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Epidemological Study of Acute Bone and Joint Infection in Pediatric Patients in Tertiary Care Centre of Central India

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ABSTRACT

Introduction: Acute bone and joint infections in children are at times difficult to diagnose and may leads to major life threatening and limb-threatening complications if not recognized and treated early. Pediatric acute bone and joint infections remain a challenging clinical issue for physicians. Objective is to assess the cause, epidemiology, diagnosis, treatment and complications of acute bone and joint infection in this study.

Material and Methods: We conducted a prospective and observational study from September 2016 to July 2018. To analyze the epidemiologic characteristics, diagnosis and treatment of acute bone and joint infections in paediatric patients treated in tertiary care centre of central india. The outcomes analyzed were: age, sex, diagnosis, etiologic agent, anatomic location, time to diagnosis, history of previous trauma and infection, laboratory tests, treatment, and complications if any.

Result: 30 patients included in our study, out of which 21 had a diagnosis of acute septic arthritis and 9 had acute osteomyelitis. Boys were predominantly affected; mean age was 6.65 years with the youngest being 4 month and the oldest being 14 years old. On comparing the laterality right sided bone and joint infection was more common(63%). The most common etiologic agent was Staphylococcus aureus. The observed peaks of the ESR reached on day 3 and peak in CRP titre generally was seen on day of admission. After peaking, ESR started a slow descent; the <20-mm/hour level was reached on day 28. CRP started a more rapid normalization, descending to less than 20 mg/L in 10 days. CRP normalizes faster than ESR, providing a clear advantage in monitoring recovery.

Conclusion: Evaluation of epidemiological and demographic characteristics, clinical features along with lab diagnosis which are useful for management of acute bone and joint infection. Future prospective studies with longer patient follow-up and development of treatment protocols are needed to improve therapeutic decision-making and the prognosis of children with osteoarticular infections.

Keywords: C-reactive protein, erythrocyte sedimentation rate, Osteoarticular infection , Osteomyelitis, pediatric, Septic Arthritis

INTRODUCTION

Acute bone and joint infections can be limb or life threatening. Timely diagnosis and appropriate treatment are paramount to minimizing complications and optimizing outcomes[1]. Acute Bone and Joint infections in children, such as osteomyelitis and septic arthritis, are a growing problem with potential

for systemic complications, since they can progress to irreversible joint destruction and sepsis. Diagnosis of joint or bone infection in children is frequently difficult, since this disease may initially be asymptomatic[2,3]. Early diagnosis and appropriate medical and surgical treatment are necessary to reduce permanent damage. Evaluation and managrment of these patients require intra departmental coordination including the emergency unit, pediatrics, orthopedics, infectious diseases, laboratory services, radiology, nursing, and social services[4-6.] Clinical manifestations of osteoarticular infections in children vary according to age and the microorganism and bone structure involved.

Acute osteoarticular infections are relatively common in pediatrics, occurring at a rate of 5.5–12/100,000 children.[7] While osteoarticular infections may cause growth changes or pathologic fractures, they often represent a diagnostic and therapeutic challenge for clinicians[8]. Illness severity has been linked to the primary infection location, and presence of infection in adjacent tissues. Other factors, including patient age and comorbidities, and the species and strain of the responsible microbe, also affect illness severity and response to treatment. There is no single test that can confirm or rule out septic arthritis or osteomyelitis. A combination of careful history, physical exam, imaging, laboratory diagnosis, and aspiration or biopsy is typically required to make a definitive diagnosis.[1]

The serum C-reactive protein (CRP) challenges the traditional position of ESR for diagnosis and follow-up of acute osteoarticular infections in childhood. The increases and decreases of CRP are so clear cut and fast (increased values are seen within 6–8 h and the doubling time is only 8 h) that they have the potential to influence treatment. Furthermore, if the infection subsides, the levels decline by approximately 50% a day [9-14]. A negative CRP measurement is of great value, because it is a strong argument against potential SA or OM [15-16].

Material and method: We conducted a prospective observational study of 30 patients at our institute from September 2016 to July 2018. In selected patients, ESR and CRP measurements were done 5 times as per pre-set protocol (on the day of admission, 3rd, 10th, 28th day and at 2nd month). We included patients with a suspected acute bone and joint infection between age 3 months and 14 years, reporting to hospital within 48 hr of initiation of symptoms of acute infection, who did not treated with antibiotics. Patients who were younger than 3 months and older than 14 years, those treated previously with antibiotics and immunodeficient patients were excluded from the study. Patients who fulfil the above mentioned inclusion criteria were then admitted. History and clinical parameters were recorded in the history sheet as per the proforma. At first visit, samples were taken for all routine investigations. Sample of all patients were sent for baseline ESR and quantitative CRP along with Blood culture and synovial fluid culture as required, X-ray and ultrasound of involved limb were done as per requirement. Broad spectrum intravenous antibiotics along with symptomatic treatment (antipyretic, analgesic, IV fluids, and slab support) were initiated after sending samples. Joint aspiration, Incision and drainage, and arthrotomy was done as required

Parameters of observation

. Age

. Sex

• Type of infection: - Septic arthritis , Osteomyelitis .

• Identification of causative organism (by culture and biopsy)

• Anatomical location and limb laterality of the infection

• History of previous illness, any trauma or infection.

. Laboratory investigation for a predetermined series of ESR, CRP measurements. C-reactive protein (CRP, normal value < 6 mg/dl) - Erythrocyte sedimentation rate (ESR, normal value < 20 mm/h).

• Treatment (conservative and surgical)-

. Duration of treatment

• Complications – if any.

Volume 4, Issue 2; March-April 2021; Page No 405-411

Observation table 1:

Age and Sex distribution			
Age group	Male	Female	Total
3 months- 3year	4	6	10
3 year - 6 year	5	1	6
6 year -9 year	1	1	2
9 year -12 year	6	2	8
12 year-14 year	3	1	4

Observation table 2:

Out of total patients, 70% cases were of septic arthritis and 30% cases were of osteomyelitis.

Total no. of cases	OM	SA
30	9	21

Observation table 3:

In our study most commonly osteomyelitis affects right lower limb with maximum no. of cases having femur involved whereas septic arthritis involves knee joints more commonly (Rt>Lt).

Limb Involved	OM	SA
Rt Upper Limb	1 (Humerus)	1(Shoulder)
Lt Upper Limb	2(Humerus)	0(Shoulder)
Rt Lower Limb	4(3 Femur,1 Tibia)	13(9 Knee,4 Hip)
Lt Lower limb	2(1 Femur,1 Tibia)	8(6 Knee,2 Hip)

Observation table 4:

Staph aureus is the most common pathogen causing osteomyelitis/septic arthritis.

Organism grown on culture(blood/synovial fluid and surgical tissue forbiopsy)	
Organism	**Number of patients**
Staphylococcus aureus	28
Pseudomonas	2

Observation table 5:

Conservative treatment with use of antibiotics stays the prime mode of treatment followed by arthotomy

Procedure	**No of Patients**
Conservative	17

Volume 4, Issue 2; March-April 2021; Page No 405-411

Arthrotomy	7
I & D	6

Statistical analysis: 30 patients were included in our study, 21 patients had a diagnosis of SA (70%) and 9 patients had acute OM (30%). Of 30 patients, 3 were lost to follow-up. Twenty-seven patients were included in calculating the final result. On applying unpaired t-test on both SA and acute OM patients with CRP and ESR on the day of admission 3rd day, 10th day, 28th day, and 2nd month. On the day of admission, mean CRP in both SA and acute OM patients was significantly high as compared to mean ESR, $P < 0.05$ which is statistically significant. Similarly, on the 10th day, mean CRP value was 18.63 mg/L and mean ESR value was 28.48 mm at 1 h, so we can deduce early normalization of CRP compared to late normalization of ESR, $P < 0.05$ which is statistically significant. Sluggish normalization of the ESR is one of the explanations why antibiotics for acute osteomyelitis have been administered for such long periods. We usually discontinued antibiotics if the CRP descended to <20 mg/L, provided the clinical response was good. Whether normalized CRP alone justifies drug discontinuation would require its own study. If surgery is performed, the tissue destruction elevates CRP transiently.[12,22] If CRP levels continue to rise or remain high on the 4th day of treatment, a complication should be suspected.[23] Unpaired t-test applied over 27 patients for correlation between patient who underwent any surgical procedure on acute OM and SA with patient who received conservative treatment. In both these groups, mean value of CRP on day 10 was >22.12 mg/L in a patient undergoing any surgical procedure, and mean CRP in nonoperative group was >15.84 mg/L on day 10. This correlation is statistically significant ($P < 0.05$). On applying unpaired t-test mean CRP of 27 patients under evaluation on day 10, to assess the correlation between patients of septic arthritis and acute OM group, the normalization of CRP was earlier in acute OM group. This correlation was statistically significant ($P < 0.05$). We have found an elevated CRP is a strong independent indicator of SA and acute OM. Levels on CRP >20 mg/L in doubtful cases strongly indicate the possibility of acute osteoarticular infection.

Observation table 6:

Student T-Test

Correlation of CRP and ESR on day 10 in septic arthirits(SA) and acute osteomyelitis(OM).

Group Statistics					
		Mean	**Std. Deviation**	**Std.Error Mean**	**P value**
CRP	SA	19.8800	6.09729	1.39881	.033
	OM	14.6000	3.79021	1.34004	.013
ESR	SA	28.5263	9.49484	2.17827	.965
	OM	28.3750	2.82527	.99888	.950

Observation table 7:

Student T-Test

Correlation of CRP on day10 in patients managed conservatively and operatively

CRP	Mean	Std. **Deviation**	Std. Error Mean	P value
Operative	21.4092	6.66674	1.92452	.013
Conservative	15.8407	4.06263	1.04897	.021

Results:

In our study 30 patients included, 21 patient had a diagnosis of septic arthritis (70%) and 9 patient had osteomyelitis (30%) . Boys were more predominantly affected (63%) then girls(37%) and the mean age was 6.65 years with the youngest being 4 month and the

Volume 4, Issue 2; March-April 2021; Page No 405-411

oldest being 14 years old. As for anatomical location of the infection, 15 patients presented septic arthritis in the knee, 6 of the hip, and one in the shoulder. The cases of osteomyelitis occurred in the following locations: 4 at the shaft and distal end of the femur,3 at the humerus, 2 at the proximal end of the tibia. On comparing the laterality right sided bone and joint infection was more common (63%). As for the etiologic agents, blood culture detected the growth of isolated pathogens in 24 patients: 22 cases of Staph aureus, 2of pseudomonas aeuroginosa. Synovial fluid aspirate culture diagnosed the growth of isolated pathogen in 6 patient: all are positive for Staph Aureus. Biopsy was sent in all cases where surgical intervention was done.

CRP level and ESR were assessed in all patients at the time of hospital admission. The average ESR on day of admission, 3rd,10th ,28th and two month was 35 mm/h, 41 mm/h and 28mm/h, 18mm/h,13mm/h. respectively average CRP on day of admission,3rd,10th,28th and two month was 80mg/l,54mg/l,17.6mg/l,8mg/l,5.5mg/l .The treatment involved intravenous antibiotic therapy during hospitalization and oral antibiotics after discharge in all patients. Therapy duration (intravenous and oral) was 3-5 weeks. Combination of Ceftriaxone + sulbactum and amikacine was the most frequent antibiotic, followed by vancomycin and meropenum.2 patient with Pseudomonas are sensitive to ceftazidime, amikacin and meropenum. Conservative treatment with use of antibiotics was the mainstay of treatment, supplemented by arthrotomy or incision and drainage if needed. Biopsy was sent in all cases where surgical intervention was done. Of the 30 patients included, 13 (43%) underwent at least one surgical procedure, which was most frequently Arthrotomy in 7 patients of septic arthritis knee, I&D in 3 patient with osteomyelitis and biopsy sample for septic arthritis hip were sent in 3 cases. The sensitivity of elevated ESR on admission to detect an osteoarticular infection was 93%. Using CRP alone gave only a slightly better sensitivity of 96% , but combining these two markers gave a sensitivity of 100%. An elevated ESR or CRP within the first 3 days was seen in all patients 100% sensitivity. The observed peaks of the ESR reached on day 3 and peak in CRP titer generally were seen on day of admission . After peaking, ESR started a slow descent; the <20-mm/hour level was reached on Day 28 . CRP started a more rapid normalization, reduced to less than 20 mg/L in 10 days. CRP normalized early in patients with OM, whereas slow normalization was in patients with SA [21]. No correlation found when comparing surgical procedure with increase titer of CRP or ESR on day of admission[21].

DISCUSSION: This study analyzed the clinical and epidemiological characteristics and treatment of acute bone and joint infections in children, based on data collected from patients treated at a tertiary care center in central india. In our study 30 patients included, 21 patient had a diagnosis of septic arthritis (70%) and 9 patient had osteomyelitis (30%) . Boys were more predominantly affected the mean age was 6.65 years, with the youngest being 4 month and the oldest being 14 years old. . As for anatomical location of the infection, 15 patients presented septic arthritis in the knee, 6 of the hip, and one in the shoulder. The cases of osteomyelitis occurred in the following locations: 4 at the shaft and distal end of the femur,3 at the humerus, 2 at the proximal end of the tibia. On comparing the laterality right sided bone and joint infection was more common(63%). As for the etiologic agents, blood culture and tissue sent for culture biopsy, detected the growth of isolated pathogens in 24 patients: 22 cases of Staph aureus, 2of pseudomonas aeuroginosa. Synovial fluid aspirate culture diagnosed the growth of isolated pathogen in 6 patient: all are positive for Staph Aureus. The sensitivity of elevated ESR on admission to detect an osteoarticular infection was 93%. Using CRP alone gave only a slightly better sensitivity of 96% , but combining these two markers gave a sensitivity of 100%. An elevated ESR or CRP within the first 3 days was seen in all patients 100% sensitivity. Of the 30 patients included, 13 (43%) underwent at least one surgical procedure, which was most frequently Arthrotomy in 7 patients of septic arthritis knee, I&D in 6 patient with osteomyelitis.

Pääkkönen et al.[12] assessed 265 children with positive culture results and found that, due to the rapid normalization of serum CRP in the first week, CRP is more sensitive for diagnosis than ESR, but the best sensitivity for diagnosis (98%) was seen with a combination of both ESR and CRP. Frederico carlos Jaña Neto et al[17] retrospectively analyzed patients admitted between September 2012 and August 2014. The outcomes analyzed were: age, sex,

Volume 4, Issue 2; March-April 2021; Page No 405-411

diagnosis, etiologic agent, anatomic location, time to diagnosis, history of previous trauma and infection, laboratory tests, treatment, and complications. Twenty two patients were included, 50% with septic arthritis, 35% with osteomyelitis, and 15% with both. Boys were predominant (80%), and the mean age was 6.6 years. The most common etiologic agent was Staphylococcus aureus. C-reactive protein value and erythrocyte sedimentation rate were elevated. The infections were treated with antibiotic therapy (intravenous and oral) and oxacillin was most frequently used. Most patients underwent at least one surgical procedure, and 35% of patients had complications. According to Dodwell et al.,[1] in there study approximately 85% of children with osteomyelitis and 100% of children with osteomyelitis associated with septic arthritis presented elevated CRP and ESR levels. Mitha et al[2] in there study found 52% of cases with septic arthritis and 41% osteomyelitis, with 80% of cases involving the lower limb. Most of the studies show that confirmation of the diagnosis of septic arthritis, osteomyelitis, or both should be based on signs and symptoms found in imaging examinations and laboratory tests. However, bone alterations only become apparent in X-rays after seven to 10 days of infection, and initial laboratory data can present within normal limits. Furthermore, approximately 30% to 50% of causative pathogens are not identified through culturing, since some microorganisms require specific culture media or a longer growth period. Chen et al.[18] studied 27 children, 55.6% children had a diagnosis of concomitant septic arthritis and osteomyelitis, Staphylococcus aureus was most common causative organism with 83.3% of cases. Kocher et al.[19] proposed guidelines to manage pediatric osteoarticular infections and mentioned the use of antibiotic therapy and surgery according to need. The patients were admitted to the hospital, treatment is started with empirical antibiotics and sample werw drwn and sent for culture. Empirical treatment is used to address the most likely pathogens, and the medication selected according to the age of the child, the local prevalence of infectious agents, and early laboratory results. When the results of culture are available, antimicrobial therapy may be modified depending on the microorganism and the pattern of susceptibility. It is recommended that treatment last a total of at least three weeks, depending on the patient's clinical response. In the sample analyzed in this study, all patients received intravenous antibiotic therapy during hospitalization and oral antibiotics after discharge, with an average total duration of four to six weeks. Pedro Fiorini Puccini1et al[20] in a descriptive study of 21 cases with patients aged zero to 14 years-old, diagnosed with acute hematogenous osteomyelitis .The incidence in males was higher than in females, and children over five years of age were the most affected ones. Fever and pain were the main symptoms, and the long bones were the most often affected. The most commonly recovered pathogen was Staphylococcus aureus. The time interval between the onset of symptoms and the diagnosis was 9.7 days, the length of hospital stay was 24.7 days, and the duration of treatment was 71.7 days. Complete resolution occurred in 71.4% of the cases and complications appeared in 28.6% of them, being chronic osteomyelitis the main one.

Limitations of this study include small sample size, and lack of long-term patient follow-up. The importance of prospective studies with longer patient follow-up is evident, as well as complete care protocols for children with suspected acute bone and joint infection which include clinical examination, laboratory diagnosis and imaging, broad spectrum antibiotic therapy, and surgical treatment if required any. Guideline of procedures for care and treatment may improve therapeutic decision-making and lead to a better prognosis for these patients.

Conclusion: The cause and Epidemiology of pediatric acute bone and joint infections identified by clinical and demographic characteristics which can help the team prepare to attend future cases. Additional prospective studies with longer patient follow-up and the creation of care protocols are necessary to improve therapeutic decision-making and the prognosis for children with suspected bone and joint infection. Further study could focus on future prospective assessments of shorter antibiotic treatment regimens, and diagnostic protocols that may allow earlier detection of causative organisms and the appropriate antibiotic therapy.

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Volume 4, Issue 2; March-April 2021; Page No 405-411

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Volume 4, Issue 2; March-April 2021; Page No 405-411