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Original Article

Current trends of microorganisms and their sensitivity pattern in paediatric septic arthritis: A prospective study from tertiary care level hospital

Girish Motwani *, Rujuta Mehta, Alaric Aroojis, Sandeep Vaidya

Department of Paediatric Orthopaedics, B.J. Wadia Hospital for Childrens, Mumbai, India

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ABSTRACT

Purpose: Early treatment of septic arthritis is essential before irreversible damage to the articular cartilage occurs. Clinicians often start empirical antibiotic therapy for symptomatic relief while awaiting a definitive culture report. In present day parlance with variations in different centres in the private and public sector and rampant antibiotic abuse, a lot of resistance is being seen in the flora and their sensitivity patterns. Hence it is imperative to document and analyze these changing trends.
Methods: The authors conducted a retrospective analysis of prospectively gathered data of 60 patients under 14 years of age. Joint arthrotomy was performed as a standard therapeutic protocol and the drained pus or synovial fluid was sent for gram stain and culture by 2 different methods: conventional agar plate method and BACTEC Peds Plus/F bottle method. Antibiotic susceptibility tests were done by the disc diffusion method of Clinical Laboratory Standards Institute (CLSI).
Results: The commonest presenting age group was below 1 year (80% patients) including 24 neonates. There were 19 hospital and 41 community acquired cases of septic arthritis. The hip (56%) was the commonest affected joint followed by knee (28%), shoulder joint (11%) and elbow (5%). Microorganism was isolated in 53% isolates of joint fluid only (36 culture positive patients). Conventional agar methods of culture showed positive report in only 42% patients (15/36 patients) while with the BACTEC method the yield was 71%. In the Community acquired septic arthritis, methicillin sensitive *Staphylococcus aureus* was isolated as commonest microbe while resistant variety of gram negative bacilli including *E. coli* and *Klebsiella* were found as predominant organism causing hospital acquired nosocomial infection of joints. The results strikingly differ in terms of response to treatment as most patients (11/19 patients) showed significant resistance to the most commonly practiced empirical antibiotic regimen of ampicillin-cloxacillin group in routine practice. When cefazolin was used as empirical antibiotic, it has shown good response and better sensitivity in 82% patients (27/33 patients).
Conclusion: *S. aureus* is still the most common organism in septic arthritis. The BACTEC system was found to improve the yield of clinically significant isolates. Though a significant resistance to common antibiotic regimen is noticed, the strain is susceptible to cephalosporin group of antibiotics. We recommend the use of cephalosporine antibiotics as an empirical therapy till culture and sensitivity report are available.

1. Introduction

Septic arthritis remains an important and serious disease of childhood because of its potential to cause permanent sequelae. Delay in its diagnosis and treatment of septic arthritis in paediatric patients can lead to disastrous complications like destruction of articular cartilage, physeal damage, and dislocation of joints.[2,4]

Despite significant advances in modern medicine with availability of better antibiotics, septic arthritis is still a major cause of morbidity. The cause is multifactorial as there is a shift in the microbiological spectra and epidemiology with emerging antibiotic resistance. This also has a distinct geographical variation. Native joint septic arthritis is usually secondary to hematogenous seeding of joint during transient or persistent bacteraemia. Early treatment is essential before damage to the articular cartilage

* Corresponding author.
E-mail addresses: gitz.dr@gmail.com (G. Motwani), rujutabos@gmail.com (R. Mehta), aaroojis@gmail.com (A. Aroojis), drsvvaidya@gmail.com (S. Vaidya).

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occurs. This mandates empirical antibiotic therapy without awaiting culture report. Although it is a disease being studied since 18th century, with the advent of more and more modern antibiotics a lot of resistance is being seen in the flora and their sensitivity. Despite the disease being rampant in India there is a paucity in literature on the subject about the Indian regional clinical scenario. Hence it is imperative to document and analyze these changing trends repeatedly.

1.1. AIMS of the our study

1. To evaluate the causative organisms for septic arthritis of children from neonates to 14 years.
2. To study the comparison of BACTEC blood culture system (Becton Dickinson Diagnostic Instrument Systems, Sparks, MD) with conventional agar culture methods for recovery of bacterial isolates from synovial fluid sample.
3. To evaluate the response to common empirical antibiotics of ampicillin-cloxacillin group versus our institutional practice of cephalosporins.

2. Materials and methods

The authors conducted a retrospective analysis of prospectively gathered data of paediatric patients under 14 years of age with diagnosis of septic arthritis (SA), treated at our institute from June 2013 to March 2016. The institute gets referrals from private clinics, NICU's and PHC's and district as well as municipal hospitals of almost whole of Maharashtra and neighbouring states of the western Indian region. Total 77 patients of septic arthritis were diagnosed and operated in 3 years from June 2013 to March 2016. Out of them, 17 patients are lost in follow-up. We have reviewed complete data of sixty children of either sex, with septic arthritis of any joint. This three-year prospective study evaluates the microorganisms and their sensitivity pattern.

Inclusion criteria: Children in the age group of 1 day–14 years presenting with

1) joint pain,
2) fever,
3) restriction of movements,
4) and elevated cell counts,
5) raised CRP and ESR values.

Additionally confirmation of diagnosis was done by (a) at least one of the following radiological or sonographic findings: increased joint space and bony changes or fluid collection on ultrasound scan with (b) purulent fluid aspiration from the joint. Informed consent was obtained from parents of all individual participants included in the study.

In management, arthrotomy done under sterile precautions in operation theatre We found that synovial fluid isolates of the patients collected after arthrotomy were cultured by 2 methods as per standard guidelines of microbiology department of B.J. Wadia hospital.

GROUP 1

Synovial sample of 36 patients were processed in conventional agar plate method which includes inoculation of synovial fluids directly onto 5% sheep blood agar and chocolate agar, which were incubated at 35 °C with 5–7% CO_2 for 2 days. In addition, approximately 0.25 ml was inoculated into thioglycolate broth, which was incubated at 35 °C with 5–7% CO_2 for 5 days.

GROUP 2

Synovial fluid isolates of 24 patients were inoculated into a BACTEC Peds Plus/F bottle and incubated for 5 days.

Sensitivity was tested against the following antimicrobial drugs: cloxacillin, amoxicillin, ceftriaxone, linezolid, and vancomycin. Antibiotic susceptibility tests were done by disc diffusion method of Clinical Laboratory Standards Institute (CLSI).

We found that empirical antibiotic therapy in the form of intravenous ampicilin-cloxacilin was given to 19 patients and cefazoline was started in 33 patients, as per the protocol of our department.

The children were treated with arthrotomy and antibiotic therapy depending on their severity and time of presentation. Definite antibiotic treatment for a period of 2–3 weeks was given as per the culture report. The children were followed up with clinical and haematological investigations every week for a period of 12 weeks.

Demographic data, clinical symptoms, laboratory findings, bacterial spectrum, method of culture, diagnostic significance of radiological tests, antiobiotic sensitivity pattern and outcomes were systematically analyzed.

3. Results

Demography: The commonest age group in the presentation was childrens below 1 years (80% patients), including most of neonates (40%) (Table 1).

Type of infection: There were 19 hospital acquired infection and 41 community acquired cases of septic arthritis.

Sex: Male children outnumbered the female children in the ratio of 2.3:1.

Presentation: 68% of children presented within a week, 24% presented in the second week, and 8% presented after two weeks.

Affected joints: Lower extremities were involved in most of the cases (56% hip, 28% knee). In the upper extremities, the involvement of shoulder and elbow joint was 11% and 5%, respectively (Table 2).

X-ray: Only 42% patients showed positive findings like increased joint space, haziness, and soft tissue changes. All these cases presented with more than one week of symptoms.

USG: Ultrasonography showed evidence of fluid collection and synovial thickening in all cases (98%) except one where the findings were equivocal.

3.1. Culture

In 47% ($n = 28$) patients, organism was not detected in culture examination (culture negative).

Out of 53% positive culture ($n = 32$), methicillin sensitive *Staphylococcus aureus* (MSSA) was isolated in 50% synovial isolates, 16% culture were positive for *E. coli* and *K. pneumoniae* was detected in 13% isolates. Rare organism found were salmonella, anaerobes and *Burkholderia cepacia*. About 10% were fungal (all candidial) septic arthritis.

Current trends of bacterial strain are showed in Table 3.

In community acquired septic arthritis, methicillin sensitive *Staphylococcus* was isolated as commonest agent while resistant variety of gram negative bacilli including *E. coli*, *Klebsiella* were

Table 1
Incidence according to age.

Age distribution	Number of patients
Neonates	24
1–3 months	10
3 months–1 year	13
1–3 years	7
>3 years	2

Table 2
Joint involvement in septic arthritis.

Joint involved	No. of joints	Percentage
Hip	39	56%
Knee	20	28%
Shoulder	8	11%
Elbow	3	5%

Table 3
Current trends of organism causing septic arthritis.

Culture positive	32 patients	53%
Culture negative	28 patients	47%
MSSA	16	50%
E. coli	5	16%
K. pneumonae	4	13%
Candida	3	10%(all neonates)
Salmonella	1	Rare
MRSA	1	Rare
Burkholderia	1	Rare
Anaerobes	1	Rare

Table 4
Microbiology according to community and hospital acquired infection.

Microorganism	Community acquired (41 patients)	Hospital acquired (nosocomial) (19 patients)
MSSA	12	4
E. coli	1	4
K. pneumonae	1	3
Candida	3	0
Salmonella	1	0
MRSA	0	1
Burkholderia	1	0
Anaerobes	1	0
No growth	21	7
Total	41	19

found as predominant organism causing hospital acquired nosocomial infection of joints (Table 4).

3.2. Method of culture

Synovial fluid isolates of 36 patients were cultured by conventional agar plate method (Group 1) where as synovial fluid isolates of 24 patients were inoculated into a BACTEC Peds Plus/F bottle (Group 2) and incubated for 5 days. Organism was isolated in only 43% culture (15 patients) processed by conventional agar methods while 71% culture (17 patients) were positive when BACTEC methods were applied (Table 4).

3.3. Antibiotic sensitivity pattern

Thirty three patients (54%) received cefazolin, 19 patients (33%) received ampicillin and cloxacillin, and 7 patients (13%) received ceftriaxone as empirical therapy. Out of 33 patients in which cefazolin was started, 27 patients (82%) responded well, which means drug was sensitive as per antiobiotic sensitivity report or had shown good clinical response (Tables 5 and 6).

While out of 19 patients in which ampicillin-cloxacillin was started as empirical therapy, 11 (55%) patients expressed resistance or poor clinical response.

All bacterial strain isolated were 100% sensitive to vancomycin and linezolid.

Depending on our findings, we will recommend cefazolin as empirical drug for septic arthritis patients, while appropriate drug should be based on culture sensitivity studies.

Table 5
Culture positivity pattern.

Culture methods	No. of patients	Positive culture	Negative culture
Group 1 (conventional agar culture method)	36 patients	15 culture +ve (43%)	21 culture −ve
Group 2 (BACTEC method)	24 patients	17 culture +ve (71%)	7 culture −ve

Table 6
Response to empirical antibiotics.

Antibiotic	No. of patients	Sensitive/good response	Resistance/poor response
Cefazolin	33	82%	18%
Ampiclox	19	45%	55%

4. Discussion

Despite extensive studies on acute septic arthritis in childhood, poor outcomes continue to occur. Most important factors determining the outcome of septic arthritis are rapid diagnosis and timely intervention in the form of effective antibiotics and surgical drainage.[2,4]

Early administration of antibiotics is widely supported in the literature and although microbiological evidence of infection is preferred, antimicrobials should not be withheld once diagnostic procedures have been performed. Conversely, there is little consensus on the choice of antibiotic, the choice often being made locally based on the most likely infecting organism.[1]

This study is an attempt to redefine effective empirical therapy and to reinforce the importance of common organisms found in these patients.

Classically, the diagnosis of septic arthritis is made on the basis of clinical examination as the child presents with high grade fever (>38 °C) and a painful swollen joint in the absence of history of trauma. Clinical signs may be subtle with irritability, low-grade fever, and limitation of movements.[1,3] Atypical clinical presentation can also be due to prior antibiotic treatment. The diagnostic tools like radiographs and ultrasound may aid in diagnosis. The diagnosis in the present study was primarily clinical which was confirmed by observing laboratory and radiological studies.

Sonography (USG) is considered as investigation of choice in diagnosis of septic arthritis world over.[1,13] Only one child in this study with mild clinical presentation had negative sonographic scan.

We agree with Buxton that radiological changes may not be noticed in 50% of the children. However its importance in diagnosis of underlying osteomyelitis cannot be denied.[6] This can alter the management protocol of the disease. Ultrasound is an excellent diagnostic tool that can reliably establish the diagnosis by indicating the presence of fluid in the joint and can guide aspiration.

The literature has enough evidence in support of ESR and CRP, which can be used as reliable markers in septic arthritis.[1,3,5] If a child who has signs and symptoms of acute hematogenous osteomyelitis initially has a moderate leukocytosis and an elevated C-reactive-protein value that increases almost twofold within twenty-four hours, the possibility of osteomyelitis with associated arthritis should be borne in mind. In children who have osteomyelitis without septic arthritis, the C-reactive protein level then usually decreases rapidly; if it does not, associated septic arthritis should be suspected. We found that when the level of the C-reactive protein on the third day was more than 1.5 times the level at the time of admission to the hospital, the likelihood ratio

that septic arthritis was also present was 6.5. Changes in the erythrocyte sedimentation rate gave the same information, but later. This study also found a raised ESR and CRP level which persistently declined with antibiotic treatment. As a prognostic marker these two parameters can fairly indicate the severity of septic arthritis.

The present study showed *S. aureus* as the most common (50%) organism causing septic arthritis in our tertiary health centre, followed by *E. coli* (16%) and *K. pneumonia* (13%).

Our findings are in similar concurrence to PELTOLA's study[14] that *S. aureus* – the most common causative agent in osteoarticular infections – is the primary target for treatment. For methicillin-susceptible strains, first-generation cephalosporins, clindamycin, and staphylococcal penicillins are first-line antibiotics of which clindamycin has retained activity even for most cases due to methicillin resistant *S. aureus*. This said, instead of clindamycin, beta-lactam antibiotics are effective also against *Kingella kingae*. Author wants to emphasize that beta-lactam antibiotics should be used as an empirical therapy over clindamycin because an often use of clindamycin may develop resistance in MRSA, so it may not be helpful drug for future. Also *K. kingae* is recently found as one of the commonest emerging microbe in bone and joint infection[8] and betalactam antibiotics are better drugs to cover *Kingella* than clindamycin.

Our study is well supported by a similar study conducted by Narang et al., who found *Klebsiella pneumoniae* and *S. aureus* as common isolates but with a much smaller sample size. Also there was a retrospective study conducted in neonates.[12] The commonly used empirical therapy in osteoarticular infection is cloxacillin/amoxicillin and clavulanic acid and amikacin combination. In large number of patients cephalosporin group of antibiotics (commonly cefexime, cefazolin ceftriaxone) is started as the initial treatment. However the present study concluded that cloxacillin-amoxicillin, and cefazoline were sensitive only in 45% and 82%, respectively. This puts question mark on their efficacy to be used as empirical drugs especially in joint sepsis which may have devastating consequences. Indirectly, this was evident as we needed to change the empirical antibiotics as per culture and sensitivity pattern in most of cases who were treated with old traditional antibiotic therapy. However, none of the organisms isolated were resistant to vancomycin and linezolid.

The results of the present study are similar to John G. Hughes[10] and it showed that statistically significantly more microorganisms were isolated from synovial fluid specimens by culture with the Peds Plus/F bottle than by culture by the conventional agar plate method.

Recent studies have demonstrated the utility of BACTEC culture methods over standard agar plate and broth methods for the isolation of microorganisms from synovial fluid. Conventional culture methods, which involve the inoculation of synovial fluid directly onto agar media, have been shown by several investigators to lack sensitivity compared to the inoculation of synovial fluid into blood culture media.[9,10] This lack of sensitivity may relate to several factors. First, the quantity of microorganisms in synovial fluid is often quite low. Culture of larger amounts of synovial fluid, which is possible by inoculation of a specimen into blood culture bottles instead of onto agar plates, should theoretically result in higher levels of recovery. Second, inhibitors, including antibiotics, in synovial fluid may inhibit the growth of microorganisms in culture. von Essen and Holtta[9] and Yagupsky and Press[11] independently observed the inhibitory effect of synovial fluid on bacterial growth near the area on culture plates where most of the synovial fluid specimen was deposited. Resins, such as those that are present in the BACTEC Peds Plus/F bottle, and the dilution effect of placing an inoculum into a liquid medium in blood culture bottles may decrease the inhibitory effects of inhibitors, including antibiotics. Third, microorganisms may be phagocytized by white blood cells in synovial fluid and therefore may not be recovered by culture. Release of phagocytized organisms by lytic agents such as saponin, which are contained in most blood culture medium formulations, may be possible.

In summary, we have demonstrated the superior performance of culture with the BACTEC Peds Plus/F blood culture bottle compared to conventional plating methods for the detection of clinically significant microorganisms in synovial fluid specimens.

Ethical responsibilities

Protection of persons and animals

The authors declare that no experiments on human beings or animals were performed for this research.

Data confidentiality

The authors declare that no patient data appear in this article.

Right to privacy and informed consent

The authors declare that no patient data appear in this article.

Conflicts of interest

The authors have none to declare.

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