the children included decreased walking ability, localized pain, redness, swelling, and/or limited motion of the affected joint. The most common symptom was localized pain, which was reported in 70% (n = 28) of the patients. Swelling of the affected site was reported in 52.5% (n = 21) of the patients. Functional impairment was observed in 55% (n = 22) of the patients, and local erythema was observed in 27.5% (n = 11) of the patients.

We reviewed the results of three inflammatory markers (total WBC count, ESR, and CRP levels) on the admission of patients with BJIs. The total WBC count on admission ranged from 2090– 27770/L, with a mean of 10561 ± 5285/L. The mean WBC count of patients with SA was 15182 ± 6546/L, whereas that of patients with OM was 8295 ± 3133/L. 80% of the patients with SA had high WBC count, and 33% of the patients with OM had high WBC count. A comparison of WBC count between patients with SA and OM was statistically significant ($p = 0.009$).

**Table 1. Baseline characteristics of 40 patients with only osteomyelitis, only septic arthritis, or a combination of osteomyelitis and septic arthritis and comparisons of the parameters between patients with only septic arthritis and only osteomyelitis**

| Variable | OM | SA | Combined infection (OM+SA) | Total | *p* value (OM vs. SA) |
|---|---|---|---|---|---|
| Number (%) | 25(62.5) | 10 (25) | 5 (12.5) | 40 | |
| Male *n* (%) | 18 (72) | 7 (70) | 3 (60) | 28 (70) | 0.884 |
| Female *n* (%) | 7 (28) | 3 (30) | 2 (40) | 12 (30) | |
| Med age (years) (iqr 25%–75%) | 9 (6.5-13) | 3 (0.6-7.7) | 6 (2-6.5) | 7 (4-12.5) | 0.007* (z= - 2.634) |
| Laboratory values on admission | | | | | |
| WBC number done | 24 | 10 | 5 | 39 | |
| Mean WBC ± s.d (/mm³) | 8295±3133 | 15182±6546 | 12102±4998 | 10561±5285 | 0.009* (t = 3.178) |
| CRP number done | 24 | 10 | 5 | 39 | |
| Med CRP mg/L (iqr) | 13.6 (2.8-55.6) | 74.1 (33.9-258) | 43.7 (24.2-258) | 34 (5.1-78.3) | 0.012* (z = - 2.495) |
| ESR, N done | 20 | 8 | 3 | 31 | |
| Med ESR mm/h (iqr) | 24 (12-63) | 63.5(35.5-85.2) | 59 | 41 (12-68) | 0.11 (z = - 1.603) |
| Treatment duration | | | | | |
| Med duration of IV therapy days (iqr ) | 8.5 (4-22.7) | 13.5 (9.2 -17.5) | 24.5 (8-44) | 12.5(6-21) | 0.461 (z = - 0.78) |
| Med duration of oral therapy days (iqr) | 37.5 (28.5-90) | 14 (10–24) | 28 (17.5- 52) | 30 (14-60) | 0.003* (z = - 2.865) |
| İmaging modalities | | | | | |
| MRI, number performed | 23 | 6 | 4 | 33 | |
| CT, number performed | None | None | 1 | 1 | |
| USG, number performed | None | 8 | 2 | 10 | |
| İmaging findings | | | | | |
| Skin and soft tissue changes | 10 | 3 | 2 | 15 | |
| Joint effusion and synovial swelling | None | 10 | 5 | 15 | |
| Bone and periost changes | 23 | None | 5 | 28 | |

OM: Osteomiyelitis; SA: Septic arthritis; OM+SA: Osteomiyelitis and septic arthritis; ;n: Number; WBC: White blood cell; CT: Computed tomography; USG: Ultrasonography; MRI: Magnetic resonance imaging; CRP: C-reactive protein, IV: Intravenous; ESR: Erythrocyte sedimentation rate; s.d: Standard deviation; Med: median; iqr: interquartile range (25%–75%)

*p < 0.05 statistically significant ;z: Mann-Whitney U test ; t: Independent samples t-test

The median ESR was 41 mm/h (IQR, 12–68). The ESR on admission ranged from 4–140 mm/h. Among patients with SA, 87.5% had high ESR levels. However, only 50% of patients with OM had high ESR levels. A comparison of ESR levels between patients with SA and OM was not statistically significant (p=0.11).

CRP level at presentation ranged from 0.13–421 mg/L, with a median of 34 (IQR, 5.1–78.3) mg/L. The initial CRP level was > 5 mg/L in 76.9% (30/39) of the patients. Upon admission, one patient had no available CRP information. In 18 of 39 (46.1%) patients, a CRP level > 50 mg/L was found. Elevated CRP levels were detected in 90% and 66.7% of the patients with SA and OM, respectively. The median CRP levels of patients with SA was 74.1 (IQR, 33.9-258), whereas that of patients with OM was 13.6 (IQR, 2.8-55.6) mg/L. A comparison of CRP levels between patients with SA and OM was statistically significant (p = 0.012).

Here, we reviewed the usefulness of the combined determination of inflammatory markers. Among the patients, both WBC and CRP were assessed, with at least one inflammatory marker testing positive in 82% of cases. Of the patients, both WBC and ESR were tested, at least one was positive in 70.5%. In the use of a combination of CRP and ESR, at least one of them was positive in 79.4% of cases. In 87% of the patients, at least one inflammatory marker tested positive when all three were simultaneously evaluated. A BJI diagnosis was established in six patients based on bacteriological and imaging modalities, although the inflammatory markers were at normal values. The baseline characteristics of the 40 patients with OM, SA, OM + SA and comparisons of the parameters between patients with only SA and only OM are shown in Table 1.

Long bones (humerus, femur, tibia) accounted for 46.6% (14/30) of the affected bones (OM, OM + SA). The large joints (shoulder, hip, knee) accounted for 93.3% (14/15) of the affected joints (SA, OM + SA). The distributions of the affected bones and joints are listed in Table 2. Microbiological analyses were performed on 30 patients using blood, synovial fluid, periosteal fluid, abscess aspirate, or bone tissue cultures. Of the 30 patients who underwent culture tests, 21 had positive microbiological results and 9 had culture-negative BJIs.

Blood cultures were performed in 36% (9/25), 50% (5/10), and 60% (3/5) of the patients with OM, SA, and OM + SA, respectively. Positive blood culture microbiology was detected in one, two, and one patient with OM, SA, and OM + SA, respectively.

Tissue culture (either bone biopsy or abscess culture) was performed in 60% (15/25) of patients with OM and was positive in 86.6% (13/15) of the patients.

The Staphylococcal species was the most frequently identified organism. Staphylococcal organisms were detected in 52.3% (11/21) of the patients with positive cultures. The most common Staphylococcal organism is *S. aureus*. Methicillin-resistant *Staphylococcus aureus* (MRSA) strains were the etiological agents in most children. The etiological organisms in patients with BJIs are shown in Figure 2.

Diagnostic imaging procedures (CT, USG, or MRI) were performed in 92% (23/25) of the patients with OM. For patients with both OM and SA and only SA, diagnostic imaging was performed in 100% of the patients. In 95% (n = 38) of the patients, at least one diagnostic imaging modality was used. USG was performed in 80% (8/10) of the patients with SA. All eight patients with SA who underwent USG revealed synovial swelling and joint effusion. During the study period, MRI was performed on 82.5% of the patients. All patients who underwent MRI showed signs consistent with those of bone infection. None of these imaging modalities were used in 5% of the patients. Patient diagnoses were determined based on the patients' clinical symptoms, inflammatory markers, and microbiological test results.

Invasive procedures were performed in 44% (11/25), 90% (9/10), and 100% of the patients with OM, SA and OM + SA, respectively. No surgical intervention was performed in a patient with SA in the metatarsophalangeal joint. Needle aspiration was performed in 90% (9/10) of the patients with SA and 40% (2/5) of the patients with OM + SA. Debridement or curettage was performed in 44% (11/25) of the patients with OM and 60% (3/5) of the patients with OM + SA. The implants were removed in 8% (2/25) of the patients with OM and 20% (1/5) of the patients with SA + OM. The two patients with OM underwent bone debridement and implant removal. The invasive procedures performed for osteoarticular infections are listed in Table 3.

**Table 2. The distribution of affected bones and joints**

| | İnfected Bones n (%) | İnfected Joints n (%) |
|---|---|---|
| **SA** | none | Knee 8 (80)<br>Hip 1(10)<br>MTP joint 1 (10) |
| **OM** | Femur 5 (20)<br>Tibia 4 (16)<br>Metatarsal bones 7 (28)<br>Talus 6 (24)<br>Calcaneus 6 (24)<br>Cuboid 2 (8)<br>Navicula 1 (4)<br>Metacarpal bones 1 (4) | none |
| **Combined infection (SA+OM)** | Femur 4 (80)<br>Humerus 1 (20) | Shoulder 1 (20)<br>Hip 2 (40)<br>Knee 2 (40) |

MTP: Metatarsophalangeal joint; OM: Osteomiyelitis; SA: Septic arthritis; OM+SA: Osteomiyelitis and septic arthritis; n: Number

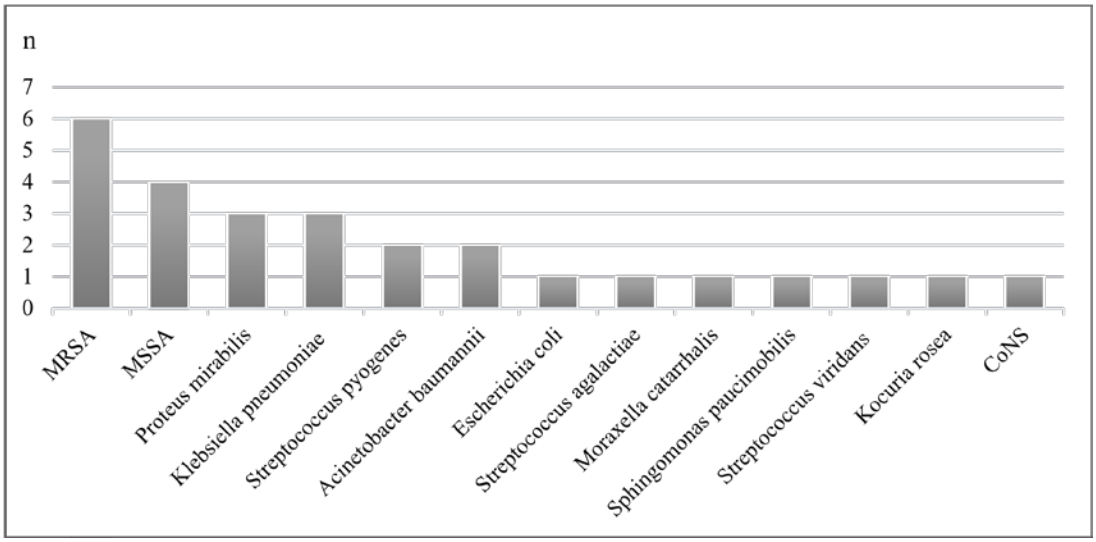


**Figure 2. The microbial growth in the cultures of patients with bone and joint infections**

CoNS: Coagulase-negative staphylococci ; MSSA; Meticillin-Sensitive Staphylococcus aureus , MRSA; Methicillin-resistant Staphylococcus aureus

**Table 3. Invasive procedures performed for bone and joint infections**

| **Procedure** | **OM**<br>***n* (%)** | **SA**<br>***n* (%)** | **OM+ SA**<br>***n* (%)** |
|---|---|---|---|
| Procedure performed | 11 (44) | 9 (90) | 5 (100) |
| Diagnostic biopsy/ needle aspiration | none | 9 (90) | 2 (40) |
| Bone debridement/curettage | 11 (44) | none | 3 (60) |
| Removal of implant | 2 (8) | none | 1 (20) |

OM: Osteomiyelitis; SA: Septic arthritis; OM+SA: Osteomiyelitis and septic arthritis; n: Number

SA was treated for 3 weeks, whereas acute OM was managed for 4-6 weeks (combining parenteral and oral antibiotics) following established guidelines [5]. Transition to oral therapy occurred in patients showing no fever, clinical improvement, or resolution of acute-phase reactants. Antibiotic discontinuation was based on improved clinical condition, imaging results, and normalization of inflammatory markers during follow-up. However, 49% of patients with OM received antibiotic treatment for >6 weeks, whereas 30% of SA patients were treated for >4 weeks.

In the study group, 50% of patients initially received empirical treatment with parenteral sulbactam ampicillin (SAM). Among these patients, 52.9% were also administered intravenous (IV) clindamycin and 5.8% were treated with a combination including teicoplanin. Other commonly used initial antibiotics included IV combinations of ceftriaxone-clindamycin (11.8%), teicoplanin-meropenem (5.9%), and vancomycin-ceftriaxone (8.8%). Following initial therapy with SAM and clindamycin, 44.4% of patients required a change to an alternative antibiotic combination due to culture results or clinical deterioration. These alternative combinations included therapies like teicoplanin-meropenem, vancomycin-meropenem, colistin-meropenem, and linezolid-meropenem. Patients with BJIs had a median duration of IV therapy of 12.5 days (IQR, 6-21). Those with OM had a median IV treatment period of 8.5 days (IQR, 4-22.7), while patients with SA had a median of 13.5 days (IQR, 9.2–17.5). Patients diagnosed with combined infections (OM and SA) had the lengthiest median IV treatment treatment duration, 24.5 days (IQR, 8-44). Although patients with only OM had a shorter median IV antibiotic treatment compared to only SA or OM + SA, this difference did not attain statistical significance ($p = 0.461$ and $p = 0.17$, respectively).

The most commonly prescribed oral discharge medication was amoxicillin-clavulanate (82.3%), with 10.7% combined with ciprofloxacin and 3.5% combined with trimethoprim/sulfamethoxazole (TMP-SMX) based on culture results. Patients with OM had a median duration of oral medication therapy lasting 37.5 days (IQR, 28.5-90), whereas SA patients had a median duration of 14 days (IQR, 10–24). Patients with combined infections had a median oral antibiotic treatment duration of 28 days (IQR, 17.5- 52). Patients with only OM received a longer median duration of oral antibiotic treatment compared to those with only SA or OM + SA ($p = 0.003$ and $p = 0.12$, respectively). During long-term follow-up, three patients developed chronic OM caused by MRSA, with one requiring reoperation.

## DISCUSSION

At initial examination, the diagnosis of osteoarticular infection is often uncertain. Strong clinical suspicion and careful observation are required for diagnosis[2]. Our study allowed us to compare inflammatory markers, microbiological analysis, imaging findings, disease location, and invasive procedures performed to identify the characteristic features for the early diagnosis of pediatric BJIs.

Our study found that patients diagnosed with SA were more likely to be in a younger age group compared to those diagnosed with OM. This is in line with recent findings from a ten-year pediatric study[8].

Localized pain was the most common clinical feature in our study. Similar to those of other studies, other clinical findings include decreased activity, skin and soft tissue changes, and joint effusions[2].

We found that inflammatory indicators could assist in the diagnosis of BJIs in our patients. Our findings indicate that sensitivity increases when all markers are combined. Our analysis revealed that incorporating numerous inflammatory markers into the diagnostic process significantly improves its accuracy. When a CRP test is combined with WBC count elevation, other diseases that may be associated with joint pain can be ruled out[2]. We observed that all patients diagnosed with SA had elevated CRP levels. A previous study showed that a negative CRP level could be a reliable indicator for ruling out SA. If a patient's CRP level was < 1 mg/dL, 87% was unlikely to have SA [7]. Monitoring CRP levels and ESR can help assess the effectiveness of therapy for BJIs[5,7]. An increase in CRP levels after the fourth day of medical therapy may indicate a complication, such as the need for additional surgical intervention[9]. Using ESR and CRP together can improve the sensitivity and negative predictive value of OM detection in children. However, ESR may not be a reliable diagnostic marker for acute infections because it increases slowly[5]. As observed in our study, six patients with a normal range of inflammatory markers were diagnosed with BJIs, proving that normal inflammatory indicators do not consistently exclude BJIs. Consistent with our findings, recent research shows that CRP alone may not be effective

in diagnosing BJIs, as 15.5% of children with BJIs had a baseline CRP of ≤10 mg/dl. Other diagnostic tests are important for accurate diagnosis[10].

Imaging techniques play an important role in the diagnosis of BJIs[2,5]. USG can accurately detect joint effusion and has an excellent negative predictive value[2,9]. The majority of our patients with SA who underwent USG revealed synovial swelling and joint effusion. Similarly our findings, in a recent pediatric study, USG findings were observed in 91% of children with SA[9]. All of our patients exhibited MR findings suggestive of osteoarticular infection, such as bone marrow edema, abscesses, sequestrum formation, and cartilage destruction. Consistent with the findings of other recently published studies, MRI showed the highest sensitivity in our study[5].

In our study, microorganisms were consistently identified in about half as many of the patients which is consistent with a recent study[8]. Similarly, children with BJIs have a microbiological confirmation rate of 58–65%[2,5]. In our study group, a quarter of the patients did not undergo microbiological analysis, which could explain the infrequent detection of bacteria. The positivity rate for blood cultures in our patients was low, which has also been observed in previous studies, with rates ranging from 17–31%[5,11]. The rate of pathogen identification in OM and SA greatly differs depending on the location of the infection, the detection method for bacteria, and the specific area where the study was conducted[5,12]. Identifying the pathogen in OM and SA is useful for diagnosis and the treatment and selection of the appropriate oral therapy after parenteral therapy[5]. A previous study reported that the rate of pathogen detection in synovial fluid cultures from patients with SA was 21% [12]. Our study showed that less than half of the patients with SA had positive synovial fluid culture results. However, positive tissue culture microbiology results (bone biopsy or abscess culture) were observed in the majority of the patients with OM. A meta-analysis of children with OM reported that the microbiological growth rate in bone biopsies was 65% [5]. The difference in microbiological analysis results between patients with OM and SA is possibly attributed to the fact the synovial fluid contains substances that can prevent the growth of bacteria in standard cultures[13].

Our study suggests that combined infections (OM + SA) are observed more frequently. Some patients with clinically suspected SA were diagnosed with OM + SA based on the MRI results in the present study. The pathogenic mechanisms involve pathogens entering the joint from the metaphysis of the bone through the transphyseal arteries[8]. Based on the results of previous studies, MRI should be consistently performed in all patients with clinical signs of osteoarticular infection to detect combined infections[9]. This is important for the treatment of BJIs, because if children with SA have concomitant OM and/or periosteal abscesses, surgery may be required at admission[14]. Delayed surgical treatment (> 4 days) can lead to long-term sequelae associated with BJIs [5].

The most common cause of SA and OM in pediatric patients of all ages is *S. aureus*[5]. In our study, *S. aureus* isolates were detected in almost half of the patients with positive specimens, and the majority of them were methicillin-resistant. The detection of pathogenic bacteria, such as *MRSA*, *Acinetobacter baumannii*, multidrug-resistant *Klebsiella pneumonia*, and *Kocuria rosea*, at varying frequencies in our patients is of concern. The patient with culture growth of multidrug-resistant *Klebsiella pneumonia* had a long hospitalization history at a different medical facility. This increase may have resulted from the procedures implemented. Our results highlight that coverage of the initial antibiotic regimen should be considered on a case-by-case basis, considering the patient's medical and hospitalization history. Rare organisms and nosocomial pathogens should be considered in patients with a complicated clinical course and risk factors. *Kingella kingae*, a common cause of BJIs in young children (aged < 5 years), rarely grows on standard agar plates. This pathogen may be a major cause of culture-negative SA and OM in this age group[3]. The rate of culture-negative BJIs was 30% (9/30), and the incidence rate of *K. kingae* was not determined in our study because the real-time polymerase chain reaction (RT-PCR) technique could not be used owing to inadequate conditions in our hospital.

SA infections can typically be treated in 2-3 weeks, whereas OM may require a treatment duration of 3-4 weeks. Nevertheless, the duration of the treatment may vary depending on the etiologic agent and the patient's response[5,9]. However, some of our patients had longer IV and total treatment durations because of the growth of unusual bacteria in cultures, the presence of complicated osteoarticular infection, and patients' clinical conditions. The patient with OM and a periosteal abscess had the longest treatment duration, lasting 4 months. Generally, patients with

OM received a shorter duration of parenteral antibiotics compared to other patient groups. Recent studies have analyzed the safety of shorter treatment periods for OM, with some suggesting that a brief IV treatment phase lasting 2-4 days can be followed by oral therapy[15]. A recent French study showed that advances in microbiological diagnosis and shorter antibiotic regimens have resulted in shorter hospital stays without an increase in complications[16]. However, concerns persist about transitioning to oral therapy too early, and larger patient studies are required[15]. Our OM patients in the study group were older than SA patients, which may have influenced the faster transition to oral treatment, possibly due to better oral therapy tolerance.

The European Society for Pediatric Infectious Diseases recommends continuing with an oral antibiotic that is similar to the IV treatment class for culture-negative infections. In regions with a high prevalence of MRSA, clindamycin/TMP-SMX ± cephalosporin is suggested, while regions with low MRSA prevalence may consider first/second-generation cephalosporin or amoxicillin–clavulanate [17]. The high rate of MRSA in our study group may provide guidance in the selection of oral antibiotics for culture-negative BJIs in our region.

Joint aspiration is a key component of the diagnosis and treatment of SA. The majority of the patients with SA underwent needle aspiration in this study because drainage and lavage are required to reduce the pressure on the joint space and remove inflamed tissue to protect the synovium [17]. In this study, in patients with OM, the indications for surgery were large involvement of the bone and soft tissues that necessitated debridement of the infected area and removal of the infected implant. The high rate of surgical procedures used to provide samples and ensure source control in our study group may have contributed to a better prognosis and fewer long-term sequelae.

The associated risks for worse outcomes reported in patients with BJIs were hip, knee, or ankle locations, recurrence of abscess, pyomyositis, and presence of MRSA OM[18]. Similarly, the causative pathogen in our patients who developed complications, such as chronic OM, was MRSA. Methicillin resistance is associated with a complicated clinical course of osteoarticular infections[5,18]. The prevalence of methicillin resistance in community-acquired Staphylococcal infections varies according to the region; therefore, epidemiological factors should also be considered when deciding the coverage of the first-line antibiotic regimen[5].

The present study has several strengths, and its findings hold substantial relevance for clinicians who treat pediatric patients with BJIs. However, it is important to address its main limitations. The study had a limited sample size as it relied on retrospectively collected data from a single center. Certain detailed analyses, such as RT-PCR, could not be performed due to inadequate facilities at our hospital.

In conclusion, combining all the inflammatory markers resulted in increased sensitivity. Considered the most informative imaging modality for BJIs, MRI provided the highest sensitivity in our study. Advanced diagnostic techniques can prevent delayed surgical intervention. Obtaining accurate microbiological specimens is crucial to effectively manage BJIs. Blood and tissue cultures can help identify the causative agent, facilitate the use of targeted antibiotic therapies, and reduce the need for treatment modifications. As the inclusion of microbiologic analyses plays a pivotal role in achieving the most accurate diagnosis and treatment of BJIs, further studies employing advanced testing methods like RT-PCR could offer more precise insights into the involvement of organisms that do not readily grow in standard cultures and their contribution to BJIs. Conducting multicenter studies involving BJIs in various hospitals across the country would be beneficial to augment the sample size. Further research is warranted to reduce hospitalization durations and the need for parenteral therapy in BJI cases, as well as to assess the efficacy of exclusive oral treatment.

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