Original Article

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IJPO
ISSN Online 2455-3905

Epidemiology and Antibiotic Sensitivity Patterns in Pyogenic Bone and Joint Infections in Children

Amit Sharma[1] MS Ortho., G Nirmal Raj Gopinathan[2] MS Ortho., Garima Sharma[3] MD Microbiology, Pallavi Sharma[4] MS ObGy., Sange Negi[1] MS Ortho.

Dr. Amit Sharma

Dr. G Nirmal Raj Gopinathan

Dr. Garima Sharma

Dr. Pallavi Sharma

Dr. Sange Negi

Abstract

Staphylococcus aureus is the most common organism causing paediatric bone and joint infections accounting for 86% of pus culture-positive cases. Methicillin resistant Staphylococcus aureus (MRSA) has become a major challenge in the tertiary care setting as the majority (56%) of all pus culture postive cases were MRSA. The male to female ratio in these infections was approximately 2:1. The lower limbs were affected in the majority of children with osteomyelitis (OM) with hip joint being the commonest (50%) followed by the knee. Broad spectrum antibiotics were used emperically in 40% of cases prior to referral to a tertiary care centre. MRSA infections were associated with a higher likelihood of complications.

Keywords: Paediatric, Pyogenic, Bone and joint infections, Antibiotic practices

Introduction

Pyogenic paediatric bone and joint infections are a major cause of morbidity and mortality [1]. Acute osteomyelitis has an incidence ranging from 1 per 10,000 children per year 2 to 13 per 100,000 children [3, 4]. Over the last few decades, several studies have recorded an increase in the rate of osteomyelitis [4] while other authors have suggested a decreasing trend in its incidence [5]. The rate of septic arthritis has not changed during the same period [6]. Higher rates have been reported in developing countries. The long-term effects of these infections include joint destruction, progressive deformity and reduced ambulation [7].

Although the exact incidence in India is unknown, the numbers may be much higher compared to the developed world on account of higher population density and the lack of widespread facilities for early diagnosis and prompt treatment. The rates of complications following MRSA infections such as deep vein thrombosis (DVT), systemic sepsis and thrombophlebitis are also reported to be on the rise [7, 8]. One of the emerging aspects is the irrational and indiscriminate use of antibiotics. This practice, while presaging the emergence of resistant organisms, also leads to worse patient outcomes. The global consumption of antibiotics has increased by 40% in the last decade. India was the world's largest consumer of antibiotics at $12.9x10^9$ units (10.7 units per person) in 20109. The crude infectious disease mortality rate in India is 416.75 per 100,000 individuals [10, 11].

Apart from environmental factors and the use of antibiotics in livestock, inappropriate use of antibiotics has been implicated in the growing menace of drug-resistant microbes [18]. The practice of over-the-counter (OTC) drug dispensing and inappropriate use of multiple antibiotics is often discussed, but not documented. In the present study, we evaluated the nature of antibiotic therapy provided at primary and/ or secondary care institutions to children with acute osteomyelitis and septic arthritis who subsequently presented to our tertiary centre. The causative

Address of Correspondence
Dr. Garima Sharma,
Department of Microbiology , Indira Gandhi Medical College, Shimla, Himachal Pradesh, India.
E-mail: garimaserene@gmail.com

[1]Department of Orthopaedics, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India.
[2]Department of Orthopaedics, Postgraduate Instiute of Medical Education and Research, Chandigarh, India.
[3]Department of Microbiology, Indira Gandhi Medical College, Shimla, Himachal Pradesh, India.
[4]Department of Obstetrics and Gynaecology, Government Medical College Hospital, Chandigarh, India.

DOI: https://doi.org/10.13107/ijpo.2023.v09.i01.149

Submitted: 12/11/2022; Reviewed: 08/01/2023; Accepted: 14/03/2023; Published: 10/04/2023

organisms and their antibiotic sensitivity patterns were studied.

Materials and Methods

An observational study was performed on children presenting with bone and joint infection from July 2017 to December 2018.

Inclusion criteria:

All children diagnosed with acute pyogenic osteomyelitis and septic arthritis (SA) between 28 days and 13 years of age.

Exclusion criteria:

1) Neonates,

2) Chronic Osteomyelitis, (Osteomyelitis greater than 3 weeks duration or presence of discharging sinus with sequestrum).

3) Immunodeficiency

4) Tuberculosis.

Patients with clinical features suggestive of septic arthritis and acute/acute on chronic osteomyelitis were considered. The details of treatment received (antimicrobials as well as surgical intervention) prior to presentation at our institution were noted. Children with multifocal or severe infection were subjected to detailed immunological evaluation including tests for retroviral infection. Where operative intervention was required, the aspirate or pus were subjected to microscopy, culture, and antibiotic sensitivity. Children were managed initially with empirical antibiotics (Cloxacillin and Ceftriaxone) after obtaining tissue samples. Once culture and sensitivity results were available, appropriate antibiotics were administered for a 6-week period with serial monitoring of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). The total duration of antimicrobial therapy was 4-6 weeks (2 weeks of intravenous treatment followed by 2 to 4 weeks of oral therapy).

Clindamycin or Vancomycin was added to empirical therapy based on the immunological status of the patient and in cases where extended coverage was required e.g. MRSA. The antibiotics were discontinued based on resolution of clinical symptoms. In doubtful cases, serum procalcitonin levels were used to ascertain resolution of the disease.

Descriptive statistics were used to examine the distribution of key outcome and predictor variables. Means and standard deviations were computed for continuous variables and percentages for categorical variables. Comparison of outcomes was performed with Chi for categorical variable. A value of < 0.05 was considered as statistically significant.

Results

A total of 90 patients were included in the study. Two patients were previous follow-ups from our institution, two patients had acute lymphoblastic leukaemia and one patient did not have an intra-operative pus culture report. These cases were excluded leaving 85 children for further analysis. 71 patients were administered antibiotics prior to presentation to us. Intra-operative pus culture was sent in all children which yielded a positive result in 50 cases.

Out of 85 patients, there were 57 boys and 28 girls. The mean age of the patients at the presentation was 6.13 years. 19 cases (22%) were less than 1 year of age. Most common symptom among the cases was fever 83(97.6%), followed by localised swelling (90.6%)and joint pain (76.5%). 16 children (19%) presented with a history of injury prior to onset of symptoms. 67 children(79%) had septic arthritis, out of which 45 were confined to the joint, 14 had an osteomyelitis component, 6 had an associated soft tissue abscess and 2 cases had associated pyomyositis (Fig. 1). Out of the 32 cases of osteomyelitis, 17 were diagnosed as OM only and 14 were associated with septic arthritis. One child had associated pyomyositis.

The most involved joints were the hip (35 joints), knee (23), ankle (5), shoulder (4) and elbow (3 joints). Some children had more than one joint involvement, resulting in a total of 70 joints. The most common bone involved in OM was the femur (17 cases), followed by tibia (11), humerus (3) and clavicle (1 case). In 89% of cases, the lower limb bones were involved (Fig. 2).

In our study, femur (53.12%) was the most commonly involved bone followed by tibia (34.37%). Hence, 87.5% bones affected were of the lower limb. The adjacent joint involvement (septic or non-septic) was present in 42% of cases of OM. 33% patients had evidence of septic joint involvement.

Complications developed in 11 cases, out of which 5 cases had

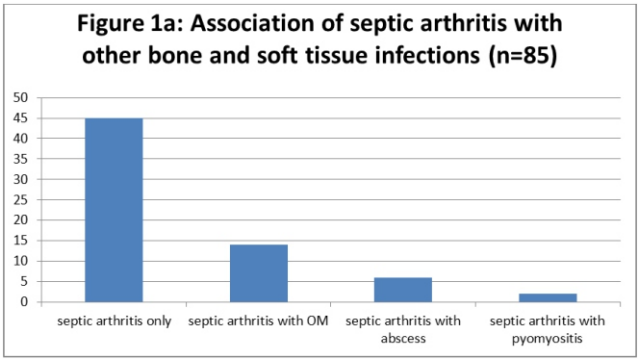


FIGURE 1b

Age Group	Number of cases
4weeks to infants (upto 1 year)	18
1 - 2	4
2 - 3	6
3 - 6	14
7 - 13	43

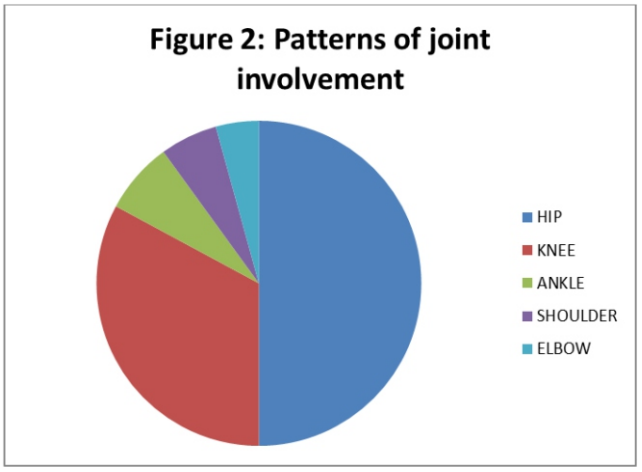


Figure 4

	Frequency	Percentage
MRSA	28	32.9
MSSA	15	17.6
Other	7	8.2
STERILE	35	41.2
Total	85	100

systemic sepsis. Five other children had pulmonary complications, out of which one child died. 1 child developed DVT and there was 1 instance of seizures.

Data regarding antibiotics administered prior to admission were collected from the parents or carers through referral notes, outpatient department slips or the discharge summary from peripheral health institutions.

The numbers of different antibiotics given were noted. The antibiotic names were written in the documents, but details regarding dosage, route of administration and duration were not always available.

Classes of antibiotics were classified as:

1) Gram-positive coverage-Penicillins (Amoxycillin, Cloxacillin)

2) Gram-negative coverage-Amikacin, Aminoglycosides, Flouroquinolones

3) Methicillin sensitive Staphylococcus aureus (MSSA) coverage- Amoxicillin, Cloxacillin, Cefuroxime, Cefadroxil.

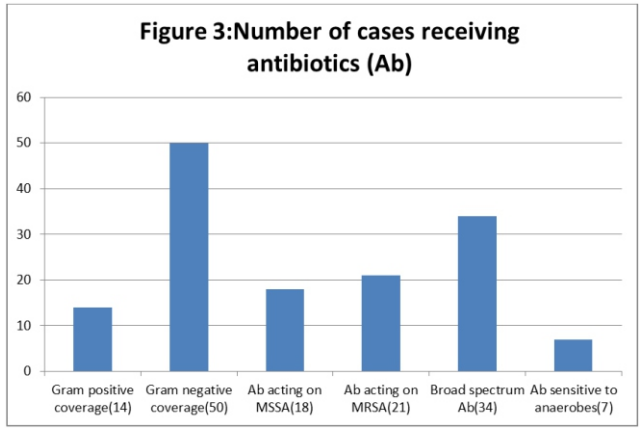
4) MRSA coverage-Vancomycin, Teicoplanin, Linezolid

5) Broad-spectrum antibiotics-Piperacillin-Tazobactam, Amoxicillin-clavulanic acid, Carbapenems, Cefoperazone-Sulbactam.

6) Antibiotics sensitive to anaerobes- Metronidazole.

Details of patients receiving each class of antibiotic are shown in Figure 3.

The details of previous culture reports were available in 7 cases. 5 cases were MSSA and 2 cases were MRSA. All cases



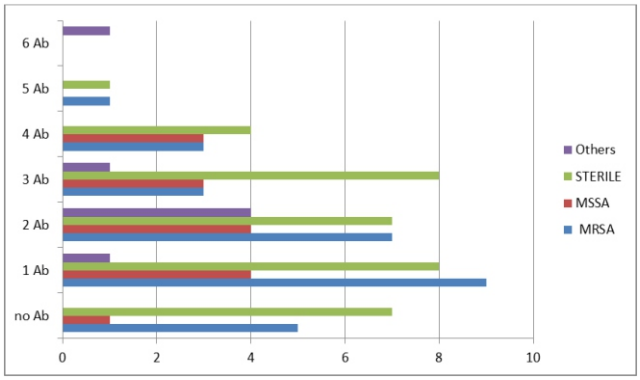


Figure 5 : (Ab-antibiotics administered) Vertical arm shows number of antibiotics administered in peripheral institutes before referral and horizontal arm shows number of patients. Colour coded bars show the pus culture results as per colour code.

underwent debridement in our institution. The intra-operative pus samples of 50 patients (59%) yielded positive culture results. The primary organism isolated from the pus culture from the cases was staphylococcus aureus followed by anaerobic organisms including E.coli, E.vulneris, Kl. pneumoniae and Acinetobacterbaumannii. Out of 43 cases of staphylococcus aureus infection, 28 samples were MRSA. Therefore, one-third of cases in this study had MRSA as the causative organism.

83.5% patients were given antibiotics prior to being referred to PGIMER. The cases, in which empirical antibiotics were given without blood or pus culture were 64(75.3%). The cases which were given two or more antibiotics in bone and joint infections were 49(57.65%). 3 or more antibiotics were given in 32.94% cases. 4 or more antibiotics were given in 15.29% cases (Fig. 5).

MRSA covering antibiotics (Vancomycin, Linezolid, Teicoplanin) were given in 21 (24.7%) cases. Broad spectrum antibiotics (Pipracillin-Tazobactum, Amoxicillin-Clavulanic acid, Carbapenems and Cefoperazone-Salbactum etc.) were administered in 34(40%) before referring the patients to our tertiary care center.

Discussion

Acute osteomyelitis typically affects the most rapidly growing ends of long bones and is more common in the lower extremity; the metaphysis of the distal femur and proximal tibia being the most common sites of infection [12, 13]. Approximately 75% of cases of septic arthritis occur before the age of three years [3]. Any joint can be infected but about 80% of cases are located in the lower extremity with the hip (in the young child) and the knee (in the older child) being the most common joints [12-14]. Our study supports the finding that lower limb is commonly affected with hip as most commonly affected joint and femur as most commonly affected bone in osteomyelitis followed by tibia. As hip joint is a deeper joint with adequate muscle cover, clinical suspicion in knee septic arthritis is more easily established as and may be treated in peripheral institutions in early stages as compared to hip joint. The delay in diagnosing hip joint infections and reluctance of performing relatively complex hip arthrotomy procedure in peripheral institutes with limited resources may have complicated the disease which may have resulted in more hip septic arthritis cases which got referred as compared to knee septic arthritis cases and presented in tertiary care institution in our study. A study on acute OM in children by Saavedra-Lozano et al states that most commonly affected bones included foot followed by femur and tibia [16]. As our study included the cases that reported in the emergency department, OM involving small bones were not encountered commonly. The incidence of joint involvement with adjacent osteomyelitis in paediatric patients in our study is comparable to other studies [14].

Many studies suggest that majority of cases of septic arthritis and acute osteomyelitis occur before the age of three years with male preponderance [3, 26, 27].

Our data suggests that in our population, male predominance is typically present in children with septic arthritis and acute osteomyelitis and the mean age of the children affected with these infections has increased as compared to the various previous studies conducted in different parts of the world.

The data also suggests that septic arthritis in younger children may have been underdiagnosed in peripheral institutions as septic sequalae cases in developing countries is more as compared to developed countries [28].

Staphylococcus aureus is most common cause of septic arthritis and acute osteomyelitis in children [3, 4, 6, 13, 15, 16]. The other common organisms causing acute osteomyelitis are skin and respiratory pathogens, such as Streptococcus pneumonia and H. influenzae with S. aureus being the most common, accounting for up to 80% of pediatric osteomyelitis [17, 18]. Kingella kingae has been increasingly recognized as an osteoarticular pathogen in children [19]. Kingella kingae infections, specifically in children younger than 2 years are reported more and more in recent studies [3, 12]. Our study suggests that Staphylococcus aureus is most frequently found offending organism in these infections, MRSA being more commonly isolated than MSSA in a tertiary care institution in India. No cases of Kingella kingae was isolated which suggests that this organism is not commonly offending organism in paediatric septic arthritis in India. This study also inferes that H. influenza is not a common pathogen in paediatric bone and joint infections. Many studies have already concluded that H. influenza as an offending organism has been on decreasing trend due to vaccination in bone and joint infections [4, 6].

The choice of antibiotic usually depends upon the clinical context and local guide lines. In a child with previously normal immune function, adequate staphylococcal cover must be included. Local incidents of MRSA determines whether the antibiotic therapy should cover this possibility [20]. Antibiotics that have proven efficacy against S. Aureus bone and joint infections include Clindamycin, first-generation Cephalosporins and Vancomycin [23]. Antibiotic therapy on the basis of antibiotic susceptibility pattern helps the clinician to choose appropriate drugs leading to successful treatment and prevention of emergence and dissemination of drug resistant isolates [24]. The lack of culture and antibiotic susceptibility test may prompt the clinician to start antibiotics that should only be used in more resistant and virulent microorganisms only.

Yu F et al. analysed the offending organisms for septic arthritis in children and their antibiotic resistance patterns for 20-years period. The major causative organisms between that period remained the same, except significant increase in MRSA infection [22]. The results of this study confirms the rising trend of MRSA in these paediatric infections.

Over-the-counter access to antibiotics is a problem, but regulations to restrict access have to be balanced against the need to maintain access for the significant proportion of the population that lacks access to doctors. Indeed, lack of access to effective and affordable antibiotics still kills more children in India than does drug resistance [21]. On the other hand, the drug resistance is increasing at the alarming rate in India due to lack of adequate antibiotic use surveillance and effective means to enforce the antibiotic usage guidelines [25]. The challenges to curb antibiotics resistance such as strengthening of surveillance data, standard operating guidelines, improvement in antibiotic prescription practices and over the counter sale of antibiotics still remain [26]. Our study concludes that the use of irrational and evidence lacked antibiotic usage is rempant in peripheral institutions. The deficiency in the facilities to perform pus culture and antibiotic susceptibility testing also results in usage of drugs which should not be used empirically.

This has led to emergence of MRSA infection in India. Implementation and follow up of intervention research should be strengthened by health care planners, managers and practitioners to identify the most appropriate strategies to improve drug use and prevent the emergence of drug resistance [25].

Conclusion

Septic arthritis and acute osteomyelitis in children remain a challenge to treat in developing countries with limited resources. Older age group children with male predominance are most common presenters with paediatric pyogenic musculoskeletal infections in tertiary care hospitals. India has been a major consumer of antibiotics in world. The indiscriminate use of antibiotics could be observed in ill equipped primary and secondary health care institutions. Due to indiscriminate use of new generation antibiotics, there is increased risk of MRSA infections as Staphylococcus aureus is the most common offending organism.

The complications related to the MRSA are more frequently severe as compared to MSSA. Appropriate antibiotic therapy is required to be effectively promoted with strict antibiotic surveillance program to prevent or curb the Herculean antibiotic resistance challenge.

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Declaration of patient consent : The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given the consent for his/ her images and other clinical information to be reported in the journal. The patient understands that his/ her names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Conflict of interest: Nil **Source of support:** None

How to Cite this Article

Sharma A, Gopinathan GNR, Sharma G, Sharma P, Negi S | Epidemiology and Antibiotic Sensitivity Patterns in Pyogenic Bone and Joint Infections in Children | International Journal of Paediatric Orthopaedics | January-April 2023; 9(1): 07-12 | https://doi.org/10.13107/ijpo.2023.v09.i01.149