Characteristics of bone and joint infections in paediatric patients complicated with disseminated sepsis

Syed Baasit Shafi Shah, Amber Bashir Mir and Iram Ali

DOI: https://doi.org/10.22271/ortho.2022.v8.i1d.3028

Abstract

Background: The bone and joint infections in the pediatric population account for one of the major causes of childhood morbidity and when complicated with sepsis, the results can be devastating. Hence the timely diagnosis and appropriate treatment are cardinal to minimize complications and improve outcomes. This study aims to evaluate the prevalence of septic arthritis and osteomyelitis in children with sepsis, the organisms implicated, and their antibiotic sensitivities.

Patients and Methods: During one year period 21 patients with bone and joint infection complicated with sepsis, severe sepsis, and septic shock were included in our study. Demographical details were collected from these patients with clinical features suggestive of septic arthritis and acute osteomyelitis, after proper clinical examination and appropriate investigations.

Results: Twenty-one patients with bone and joint infections complicated with sepsis, severe sepsis, and septic shock were included of which 13 patients were males and 8 were females. The median age at presentation was 6.7 years. The median interval between symptom onset and hospital admission was 8 days. Septic arthritis was seen in 14 patients, and osteomyelitis was seen in 7 patients. Multiple sites were involved in 2 patients. The most common joint was the knee (28.5%) followed by the hip (19%), and the most common bone involved was the femur (23.8%) followed by the tibia (9.5%). C-reactive protein (CRP) was raised among all patients with a median of 96 mg/L (range 48-170 mg/L). 14 [66.6%] cases were culture positive and Staphylococcus aureus (MRSA) was detected either in their blood or aspirate in 12 [85.6%] of such patients.

Conclusion: Acute osteomyelitis and septic arthritis are relatively common serious bacterial infections that can progress to disseminated sepsis and septic shock. A multidisciplinary approach including the consideration of combined medical and surgical management should be considered in these patients.

Keywords: Disseminated sepsis, acute osteomyelitis, septic arthritis, Methicillin-resistant staphylococcus aureus

Introduction

Pediatric bone and joint infection account for one of the major causes of childhood morbidity and mortality, with the incidence being up to 200 for osteomyelitis and 10-20 for septic arthritis per 1 lakh individuals in developing countries and mortality of up to 1% and morbidity up to 29%. [1, 2, 3].

In children, these infections are most often caused by the dissemination of the pathogenic bacteria through blood [3]. Acute osteomyelitis [AO] can be a devastating disease unless it is diagnosed promptly and treated appropriately [3]. Septic arthritis [SA] causes morbidity due to the destruction of articular cartilage and underlying epiphysis with long-term complications [4]. Timely diagnosis and appropriate treatment are cardinal to minimize complications and improve outcomes.

Staphylococcus aureus is an important cause of AO and Septic arthritis in children and is incriminated as an important cause of disseminated sepsis [5, 6] which has led to significant mortality and morbidity in the pediatric age group. The emergence of Methicillin-resistant Staphylococcus aureus (MRSA) has become a challenge in deciding the empirical treatment in such patients. Limited data is available from our region regarding acute bone and joint infection [AO and Septic arthritis] that complicates as disseminated sepsis and shock in children.
Materials and Methods
Our study was a prospective study conducted in the tertiary care hospital of Kashmir. All the children admitted from October 2018 to October 2019 who had any form of acute bone and joint infection [AHO and SA] complicated with sepsis, severe sepsis, and septic shock were included in our study.
Sepsis is a systemic inflammatory response syndrome due to infection. Severe sepsis is defined as sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Septic shock is defined as hypoperfusion and hypotension despite adequate resuscitation [7]. Demographical details were collected and patients with clinical features suggestive of septic arthritis (fever, general malaise, painful joint motion) and acute osteomyelitis (fever, general malaise, local pain, and tenderness) during their entire stay in hospital were considered after appropriate clinical examination and investigation.
All the patients were subjected to a panel of blood tests including complete blood count, Kidney function test, Liver function test. Septic panel including C-Reactive protein, ESR, and blood culture. Bone and/or joint aspiration was done, and aspirated material was sent for gram stain, aerobic bacterial culture, TB culture, and fungal culture, and sensitivity. Roentgenograms and an ultrasonographic examination were carried out as per indication. Patients with severe sepsis and septic shock were managed in the Intensive care unit of our hospital. Specific management included antimicrobial therapy, thorough surveillance to search for collections and their surgical drainage. Supportive care included maintenance of blood pressure, fluid and electrolyte balance, analgesia, prevention of bed-sores, physiotherapy, asepsis, and early enteral nutrition [8].
As per the institutional protocol, empirical antibiotic therapy included a combination of intravenous vancomycin and ceftriaxone. Empiric use of Glycopeptide Antibiotics in children with disseminated sepsis is because we have a high incidence of Methicillin resistance staphylococcus aureus in an intensive care unit.

Results
During the defined period of one year from 21 patients with bone and joint infection complicated with sepsis, severe sepsis, and septic shock were admitted to our hospital of which 13 patients were males and 8 were females. The median age at presentation was 6.7 years [IQR 6.3-8.6 years]. The median interval between symptom onset and hospital admission was 8 days [IQR 6-11.5]. The predisposing injury was present in 5 (23.8%) patients (3-trauma and 2-skin infection /cellulitis). Patients had a history of non-significant trauma to the extremities. [Table 1]

Table 1: Demographic profile of patients

| Male | Female |
|------|--------|
| N=13 | N=8 |
| The median age of presentation | 6.7 years [range 6.3-8.6 years] |
| The median time between the onset of symptoms and treatment | 8 days [range 6-11.5 days] |

| Predisposing factors | Non-significant trauma | skin abscess / boil/cellulitis |
|----------------------|------------------------|-----------------------------|
| 5 (23.8%) | 3 (14.2%) | 2 (9.5%) |

Thirteen patients had fever on presentation. Local symptoms of decreased joint movements and pain was seen in 11 patients. Swelling and redness and warmth were the presentation at admission in 5 patients each. Predominantly systemic manifestation with generalized malaise was present in 8. Hypotension with cold extremities was present in 2 patients whereas another 2 patients were admitted with altered sensorium. [Table 2]

Table 2: Presenting signs and symptoms of patients

| A. Fever | 13 |
|----------|----|
| B. Local signs and symptoms | |
| 1. Decreased range of movements, painful movements | 11 (52.3%) |
| 2. Redness and warmth | 5 (23.8%) |
| 3. Localized swelling | 5 (23.8%) |
| C. Systemic signs and symptoms | |
| 1. Generalised malaise and fatigue | 8 (38.1%) |
| 2. Altered sensorium | 2 (9.5%) |
| 3. Hypotension | 2 (9.5%) |

Septic arthritis was seen in 14 patients, and osteomyelitis was seen in 7 patients. Multiple sites were involved in 2 patients. The most common joint was the knee (28.5%) followed by the hip (19%), and the most common bone involved was the femur (23.8%) followed by the tibia (9.5%). [Table 3]

Table 3: Pattern of Musculoskeletal involvement

| 1. Osteomyelitis | 7 (33.3%) |
|-----------------|----------|
| a) Femur | 5 (23.8%) |
| b) Humerus | - |
| c) Tibia | 2 (9.5%) |
| 2. Septic arthritis | 14 (66.6%) |
| a) Hip | 4 (19%) |
| b) Knee | 6 (28.5%) |
| c) Shoulder | 1 (4.7%) |
The median total leukocyte count (TLC) was 18,970/mm³, with interquartile range [13,400 -22,750]. C-reactive protein (CRP) was raised among all patients with a median of 96 mg/L (range 48-170mg/L). The median erythrocyte sedimentation rate was 44mm/hr [range 23.5 – 49]. [Table 4].

**Table 4:** Septic screening /laboratory parameters of all patients [N=15]

| Parameter                | Value          |
|--------------------------|----------------|
| Total leucocyte count    | 18,970 (median) |
| Platelet count           | 2,50,700       |
| C reactive protein       | 96 mg/dl (median) |
| ESR                      | 44 mm/hr       |

The microbiological confirmation was obtained by performing blood culture and culture of the aspirate. 14 [66.6%] cases were culture positive of which 7 [33.3%] had positive culture of aspiration fluid.5 [23.8%] patients had microbial growth in blood and in 2 patients [9.5%] organisms were isolated both from blood and aspiration fluid.[Table 4]. Staphylococcus aureus (MRSA) was detected either in their blood or aspirate in 12 [85.6%] patients. Escherichia coli and Coagulase-negative Staphylococcus Aureus was isolated in 1 [7.1%] patient each.

**Table 4a:** Microbiological confirmation

```
| Parameter                  | N =21 [%] |
|----------------------------|-----------|
| Blood culture positive     | 5 [23.8%] |
| Joint culture positive     | 7 [33.3%] |
| Both blood and joint culture positive | 2 [9.5%] |
| Culture negative           | 7 [33.3%] |
```

**Table 4b:** Microbiological distribution

```
| Organisms                   | N = 14 [%] |
|-----------------------------|------------|
| Methicillin-Resistant Staphylococcus Aureus (MRSA) | 12 [85.7%] |
| Escherichia coli            | 1 [7.1%]  |
| Coagulase-negative Staphylococcus Aureus | 1 [7.1%]  |
```

**Treatment**

All the patients received intravenous antibiotic therapy. Empiric antibiotics were vancomycin and a third-generation cephalosporin. Our intensive care unit has a very high incidence of oxacillin resistance henceforth vancomycin is started empirically. The average duration of intravenous antibiotics was 4 to 6 weeks. Intravenous antibiotics were stopped depending on the improved clinical parameters such as fever, improved joint range of motion, and reduced inflammatory markers like TLC, ESR, and CRP. After IV antibiotics, oral antibiotics were given for 2 weeks. Intravenous inotropes and fluid resuscitation were done for patients presenting with hypotension and shock as per protocol. Four patients were on ventilatory support of which 3 were extubated and 1 patient expired due to disseminated sepsis. In one patient with coagulase-negative staph sepsis echocardiography revealed large vegetation and was managed as infective endocarditis. Surgical intervention was done in 19 patients that included arthroscopy of the affected joint and incisional drainage with bone drilling in cases with acute osteomyelitis.

**Discussion**

Despite many studies of septic arthritis and osteomyelitis in children, there is a paucity of studies regarding the clinical profile and risk factors that lead to disseminated sepsis in these children.

Our study confirms epidemiological data previously well described in the literature [9]: AO and septic arthritis is more commonly reported in males and young children, and the patient's history is commonly positive for a recent trauma or a febrile episode. In our study, the median age of presentation is 6.7 years which is in concordance with previous studies where young age was found to be a risk factor for complicated bone and joint infections [10]. This is possibly related to delays in the diagnosis and initiation of treatment, as well as differences in the response of younger children to antibiotic therapy. In our study, the median time between initial symptoms and treatment was 8 days. Besides, in our part of the world, the lack of education and low socio-economic factors cause a delay in seeking medical attention.

In our study, fever at admission was present only in 61.9% of children. This finding is similar that one reported by Dartnell et al. [11] who observed fever as the presenting symptom only in 61.7% of children. Local symptoms of decreased joint movements and pain were seen in 52.3% patients. Swelling and redness and local warmth were present in 23.8%. Systemic symptoms of generalized fatigue and severe malaise were seen in 38.1%. Altered sensorium and hypotension were present in 9.5% respectively. The pleuropulmonary disease was seen in 68% of patients in a study by Sodavarapu et al. [12]. Paterson noted in his study that systemic involvement in form of pneumonia and empyema were detected in 87% and 53%, respectively, among the 38 patients with osteoarticular infection with the disseminated staphylococcal disease [13]. The knee (42.8%) and hip (28.5%) were the most common joints involved in septic arthritis. For osteomyelitis, the femur was most commonly involved (71.4%). Previous studies also ascertained this finding with the hip and knee are common sites for septic arthritis and femur was found to be the most common site among osteomyelitis [14]. Paterson found out that hip was commonly involved among septic arthritis (55.5%), and the involvement of tibia (48.8%) and femur (41.4%) was higher in osteomyelitis among the patients of disseminated staphylococcal disease in his study [15].

Our study revealed a median leucocyte count of 18,970. Median CRP 96 mg/dl and median ESR of 44 mm/hr. Leucocytosis was less remarkably seen in patients than markedly elevated C-reactive protein and ESR. In the study by Chiappini et al. [15] the high CRP and ESR were associated with complicated osteomyelitis. In a study of culture-positive AO and SA, the reported sensitivity of CRP at diagnosis was 95% (CI 91% to 97% CI). ESR and CRP both peaked on day 2 of presentation, with the level of CRP normalizing in 10 ± 0.5 days. In this cohort of 265 children with confirmed osteoarticular infections, all had an elevated CRP and/or ESR within 3 days of admission [16].

Microbiological confirmation was done by performing blood culture and culture of aspirate. [Table 4a,4b]. Culture positivity of either blood or aspirate was seen in 14[66.6%]. Culture negative results may be due to less virulent organisms, due to slow-growing organisms, due to the low burden of disease, or due to the administering of antibiotics. A microbiological diagnosis is achieved in barely more than half of all cases. In their systematic review, Dartnell et al. reported...
that microbiological diagnosis is achieved in approximately 50% of all cases of musculoskeletal infection \[11\].

In our experience, Gram-positive cocci represented 85.7% of all isolates. Escherichia coli from 2 [18.1%] isolates and 1 [9.09%] revealed Klebsiella. S. aureus is a major cause of acute osteomyelitis in children. Methicillin resistance among S. aureus isolates has become an emerging problem in pediatrics. The prevalence of MRSA varies among countries as well as among hospitals. MRSA strains are typically viewed as hospital pathogens, but this image is now changing. Outbreaks of community-acquired MRSA infections have recently been described worldwide, mainly in previously healthy children with no recognizable risk factors \[13\]. In a recent study in a tertiary care center in India, MRSA was the predominant isolate in 13% of young infants with septic arthritis \[18\].

In our series, all patients received antibiotic treatment, and 19 [66.6%] also needed open surgical drainage which include either arthrootomy of the affected joint or incisional drainage and bone drilling in cases with osteomyelitis. The median duration of treatment was 4 to 6 of Intravenous antibiotics and two weeks of oral antibiotics. Vancomycin, along with third-generation cephalosporin, can be the preferred choice of antibiotic in cases of disseminated disease with suspected osteoarticular infection, as all cases of Staphylococcus aureus were sensitive to vancomycin in our study, but further studies are required to ascertain its use before recommending it as a first choice drug as suggested by other studies \[19\].

**Conclusion**

Acute Osteomyelitis and Septic Arthritis are relatively common serious bacterial infection of children that can progress to disseminated sepsis and septic shock. Early diagnosis and initiation of appropriate antibiotics is a sine qua non in preventing life-threatening complications like endocarditis. While this disease can be caused by a wide variety of pathogens, S. aureus is the predominant etiology. MRSA is emerging as community-acquired bacteria. A multidisciplinary approach including the consideration of combined medical and surgical management should be considered in these patients.

**References**

1. Sukswai P, Kovitvanicha D, Thumkunanon V, Chotpitayasunondh T, Sangtawesin V, Jeerathanyasakun Y. Acute hematogenous osteomyelitis and septic arthritis in children: clinical characteristics and outcomes study. Journal of Medical Association of Thailand. 2011;94:S209-S216.

2. Akinkugbe O, Stewart C, McKenna C. Presentation and investigation of pediatric bone and joint infections in the pediatric emergency department. Pediatric Emergency Care. 2019;35:700-704. https://doi.org/10.1097/PEC.0000000000001431

3. Iliadis AD, Ramachandran M. Paediatric bone and joint infection. EFORT Open Reviews. 2017;2:7-12. https://doi.org/10.1302/2058-5241.2.160027

4. Borella L, Goobar JE, Summitt RL, Clark GM. Septic arthritis in childhood. Journal of Pediatrics. 1963;62:742-747. https://doi.org/10.1016/s0022-3476(63)80044-x

5. McCarthy JJ, Dormans JP, Kozin SH, Pizzutiello PD. Musculoskeletal infections in children: basic treatment principles and recent advancements. Instructional Course Lectures. 2005;54:515-528.

6. Watson RS, Carcillo JA, Linde-Zwirble WT, Clermont G, Lidicker J, Angus DC. The epidemiology of severe sepsis in children in the United States. American Journal of Respiratory and Critical Care Medicine. 2003;167:695-701.

7. Mandal K, Roy A, Sen S, Bag T, Kumar N, Moitra S. Disseminated staphylococcal disease in healthy children: experience from two tertiary care hospitals of West Bengal. Indian Journal of Pediatrics. 2014;81:133-137. https://doi.org/10.1007/s12098-013-1034-7

8. Singhi S. Intensive care of pediatric patient. In H. P. S. Sachdev, R. K. Puri, A. Bagga, &P. Choudhury (Eds.), Principles of pediatric and neonatal intensive care (pp. 329-353). Jaypee Brothers. 1994.

9. Arnold GC, Bradley JS. Osteoarticular infections in children. Infect. Dis. Clin. N. Am. 2015;29:557-574.

10. Bradley JS, Kaplan SL, Tan TQ, et al. Pediatric pneumococcal bone and joint infections. The Pediatric Multicenter Pneumococcal Surveillance Study Group (PMPSSG). Pediatrics. 1998;102:1376-1382.

11. Darnell J, Ramachandran M, Katchburian M. Haematogenous acute and subacute paediatric osteomyelitis: A systematic review of the literature. J. Bone Joint Surg. Br. 2012;94:584-595.

12. Praveen Sodavarapu, Pebbam Sudesh, Nirmal Raj Gopinathan. Characteristics of Musculoskeletal Involvement in Pediatric Patients with Disseminated Sepsis in a Tertiary Care Center Indian Journal of Orthopaedicshttps://doi.org/10.1007/s43465-021-00488-1

13. Paterson MP, Hoffman EB. Severe disseminatedstaphylococcal disease associated withheotisitis and septic arthritis. Journal of Bone and Joint Surgery. British Volume. 1990;72:94-97.

14. Maraqo NF, Gomez MM, Rathore MH. Outpatient parenteral antimicrobial therapy in osteoarticular infections in children. Journal of Pediatric Orthopedics. 2002;22:506-510.

15. Elena Chiappini, Caterina Camposampiero, Simone Lazzeri. Epidemiology and Management of Acute Haematogenous Osteomyelitis in a Tertiary Paediatric CenterInt. J. Environ. Res. Public Health 2017;14:477. Doi:10.3390/ijerph14050477

16. Pääkkönen M, Kallio MJ, Kallio PE. Pseudomonas aeruginosa. Int. J. Environ. Res. Public Health 2017;14:477. Doi:10.3390/ijerph14050477

17. Eady EA, Cove JH. Staphylococcal resistance revisited: community-acquired methicillin resistant Staphylococcus aureus – an emerging problem for the management of skin and soft tissue infections. Curr. Opin. Infect. Dis. 2003;16:103-124.

18. Sankaran G, Zacharia B, Roy A, Purayil SP. Current clinical and bacteriological profile of septic arthritis in young infants: a prospective study from a tertiary referral centre. European Journal of Orthopaedic Surgery and Traumatology. 2018;28:573-578.

19. Kabak S, Halici M, Akcakus NC, Narin N. Septicarthritis in patients followed-up in neonatal intensive care unit. Pediatrics International. 2002;44:652-657. https://doi.org/10.1046/j.1442-200x.2002.01649.x