Acute Osteomyelitis and Septic Arthritis in Children – Current Concepts in Diagnosis and Management

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Abstract

Acute osteomyelitis and septic arthritis are the most common cause of morbidity in childhood. These occur more commonly in children upto 5 years of age. The most common organism responsible is Staphylococcus aureus, however, many other organisms are also known to cause osteoarticular infections in children. These infective conditions demand a prompt diagnosis and management, as any delay can lead to joint destruction, instability, deformity and significant limb length discrepancy. Thus early diagnosis and prompt management are of importance to achieve optimal goals. The clinical presentation of a child with osteoarticular infection is typical; with presence of fever, swelling and inability to move the affected extremity. However, sometimes the typical clinical findings are missing. Therefore it is important to follow a specific clinical, laboratory and imaging work-up to reach a definitive diagnosis. Following appropriate diagnosis, the further management protocol should be followed, with appropriate choice and dose of antibiotics and surgical debridement as required. The aim of this review article is to discuss the current concepts in acute osteomyelitis and septic arthritis in children. This article discusses the recent literature on etiological organisms, pathophysiology, current trends in investigations and management of osteoarticular infections in children.

Keywords : Acute osteomyelitis, Septic arthritis, Osteoarticular Infection

Introduction:

Musculoskeletal infections in the paediatric age group are an important cause of morbidity. They comprise of a spectrum of disorders depending on the localisation of infection, such as, osteomyelitis, septic arthritis, a combination of both or spondylodiscitis. The source of infection may be haematogenous, secondary to contiguous infection, or secondary to direct inoculation from trauma and surgery. Most are primarily haematogenous in origin and result from symptomatic or asymptomatic bacteraemia in otherwise healthy individuals [1]. Acute haematogenous osteomyelitis (AOM) and septic arthritis (SA) are most common in childhood, with a peak incidence in neonates and children up to five years of age. Acute haematogenous osteomyelitis often occurs concurrently with adjacent joint sepsis, leading to long term morbidity. Acute osteomyelitis and septic arthritis in childhood demand a prompt diagnosis and management, as any delay can result in catastrophic sequelae including joint destruction, instability, deformity and significant limb length discrepancy. Management goals have progressed from survival, to limb preservation, to maintenance of normal limb development and function [2].

Demography And Epidemiology:

The reported incidence of osteomyelitis in developed countries varies between 1 and 13 per 1,00,000 population, with higher values of up to 200 per 1,00, 000 reported for developing countries [3]. While some authors report a decrease in incidence of over 50% in the last three decades, others report increasing incidence. This increase may actually be due to advances in microbiological diagnosis [4]. Septic arthritis and acute hematogenous osteomyelitis can occur at any age but two distinct groups have a greater susceptibility, which are, infants and children upto 5 years of age. Almost 50% of all cases of acute hematogenous osteomyelitis occur in children less than 5 years of age [1]. There is a seasonal variation; the hospital admission rate for osteomyelitis peaking in late summer in both the Northern and Southern

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Figure 1: Clinical picture of 5 year old boy with right proximal radius osteomyelitis. Note the swelling and redness in the proximal forearm

Figure 2: Clinical picture of an eight month old child with painful movements of the right hip associated with high grade fever and irritability since 3 days. Note the flexion deformity of the right hip joint and associated swelling in the buttock and groin, which is usually diagnostic of joint infection. Passive movements of the affected joint are painful & severely restricted

hemispheres. The incidence is greater in boys than girls and the male to female sex ratio increases with age [5]. The higher incidence in males is most likely because they are more physically active, which predisposes them to repeated microtrauma. Common joints involved, in order of frequency, are the hip, knee, elbow and shoulder. Occasionally, multiple joints may be involved especially in the setting of septicemia.

Organisms:

A variety of organisms have been implicated in the causation of musculoskeletal infections, depending on the age of the child and prevailing

risk factors. They are broadly classified as community based infections and hospital based / nosocomial infections. The differentiation between the two groups is important with respect to the common infecting pathogens, risk of antibiotic resistance and prevalence of predisposing factors, which is more commonly seen in the latter group.

The most frequent pathogen responsible for osteomyelitis and septic arthritis in any age group is staphylococcus aureus. It is responsible for up to 70%–90% of confirmed cases. There has

also been an increase in cases of infection due to methicillin-resistant strains of S. aureus (MRSA) in pediatric patients that should be considered when choosing an empirical antimicrobial treatment [6]. The increase in incidence is from 4% previously reported to 40% [7]. These organisms are associated with increased severity of acute osteoarticular infections and higher risk of subperiosteal abscess formation requiring surgical intervention.

In children less than two months of age, Streptococcus agalactiae and other

Figure 3: (A and B) - Radiograph of a child presenting with swollen forearm on day one (Fig. 3A) and 6 weeks post presentation (Fig. 3B) showing periosteal elevation and sequestration of entire radius.
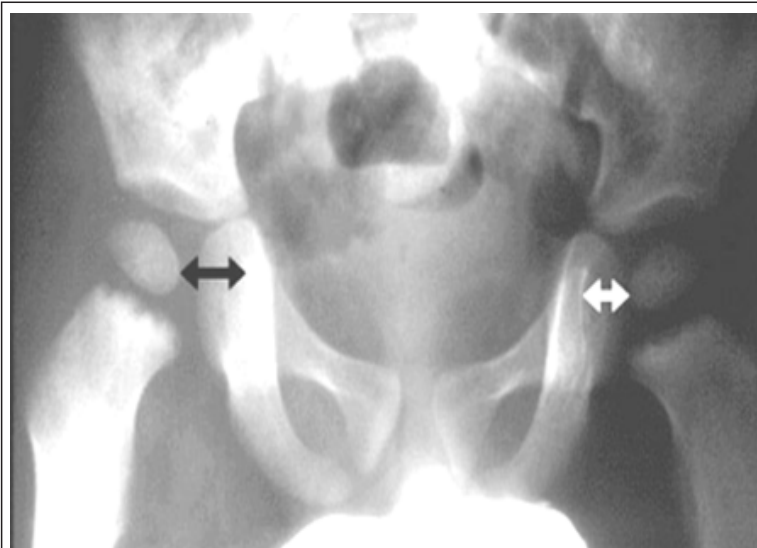

Figure 4: Radiograph of both hip joints showing increased medial joint space, indicating fluid / pus collection in the right hip joint
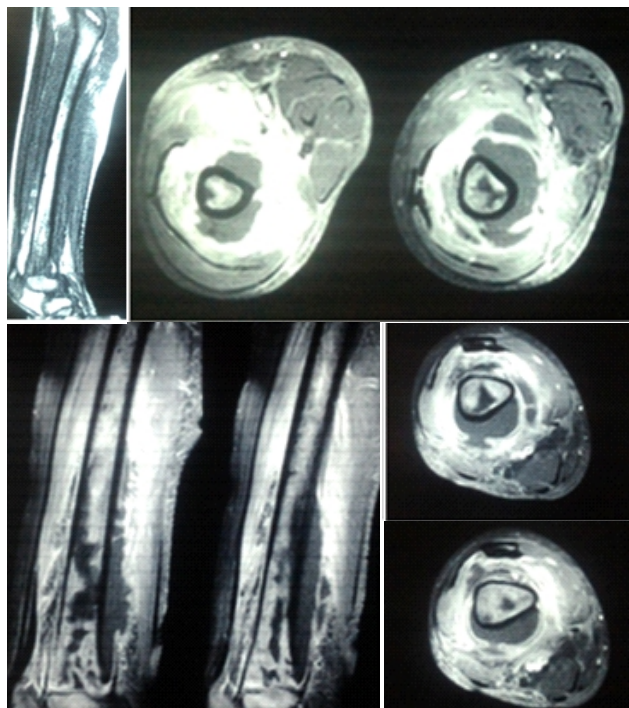
Figure 5: MRI images showing acute osteomyelitis of distal femur and sub-periosteal abscess collection.
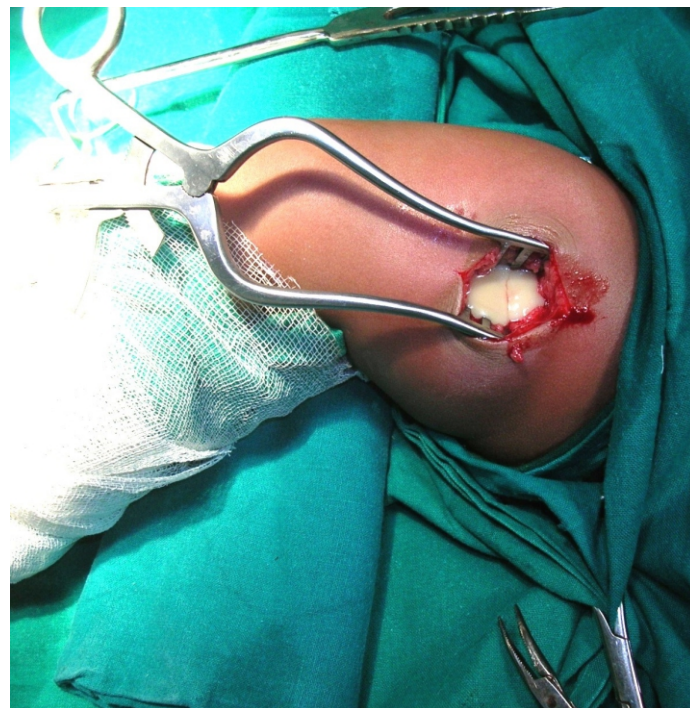

Figure 6: 1 year old child with high grade fever, irritability and refusal to move left lower limb since 2 days. Urgent incision and drainage revealed a large pus collection in the proximal thigh, which was drained.

Gram-negative organisms are recognized as potential pathogens. However, in children between two and five years of age, Streptococcus pyogenes and Streptococcus pneumoniae should be considered [8]. Since the decline in H. influenzae osteomyelitis and septic arthritis in children under the age of 3 years following introduction of H. Influenzae vaccination, there has been an increasing prevalence of gram negative organisms [9]. The incidence of infection by Group A beta hemolytic streptococci is on the rise and is commonly seen in association with varicella zoster infection. Diagnosis is difficult and often delayed in absence of overt clinical signs and equivocal investigations [10]. Candida albicans and other fungi are also emerging as frequent pathogens especially in the ICU settings due to long term hyperalimentation, prolonged intravenous access, use of potent broad spectrum antibiotics and ventilatory

support for critically ill neonates. About 25-30% of cases have no identifiable causative organism.

Table 1 enumerates the list of common organisms in different age groups

Pathology And Pathophysiology :
Infection in case of acute osteomyelitis is almost always haematogenous due to colonization of bones by bacteria. The metaphysis of long bones is the most usual site. Theories to account for this fact include decreased blood flow in sinusoidal vessels and relative paucity of phagocytic cells in this area. Trauma also plays a part in the pathogenesis as shown in animal models, in which, isolated bacteremia does not lead to osteomyelitis but bacteremia plus a traumatic injury to the metaphysis produces significant osteomyelitis [11].

Acute hematogenous osteomyelitis typically begins in the metapyhseal venous sinus which has vascular loops and terminal branches with low oxygen tension and paucity of leucocytes leading to inhibited phagocytosis. Such an environment is conducive for bacterial growth following the bacteremia. Bacteria lodged in these loops lead to bacterial proliferation and eventually lead to thrombosis of the venous sinuses. The resultant loss of medullary blood supply further reduces

Table 1 – List of common organisms in different age groups

Age group	Common organisms
Age < 2 months	Staph. Aureus
	Streptococcus agalactiae
	Gram-negative enteric bacteria
	Candida
< 5 years	S. aureus
	Streptococcus pyogenes
	Streptococcus pneumonia
	Kingella kingae
	Heamophilus influenza type b
>5 years	Staph. Aureus
	Streptococcus Pyogenes

the movements of phagocytes. By 72 hours inflammatory exudate is formed. This exudate exits the bone through the porous cortex and can cause a subperiosteal abscess, or if the area involved is the proximal femur where the metaphysis is intracapsular, the exudate can cause concomitant septic arthritis. The elevation of periosteum induces new bone formation (involucrum), and the underlying bone can become nonviable to form a sequestrum.

Inoculation of the joint occurs most commonly by hematogenous route. It also occurs by contiguous spread from adjacent focus or by direct inoculation. Hematogenous spread occurs from a distant focus of infection such as pyoderma, otitis media, respiratory tract infections, umbilical sepsis etc., with seeding of organisms during the bacteremic episode. Contiguous spread occurs from an adjacent focus such as osteomyelitis of an intracapsular metaphysis such as the hip joint. Direct inoculation occurs following femoral venepuncture and accidental joint penetration.

Following an inoculation of the organism into a joint, there is an acute inflammatory reaction with an outpouring of white cells into the joint fluid and release of proteolytic enzymes. This inflammatory exudate is initially thin and turbid, but later becomes frankly purulent. Degradation of the articular cartilage by the proteolytic enzymes begins within 8 hours of infection manifested by glycosaminoglycan and collagen breakdown mediated via polymorphonuclear cells and cytokines secreted by the chondrocytes. The joint is surrounded by granulation tissue and pockets of pus and adhesions occur in the joint. Pathological subluxation and dislocation or avascularity may occur.
DIFFERENTIAL DIAGNOSIS:

The various differential diagnosis of Osteo-articular infections include,
• Transient synovitis
• Rheumatic fever
• Other rheumatological conditions
• Metabolic conditions like scurvy.

Clinical Picture:
Children with musculoskeletal infection typically present with a combination of high grade fever, pain, loss of mobility and dysfunction involving the spine, pelvis, or extremities. This clinical picture is less pronounced when it presents in very young children and a high degree of suspicion is required to pick up these children early and manage them [12]. In children, infection in almost every bone and every joint has been reported in literature. Among the most important and commonly involved are that of femur, tibia and humerus among bones and hip, knee, elbow and shoulder among the joints. The clinical symptom with which the child presents with depends on the demographic factors including age, host resistance, virulence of the organism, predisposing and co-morbid factors in the host [9]. Although isolated abscesses and cellulitis of the spine pelvis & extremities are not necessarily orthopaedic problems, these conditions my be indistinguishable from deep infection of bone, joint or muscle [13]. Refusal to feed and to weight bear on the affected extremity are important clinical findings, especially in very young children. In case of lower limb involvement, the affected limb shows antalgic gait with the trunk swaying to the affected side [14].

In cases of osteomyelitis (OM), fever and localized bone tenderness are among the hallmark of the findings (Figure 1). The patient may also show adjacent sympathetic joint effusion with joint irritability and a restricted range of motion. These patients have to

be diagnosed and treated early before joint involvement and full-blown septic arthritis develops. In case of neonates and immunocompromised patients, the findings of sepsis may be clinically silent till a large amount of pus is accumulated [15].

In septic arthritis (SA), the affected joint is swollen and local signs of inflammation are present, with the attitude of the limb kept in position of ease and in maximum capacity of the involved joint (Figure 2). For the hip joint it is about 30 to 45 degrees of flexion, 15 to 20 degrees of abduction and external rotation and for the knee it is about 30-45 degrees of flexion. There is associated spasm of the adjacent muscles and restriction of range of motion of the joint (both active and passive). Severe tenderness is elicited by palpation, with swelling and redness visible in cases of superficial joints [16].

One clinical setting which requires a high index of suspicion and awareness is the children who are at high risk and critically ill in NICU (especially the preterm neonates). The peculiar anatomy and vascularity of the proximal femur in this age group, the failure of systemic response, the often delayed and missed diagnosis of sepsis foci elsewhere which can lead to consequent irreparable damage to the joint if inadequately treated, makes this entity a unique problem to deal with. Certain infections are life threatening, and or/ with multifocal involvement especially those that lead to a diathesis of septic shock and multisystem organ failure (group A beta-hemolytic streptococcal pyomyositis, MRSA infection and necrotizing fasciitis) [17].

Investigations:
One of the most important components in management of Osteo-articular infections is the judicious use of laboratory investigations and imaging

Table 2 – List of common investigations in osteoarticular infections

Essential Investigations

✓ LAB – WBC count, CRP, PCT, Blood Culture, Tissue Culture and PCR

✓ IMAGING- X-rays, USG, Bone Scan MRI and CT scan.

PCR- Polymerase Chain Reaction, PCT -Procalcitonin

Table 3 – Guidelines of Infectious Disease Society of America for treatment of MRSA positive infection.

Condition	Treatment	Comments
Bacteremia	Vancomycin OR Daptomycin	No rifampin unless prosthetic valve
Osteomyelitis	Vancomycin, Linezolid, Clindamycin, Daptomycin, TMP-SMX	Some experts recommend adding rifampin

modalities (Table 2).

Over the years, various blood parameters have been studied for musculo-skeletal infections that include, Complete Blood Count (CBC), Differential Count (DC), Peripheral smear studies (to rule out leukemic conditions), Erythrocyte Sedimentation Rate (ESR), C-Reactive Protein (CRP) and Blood Culture. An elevated white blood count (WCC) more than 13,000 cells /cumm, and ESR more than 20mm at the end of first hour are seen in the majority of patients. However, these tests have poor reliability in neonates and children with concomitant osteomyelitis. Previous studies have shown that, the WCC is elevated in only 35 to 40% of cases while ESR is greater than 20 in 70 to 92% of cases [18]. C-reactive protein is the most sensitive test, being an acute phase reactant; and levels more than 20 mg/Lit (mean 60-80 mg/lit) were found to be raised in up to 98% of patients at the time of admission. CRP also is a good indicator of response to

treatment, with normal levels (20 mg/Lit) reached within a mean of 10 days [19]. Chou studied the utility of CRP as a follow up parameter in musculoskeletal infections and proposed that, more than 50% reduction in CRP from original value after the start of antibiotics, provided a favourable outcome [20]. The best sensitivity for OAI was with combined elevation of ESR and CRP (98%).

A high index of suspicion and awareness should be maintained to rule out septic arthritis and acute osteomyelitis. Kocher's criteria [21] were devised to differentiate true septic arthritis from transient synovitis. Here, fever > 38 deg., ESR>40mm, WBC count > 12000/cu.mm and inability to weight bear were the factors considered. There was a positive predictive value of 99% of a septic arthritis if all 4 factors were present. Caird et al [22] added CRP (level > 20mg/L) to the Kocher's criteria, for diagnosis of musculoskeletal infections. Rosenfeld studied concomitance of SA and OM in acute presentations and five factors – age > 3.6 years, CRP > 13.8, duration of symptoms > 3 days, platelet count > 3.14 lac and ANC > 8600 were proposed [23]. More than 90% positive

predictive value was found if 3 or more factors were positive. In recent studies, evidence suggests that the magnitude of elevation of the CRP level obtained at the time of admission had some usefulness in identifying the child at increased risk for developing DVT. In this study, the children in whom the CRP level at the admission was >6 mg/dL, had a 40% incidence of DVT [17].

In recent years, Procalcitonin (PCT) has been identified as another potential biomarker of bacterial infection. Maharajan et al [24] prospectively evaluated WBC, ESR, CRP, and PCT in both infectious and non-infectious inflammatory conditions. The authors had shown that a PCT > 0.4ng/mL was the most sensitive (85.2%) and specific (87.3%) test to differentiate OAI from noninfectious diagnoses. At this time, the value of PCT as a reliable biomarker of OAI is unclear and randomized control trials and larger cohort studies are required to prove the reliability and efficacy of PCT in musculoskeletal infections.

Culture (Blood culture/ pus culture and/ or tissue culture) is one of the gold standard investigations in OAIs. Blood culture will be positive in 30 to 50% of patients and the organism detection rate is increased to 75% to 80% by aspiration of the affected bone, only if done before the start of antibiotics. Sometimes poor yield of the blood culture and well as tissue/pus culture is due to the presence of fastidious organisms like Kingella kingae [25] which is proposed to be responsible for most of the culture negative infections in the recent times. Aspiration is critical for bacteriological diagnosis and should be performed earlier under all aseptic precautions. The joint should be aspirated with a 16 or 18 G needle and is ideally performed

under image intensifier. The aspirate should be subjected to direct smear for pus cells and organisms. In SA the joint fluid is usually turbid with elevated proteins and WBC count and reduced glucose. In case of acute osteomyelitis, aspiration should be done from the point of maximum tenderness by extraperiosteal, subperiosteal or intra osseous route. Various recent methods like BacTec, BacT/ Alert, Isolator 1.5 Microbial tube and Hemoline DUO have been found to improve the yield of organisms [26].

Utility of PCR was investigated by Song [27] who proposed that the current PCR methods were not superior to standard bacterial culture methods when applied to children with presumed bone and joint infections. However Choe et al [28] investigated the use of real-time PCR for the diagnosis of septic arthritis in children and found that PCR had a success rate of 100% in differentiating between gram negative and gram-positive infections. The use of real-time PCR was found to help in guiding antibiotic therapy while the results from traditional microbiological culture are still pending.

Imaging:

Plain radiographs are normal till 7 to 10 days and difficult to interpret. The earliest sign in case of osteomyelitis is deep soft-tissue swelling and loss of soft tissue planes, which can be seen in fist few days of the infection. The periosteal and lytic changes are not seen until substantial bone destruction has occurred, which is usually 2 to 3 weeks after the onset of the symptoms (Figure 3). Prospective studies have shown that only 70% of children with culture proven osteomyelitis will have bone changes at three weeks [29]. In

case of septic arthritis, the earliest finding is the evidence of capsular distention, detected by increased joint space and displacement of fat planes (Figure 4). Later, the epiphysis may show destructive changes and may disappear completely. Metaphyseal erosion with concomitant osteomyelitis especially in the hip joint and pathologic subluxation and dislocation may be evident in late presentations.

Ultrasonography (USG) has been a traditional and useful investigation in the diagnosis of early osteomyelitis and septic arthritis. It is quick and easy to perform without the need of sedation or anesthesia but operator dependent. Laine investigated the usefulness of USG in OAI and proposed that, USG is a quick and relatively accurate method to detect joint effusions especially hip, but higher investigations like MRI are required only if adjacent infection or unresolving collection is suspected [30]. Deep soft-tissue swelling is the earliest sign of acute osteomyelitis followed by periosteal elevation and a thin layer of subperiosteal fluid, and in some cases a subperiosteal abscess [31].

Technetium-99m bone scintigraphy can be useful in the setting of normal radiographs and clinical suspicion of osteomyelitis. It is positive within 24 to 48 hours of the onset of symptoms. The reported sensitivity ranges from 84% to 100% for detection of osteomyelitis and the specificity, from 70% to 96% as reported in literature. The use of pinhole collimated views and single-photon emission computed tomography (SPECT) has increased both sensitivity and specificity. In the early stages of an infection, scintigraphy shows a decreased uptake because of the relative ischemia caused

by the increased pressure from the presence of purulent material Such "cold" scans have been reported to have a positive predictive value of 100%, compared with a positive predictive value of 83% for "hot" scans. Scanning with indium111–tagged WBCs can be helpful in those rare situations in which osteomyelitis are suspected but the Tc-99m scan appears normal.

Magnetic resonance imaging (MRI) is one of the most sensitive and specific imaging modality used for the diagnosis of osteomyelitis and septic arthritis, particularly for infections in the axial skeleton (Figure 5). Browne [32] in his study proposed a sensitivity of around 98 percent for MRI (USG – 40% and Bone Scan – 53%). It was found to be useful in ruling out non-hip causes of pain, diagnosing concomitant osteomyelitis and pelvic pyomyositis. The cost for MRI is significant and it lacks specificity to demonstrate whether the abnormal changes are due to osteomyelitis or tissue oedema. The role of gadolinium enhancement on MRI was proposed by Kan who concluded that the only advantage was in detecting deep-seated small abscesses that were not drainable [33]. Although MRI is the imaging modality of choice in the workup of acute OAI, it is uncertain whether it is the modality of choice in the assessment of the post treatment course of OAI. Post treatment MRI, especially in the postoperative period can be abnormal even after successful treatment of the infection.

Treatment:

The general principles of treatment for acute hematogenous osteomyelitis and septic arthritis are similar to those for other infections. The focus is on identifying the organism and its

sensitivity and use of the correct antimicrobial treatment.

Acute Osteomyelitis:

The successful treatment of osteomyelitis depends on the appropriate selection and initiation of antibiotic therapy and surgical management as needed. Appropriate empiric antibiotic selection is based on the child's age and the most likely causative organism within a local community. The initial anti-microbial therapy is targeted against the common pathogens according to the age and associated abnormal findings.

The initial regimen includes Cloxacillin / cefazolin / clindamycin, with or without MRSA cover. Recent studies have shown that delaying MRSA cover by 2 days until the preliminary report is obtained, did not affect the complication rate. When culture results are available, antibiotic therapy is modified depending on the organism and the susceptibility pattern. If no organism is isolated, but the patient is improving, initial empirical coverage is continued. If the patient is not improving, further diagnostic testing should be considered, including bone biopsy for histopathology and culture if not previously obtained or imaging studies to rule out areas of infection that may require surgical drainage or debridement.

The antibiotics are administered according to the sensitivity pattern and parenteral therapy is continued for at least 1-2 weeks (2 weeks in bacteremia or blood culture positive children). Oral therapy is initiated once local signs of inflammation have subsided, the WBC counts are normalized and CRP becomes negative. The use of an oral agent with good bioavailability and in proper

doses as per sensitivity is recommended, usually cephalexin in doses of 75-100 mg/kg/day or Cloxacillin in combination with Ampicillin. The total duration of antibiotic therapy (parenteral + oral) is around 4-6 weeks. The oral doses of clindamycin, trimethoprim-sulfamethoxazole, fluoroquinolone antibiotics, and linezolid can be used because of the excellent bioavailability of these drugs [34, 35].

Infection caused by MRSA is increasingly common in many communities. Many isolates of CA-MRSA are susceptible to clindamycin. Alternative drugs to consider for treatment of osteomyelitis caused by MRSA include intravenous vancomycin, trimethoprim-sulfamethoxasole, and linezolid. Bone and joint infections caused by MRSA should be managed in consultation with an expert in infectious disease. Empirical use of these antibiotics before organism identification and susceptibility testing depends on severity of illness and incidence of MRSA in the community [36].
In an open-label, noncomparative, nonrandomized, compassionate use study, linezolid was used to treat serious infections caused by resistant gram-positive bacteria. Microbiologic cure for the cases of osteomyelitis caused by MRSA was 72%. The treatment of MRSA osteomyelitis may need to be longer (sometimes upto 6-12 weeks) and recent studies recommend to avoid linezolid for empirical therapy of osteomyelitis (anti TB drug also)

As per the guidelines of Infectious Disease Society of America the treatment of MRSA positive infection is as follows [Table 3]

Surgical debridement is done in case

of acute hematogenous osteomyelitis if the infection is refractory to medical treatment or if an abscess is identified. If the child doesn't respond to antibiotics within thirty six hours, surgical debridement should be considered. The primary role of surgery is to evacuate purulent material (Figure 6). If the pus accumulates under the periosteum for any length of time, the periosteum can be destroyed. The periosteum may serve as the only source of osteogenic regeneration of dead bone. If the bone does not regenerate, a permanent defect may result. Surgery is also very effective in removing sequestrate to clear up chronic infections.

Septic Arthritis:
The successful management of pyogenic arthritis depends on timely decompression of the joint space and institution of appropriate antibiotic therapy.
The treatment of acute septic arthritis is divided into two broad perspectives:
· Joint decompression.
· Control of infection by antibiotics
1) Joint decompression:
 Once the diagnosis of SA is confirmed by USG and aspiration, a formal arthrotomy and joint lavage should be carried out for joint decompression. This should be carried out on an emergency basis as delayed treatment will lead to cartilage and joint destruction. If the joint is not decompressed in time, the increased intraarticular pressure can cause tamponade of epiphyseal vessels with resultant avascular necrosis. Following arthrotomy, the capsule is left open but the wound is closed over suction drainage [37].
Joint decompression can also be done by
 i) Aspiration and lavage
 ii) Arthroscopy assisted joint lavage:
This is a useful modality for superficial

and large joints like the knee, elbow, and shoulder.

2) Control of infection by antibiotics:
As with osteomyelitis, a child should be treated with intravenous antibiotics until there is significant clinical improvement, inflammatory markers are returning to normal, and the child's oral intake is normal.

The doses of oral antibiotics used are the same as doses used to treat osteomyelitis as described in the osteomyelitis section. Currently, the clinical response to treatment as well as laboratory values (usually the C-reactive protein level) is used to

determine whether switching to oral medications is appropriate. The duration of therapy for uncomplicated pyogenic arthritis depends on the response to therapy and the suspected organism. Generally, infections caused by S. aureus or gram-negative enteric bacteria are treated for 3 to 4 weeks.

Conclusion:
Bacterial bone and joint infections cause significant morbidity, especially in children. There is a rising incidence of resistant infections like MRSA positive infections and resistant gram negative bacterial infections which needs appropriate antibiotic therapy,

and surgical management if required. Every attempt should be made to obtain an appropriate microbiologic diagnosis. The anti-microbial usage must be appropriate and right in sensitivity, dosage, route and duration. In a subset of patients with un-complicated infections early switch to oral therapy and shorter duration of antibiotic regimen can be adopted. A short course steroids provides a successful and early recovery, especially in septic arthritis.

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