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RESEARCH ARTICLE

AN OBSERVATIONAL COMPARATIVE STUDY OF CRP AND ESR IN EVALUATION AND MANAGEMENT OF ACUTE BONE AND JOINT INFECTION IN PEDIATRIC PATIENTS IN TERTIARY CARE CENTRE OF CENTRAL INDIA

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Abstract

Introduction : Acute osteomyelitis of childhood usually affects the long bones of the lower limbs. Although almost any agent may cause acute osteomyelitis, Staphylococcus aureus is the most common bacteria. We conducted a prospective and observational study from July 2019-December 2020. Aims and Objects: Our study included 36 children between the ages of 5 months and 14 years, with suspected acute osteoarticular infection, with a predetermined series of ESR, CRP measurements.

Material and Methods: We included 36 patients in our study out of which 25 patients had a diagnosis of acute osteomyelitis (70%) and 11 patients had acute septic arthritis (SA) (30%). Boys were predominantly affected (64% boys as compared to 36% girls), and the mean age was 6.12 years. The average ESR on day of admission, 3rd, 10th, one month and two months was 36 mm, 51 mm, 37mm, 20mm and 14 mm at one hour respectively. Average CRP on day of admission, 3rd, 10th, one month and two months was 86 mg/l, 64mg/l, 19.6mg/l, 10mg/l, 5mg/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 end of one month. 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, where as 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.

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Introduction:-

Acute osteomyelitis is defined as an acute infection of the bone or bone marrow diagnosed within 2 weeks from the onset of signs and symptoms.^[1] Further definitions vary, but the usual consensus is that if the history is longer than 2 weeks the disease is subacute, and if much longer (months) then osteomyelitis is chronic. Acute bone & joint infections in children, such as osteomyelitis and septic arthritis, are a growing problem with potential for systemic after effects, because disease can progress to irreversible joint damage and sepsis. For evaluation and management physicians pay attention to fever, malaise, or local symptoms such as swelling, pain, or restricted motion of the affected limb. Laboratory parameters are used to help the clinician with evaluation.^[2,3,4,5] The routes by which bacteria reach to bone are direct spread from an adjacent infected soft tissue or joint, direct inoculation during trauma or a surgical procedure, by haematogenous seeding.^[2,6] In children, haematogenous spread is most common. The anatomy of growing bone plays a major role in the pathogenesis. Acute osteomyelitis usually commences from the metaphysis of a long tubular bone. As already suggested sluggish blood flow in the sinusoids of the epiphyseal-metaphyseal junction and a defective reticuloendothelial system with impaired phagocytosis allow bacteria to stick in the sinusoidal structures.^[6,7,8] It also has been hypothesised that acute articular infection develops by two different mechanisms.^[9] The more common is local: blunt trauma causes oedema and haematoma and this local process is secondarily infected haematologically by bacteria that occasionally gain access to the bloodstream. Alternatively, one or multiple non-traumatised locations are infected during primary septicaemia.^[9] Classical AHOM manifests as local pain in the affected limb. A distinctive feature is gradual worsening of the symptoms and signs within days.^[6,10] Local swelling and redness may be present, more commonly in infants and young children, but may be inconspicuous and appear only after spread of the infection to beneath the periosteum (subperiosteal). Acute bone & joint infections of childhood comprise essentially three entities, septic arthritis (SA), osteomyelitis (OM), and their combination (OM + SA). Laboratory parameters are used to help the clinician with evaluation. ESR is still the main yardstick in monitoring the course of illness.^[11,12,13,14] The serum CRP challenges the traditional position of ESR for diagnostics and follow up of invasive bacterial infections such as osteoarticular infections of childhood. The increases and decreases of CRP are so clear cut and fast (increased values are seen within 6 to 8 hours, and the doubling time is only 8 hours) that they have the potential to influence treatment. Furthermore, if the infection subsides, the levels decline by approximately 50% a day^[15]. A negative CRP is of high importance, because it is a strong indicator against potential osteoarticular infection. If in doubt, CRP should be checked after 6 to 8 hours, and if still less than 20 mg/L^[16], the risk of acute osteoarticular infection is very low.^[17,18,19]

Material and Method:-

We conducted an observational study of 36 patients at our center between July 2019- Dec 2020. In these selected patients, ESR and CRP measurements were done 5 times (on the day of admission, 3rd, 10th, one month and at two months). We included patients with a suspected acute osteoarticular infection between age 5 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 5 months and older than 14 years, those who received previous antimicrobial 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 withdrawn 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 (analgesic, antipyretic, IV fluids, and splintage) were started after sending samples. Incision and drainage, joint aspiration, or arthrotomy was done as required.

Parameters of observation:

The level of CRP measured on the day of admission 3rd, 10th, one month, 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, one month, and 2nd month. ESR value >20 mm at 1 h was highly suggestive of acute osteoarticular infection.

Demography-Age and sex distribution;

A total of 36 patients were included in the study out of which maximum number of cases were seen to fall in the age group between 5 months and 3 years with female predominance. After the age of 3 years, male patients predominated. Male predominance was observed with 64% of patients being male and 36% female [Table 1].

Disease Distribution-case wise:

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

Laterality-limb involvement:

In our study, most commonly OM affected the left 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.

Blood/Synovial culture:

Staphylococcus aureus was the most common pathogen causing OM/SA [Table 2].

Surgical Procedure:

Conservative treatment with use of antibiotics was the mainstay of treatment supplemented by arthrotomy or incision and drainage if needed [Table 3]. Biopsy was sent in every case where surgical intervention was done.

Observation table :**Table 1:-**

Age and Sex distribution			
Age group	Male	Female	Total
5 months- 3year	5	7	12
3 year - 6 year	5	2	7
6 year -9 year	2	1	3
9 year -12 year	6	3	9
12 year-14 year	3	2	5

5 months- 3year age group children most communally affected.

Table 2:-

Organism grown on culture (Blood/ Synovial fluid/ Biopsy specimen after surgical procedure)	
Organism Number of patients	
Staphylococcus aureus	34
Pseudomonas	2

Staphylococcus aureus -most common organism

Table 3:-

Procedure	No of Patients
Conservative	25
Arthrotomy	8
I & D	3

Results:-

The sensitivity of elevated ESR on admission to detect an osteoarticular infection was 94%. Using CRP alone give a slightly better sensitivity of 96%, but combination of these two markers gave a sensitivity of 99%. An elevated ESR or CRP within the first 3 days was seen in all patients with 100% sensitivity. The observed peaks of the ESR and CRP generally were reached on Day 3 and on day of admission. After peaking, ESR started a slow descent; the 20-mm/hour level was reached at end of one month. CRP started a more rapid normalization, descending to less than 20 mg/L in 10 days. ESR and CRP normalized fastest in patients with OM, whereas normalization was slowest in patients with SA. In our study, 36 patients were included, 25 patients had a diagnosis of SA (70%) and 11 patients had acute OM (30%). All 36 patients, were included in calculating the final result. On the day of admission, mean CRP in both SA and acute OM patients was significantly high as compared to mean ESR. Similarly, on the 10th day, mean CRP value was 19.6mg/L and mean ESR value was 37 mm at 1 hr, so we can estimate early normalization of CRP compared to late normalization of ESR. Slow normalization of the ESR is one of the explanations why antibiotics for acute osteomyelitis have been administered for such long periods. We have found an elevated CRP is a strong independent indicator of SA and acute OM. Serum C-reactive protein (CRP) is a good guide in monitoring the course of illness, and the antimicrobial can usually be discontinued if CRP has decreased to <20 mg/L. Newer and costly agents, such as linezolid, should be reserved for cases due to resistant *S. aureus* strains.

Discussion:-

Diagnosing and monitoring pediatric osteoarticular infections start with a clinical evaluation. Attention is directed to local symptoms and signs such as pain, tenderness, swelling, or restricted motion of the affected limb or constitutional symptoms such as fever, malaise, nausea or refusing food. Unfortunately, many inflammatory conditions such as transient synovitis, reactive arthritis, or juvenile rheumatoid arthritis can clinically mimic septic arthritis.^[8] To counter this problem, ESR and CRP have been used to diagnose osteoarticular infections for decades, but the sensitivities of these markers have not been described in previous reports of these infections.^[8, 17, 19, 20] The benefits of CRP for monitoring patients have been described, but owing to the rarity of septic osteoarticular infections, the study sizes tend to be small, as are studies comparing the behavior of laboratory markers in SA, OM,^[17, 19, 20] Sensitivity to detect a bacterial osteoarticular infection on admission was 94% for ESR and 96% for CRP, higher than reported previously^[19, 21]. Most importantly, combining these two markers provided an even better sensitivity of 99%, virtually ruling out bacterial osteoarticular infection if ESR and CRP remain normal for 3 days. This information benefits clinicians when wondering whether to start antimicrobial treatment for a suspected osteoarticular infection. In monitoring the course of diseases, CRP proved a good yardstick.^[17, 19, 20] The pattern followed by the ESR and CRP values (WBC was not measured with the same schedule) was similar in SA, and OM, such rapid ascend that increased values usually were seen on admission, a peak on the second or third day of treatment, and then a fast descent, provided no complications developed. The speed of normalization differed substantially in favor of CRP, being at least 15-18 days quicker than for ESR. Other investigators reported, if CRP in OM and SA was not clearly descending on the fourth day of treatment, a complication was likely.^[22] Regardless, an exceptionally high CRP value on admission was a warning sign to the clinician to take into account this possibility. A physician who puts CRP in the context of the entire clinical situation gains much from sequential CRP measurements. Modern technology has made it possible to measure CRP quantitatively from a finger prick whole-blood sample. A precise value is obtained so quickly that the procedure is easily possible even on site of clinic.^[3, 10, 11] A complex hospital laboratory is not needed (unless many samples are analyzed) if the small instrument is at hand. CRP is an inexpensive and useful method to diagnose and monitor acute osteoarticular infections of childhood. The concentration of serum CRP, an acute phase protein, initially rises and thereafter decreased 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. Serum CRP is a good guide in monitoring the course of illness, and the antimicrobials can usually be discontinued if the symptom and signs subside and CRP has decreased to <20 mg/L.^[23] 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. 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 post operative CRP levels in pediatric patients with OM with adjacent SA.^[17, 24] In the present study, comprising of 36 children of age 5 months –14 years (mean, 6.12 years) with infective organism confirmed acute OM and SA. After having the highest levels on the day 3 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 at 1 h was one month 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 30 days. Sluggish normalization of the ESR is one of the explanations why antibiotics for AHOM have been administered for such long periods.^[25-29] 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. 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 36 patients of acute osteoarticular infection, the most common etiologic agent was *S. aureus*. CRP values were elevated on the day of admission in all cases. CRP values peaked on the day of admission in most of the cases, and 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.

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. These tests will never be

gold standards, and they need to be used in conjunction with clinical history and physical examination, cultures, pathology or imaging. But these biomarkers are available, and some of them are being widely used.

Sponsorship:

No.

Conflict of interest:

No conflicts of interest.

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