Abstract

Background: Acute bone and joint infections in children are at times difficult to diagnose and pose serious consequences if not diagnosed and treated in time. We conducted a prospective and observational study from September 2016 to July 2018. Aims and Objectives: Our study included 30 children between the ages of 3 months and 14 years, with suspected acute osteoarticular infection, with a predetermined series of ESR, CRP measurements. Material and Methods: 21 patient had a diagnosis of acute septic arthritis (SA) (70%) and 9 patient had acute osteomyelitis (OM) (30%). Boys were predominantly affected (63% boys as compared to 37% girls), and the mean age was 6.65 years. The average ESR on day of admission, 3rd, 10th, 28th day and two month was 35 mm, 41 mm, 28 mm, 18 mm and 13 mm at one hour respectively. Average CRP on day of admission, 3rd, 10th, 28th day and two month was 80 mg/l, 54 mg/l, 17.6 mg/l, 8 mg/l, 5.5 mg/l respectively. Results: 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. CRP normalized earlier in patients with OM, whereas normalization was slower in patients with SA. Conclusion: Serial measurements of ESR and CRP not only help in diagnosing Acute bone and joint infections in children but also help in monitoring response to treatment and duration of antibiotics.

Keywords: Acute osteoarticular infection, C-reactive protein, erythrocyte sedimentation rate

INTRODUCTION

Acute osteoarticular infections in children, such as acute osteomyelitis (OM) and acute septic arthritis (SA), are serious problems with the potential for systemic after effects since they can progress to irreversible joint damage and sepsis. The diagnosis of acute osteoarticular infection in children is frequently difficult, since this disease may initially be asymptomatic.[1] Early diagnosis, pharmaceutical, and surgical treatment are necessary to reduce permanent damage.

Acute osteoarticular infections may develop as a result of hematogenous seeding, direct inoculation or extension from a contiguous focus of infection. The pathogenesis of acute SA is multifactorial and depends on the interaction of the host immune response and the adherence factors, toxins, and immunovoidance strategies of the invading pathogen.[2]

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Role of Quantitative C-Reactive Protein and Erythrocyte Sedimentation Rate for Evaluation and Management of Acute Osteoarticular Infections in Pediatric Patients

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the capillaries. Large colonies of bacteria surrounded by glycocalyx obstruct capillary lumens, impairing phagocytosis, and antibiotic penetration.

Acute osteoarticular infections of childhood comprise essentially three entities, SA, OM, and their combination (OM + SA).

Laboratory parameters are used to help the clinician with evaluation. Erythrocyte sedimentation rate (ESR) has been the main yardstick in monitoring the course of illness. 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.

A negative CRP measurement is of great value, because it is a strong argument against potential SA or OM.

**Materials and Methods**

We conducted a prospective observational and interventional study of 30 patients at our center between September 2016 and July 2018. In selected patients, ESR and CRP measurements were done 5 times (on the day of admission, 3rd, 10th, 28th day and at 2nd month). We included patients with a suspected acute osteoarticular infection between age 3 months and 14 years, presenting within 48 h of onset of symptoms of acute infection with no previous antibiotic therapy.

Patients who were younger than 3 months and older than 14 years, those who received previous antibiotic therapy and immunodeficient patients were excluded from the study.

The selected patients who satisfied the above inclusion criteria were then registered, all history and clinical details were recorded in the history sheet as per the pro forma.

On arrival, samples were drawn for all routine investigations along with differential and total leukocyte count. All patients were investigated for baseline ESR and quantitative CRP. Blood culture and synovial fluid culture were sent as required, X-ray and ultrasonography of affected part were done as per requirement. Broad spectrum intravenous (IV) antibiotics along with symptomatic treatment (analgiesic, anti-pyretic, IV fluids, and splintage) were started after sending samples. Incision and drainage if needed were done.

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**Parameters of observation**

The level of CRP measured on the day of admission 3rd, 10th, 28th day, and 2nd month. Baseline CRP value >20 mg/L was highly suggestive of acute bone and joint infection. The level of ESR on treatment measured on the day of admission 3rd, 10th, 28th day, and 2nd month. ESR value >20 mm at 1 h was highly suggestive of acute osteoarticular infection.

**Age and sex distribution**

A total of 30 patients were included in the study out of which maximum number of cases were seen to fall in the age group between 3 months and 3 years with female predominance. After the age of 3 years, male patients predominated. Male predominance was observed with 63% of patients being male and 37% female.

**Total osteomyelitis and septic arthritis case distribution**

Of total patients, 70% of cases were of SA and 30% of cases were of acute OM.

**Laterality**

In our study, most commonly OM affected the right lower limb with maximum number of cases having femur involved whereas SA involved knee joints more commonly (right > left). All cases in our study had unilateral involvement except for one which had bilateral SA of the knee joint.

**Blood culture**

*Staphylococcus aureus* was the most common pathogen causing OM/SA.

**Procedure**

Conservative treatment with use of antibiotics was the backbone of treatment supplemented by arthrotomy or incision and drainage if needed.

Biopsy was sent in all cases where surgical intervention was done.

**Statistical analysis**

In our study, 30 patients were included, 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 hematogenous OM (AHOM) 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. If CRP levels continue to rise or remain high on the 4th day of treatment, a complication should be suspected.

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 ($P < 0.05$) [Table 5].

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.

**DISCUSSION**

We studied 30 children aged 3 months–14 years with acute osteoarticular infection with a predetermined series of ESR, CRP measurements, and assessed their role in diagnosis and management.[13]

The concentration of serum CRP, an acute phase protein, initially rises and thereafter decreases rapidly during acute bacterial arthritis or OM in children. On the contrary, ESR rises slowly during several days and then normalizes slowly during several weeks.

The question is what additional benefit is achieved using CRP determinations in addition to ESR (and to a lesser extent, white blood cell) in diagnosis and especially follow-up of acute OM or SA in children. There are three important reasons for using CRP in addition to ESR determinations.[14]

First, CRP is a simple test carried out with readily available laboratory equipment, nephelometer or turbidimeter, and it requires only a finger prick sample of blood. Ease of sampling and determination of CRP means that it can be done frequently during the acute phase of the illness. The CRP values should be measured quantitatively, and the test result must be obtained on the same day because the information reflects the actual situation of infection more reliably than any other simple laboratory test. Measuring CRP from a finger prick is even easier now that an apparatus is available in which whole blood, instead of serum, is used without the need for centrifugation.[14]

Second, CRP increases and decreases much more quickly than ESR. CRP was clearly elevated on admission, peaked within 48 h and normalized in about 1 week. In contrast, ESR started a slow descent; the 20-mm/h level was reached on day 28. CRP started a more rapid normalization, descending to less than 20 mg/L in 10 days. ESR and CRP normalized faster in patients with OM, whereas normalization was slower in patients with SA.

In our study, the correlation between increased value of CRP or ESR on the day of admission and patients who required surgical procedure was not proven statistically significant, $P > 0.05$.

In all cases, CRP peaked and normalized significantly earlier than the erythrocyte sedimentation rate. In our study, it was observed that on the 10th day of treatment, the normalization time of CRP was more in patients who required surgical procedure, mean CRP on 10th day in operated patients was >20 mm/h and in nonoperated cases <20 mm/h, and it is statistically significant ($P < 0.05$). It was also found that CRP normalization in acute OM patients was statistically more significant compared to SA patient population on 10th day of follow-up ($P < 0.05$).

Previous studies did not reveal any rise of postoperative CRP levels in pediatric patients with OM or OM with adjacent SA.[12,15]

In the present study, comprising of 30 children of age 3 months–14 years (mean, 6.65 years) with bacteriologically confirmed acute OM and SA. After having the highest levels on the day of admission, during treatment, CRP commenced a rapid normalization and values at <20 mg/L were reached in 10 days. The mean time to reach a level at <20 mm/h at 1 h was 28 days for ESR. The difference between the normalization time of CRP and ESR is statistically significant ($P < 0.05$).
The ESR decreases slowly, and a value of 20 mm at 1 h is reached on average only after 25 days. sluggish normalization of the ESR is one of the explanations why antibiotics for AHOM have been administered for such long periods. [38,34] We recommend to discontinue antibiotics if the CRP has 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. [12,16]

Our study proves that quantitative CRP and ESR done serially in acute osteoarticular infections are very helpful in first the diagnosis and second the monitoring of treatment.

In our study of 30 patients of acute osteoarticular infection, the most common etiologic agent was S. aureus. CRP values and ESR were elevated on the day of admission in all cases. CRP values peaked on the day of admission in most of the cases, and ESR peaked on day 28. CRP normalized to <20 mg/L on day 10. ESR normalized <20 mm at 1 h on day 28. The infections were initially treated with broad-spectrum antibiotics such as third generation cephalosporins and aminoglycosides. Once the culture sensitivity reports were available, antibiotics were changed accordingly. 13 patients out of 30 underwent at least one surgical procedure.

No correlation was observed between the need of a surgical procedure and raised titer of CRP or ESR on the day of admission. The normalization of CRP was earlier in acute OM cases as compared to SA cases. Serum CRP is a good guide in monitoring the course of illness, and the antimicrobials can usually be shifted to oral if the symptom and signs subside within a few days, and CRP has decreased to <20 mg/L. In our study, CRP levels decreased to <20 on day 10 and once this happened with clinical resolution of symptoms, IV antibiotics were stopped and oral antibiotics were started which were continued till CRP <10.

Conclusion

Those serial measurements of quantitative CRP and ESR in patients of acute osteoarticular infections in children used together are very useful for diagnosis as well as monitoring treatment progression. We advocate further studies to use serial measurements of CRP and ESR in these patients to frame guidelines for performing a surgical procedure and to decide the duration of antibiotic treatment.

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Conflicts of interest

There are no conflicts of interest.

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