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ORIGINAL RESEARCH

Assessment of Serum Procalcitonin as a Diagnostic Marker for Acute Bacterial Septic Arthritis: A Comparative Study with Synovial WBC Count, ESR, and hs-CRP

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ABSTRACT

Introduction: Septic arthritis is a prevalent and severe condition. Timely detection and immediate treatment significantly enhance patient outcomes. **Objective:** This study aims to assess serum procalcitonin as a diagnostic marker for acute bacterial septic arthritis and compare its diagnostic efficacy with synovial white blood cell (WBC) count, erythrocyte sedimentation rate (ESR), and high-sensitivity C-reactive protein (hs-CRP). **Methods:** We conducted a prospective cross-sectional study involving 100 patients presenting with acute arthritis. Patients with concurrent infections were excluded from the study. Out of 100 cases, 36 patients were diagnosed as acute bacterial septic arthritis and 64 with acute inflammatory arthritis. Blood samples were obtained for complete blood count, ESR, hs-CRP, procalcitonin, and blood culture. Additionally, synovial fluid was analyzed for cell count, Gram stain, crystal identification, and culture. **Results:** In a study involving 100 patients, 36 were diagnosed with acute bacterial septic arthritis, primarily caused by *Staphylococcus aureus and Streptococcus group B.* Another 64 patients had acute inflammatory non-septic arthritis, including conditions like gout and rheumatoid arthritis. Serum procalcitonin (PCT)≥0.5 ng/mL showed 59.3% sensitivity, 86% specificity, and a 75.3% positive predictive value for diagnosing septic arthritis. C-reactive protein (CRP) > 10 mg/dL had 78.2% sensitivity, but only 19% specificity. Erythrocyte sedimentation rate (ESR) ≥ 20 mm/h exhibited 95% sensitivity and 19% specificity. White blood cell count (WBC) > 15 × 10^9/L showed 39.1% sensitivity and 66.6% specificity. **Conclusion:** Serum procalcitonin shows promise in diagnosing acute bacterial septic arthritis, especially when arthrocentesis is not feasible.

Keywords: Diagnosis, High-Sensitivity C-Reactive Protein, Procalcitonin, Septic Arthritis

INTRODUCTION

Septic arthritis must be promptly considered in adults presenting with acute monoarticular arthritis due to its potential for permanent morbidity and mortality if not treated swiftly. Delayed initiation of appropriate antibiotic therapy within 24 to 48 hours can lead to sub-cartilaginous bone loss, cartilage destruction, and irreversible joint dysfunction.[1] The reported incidence ranges from four to 29 cases per 100,000 person-years, with higher risks associated with advanced age, immunosuppressive medication use, and lower socioeconomic status.[2] Intra-articular infections typically manifest as monoarticular, although up to 20% of cases can involve multiple joints (oligoarticular or polyarticular). Hematogenous spread from bacteremia is the most common route of joint infection, predominantly caused by Staphylococcus aureus and Streptococcus species. Diagnosis hinges on laboratory tests, particularly synovial fluid analysis.[3] Acute bacterial septic arthritis is a

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significant medical emergency with an annual incidence of 0.002% to 0.01%, carrying substantial mortality (10-15%) and morbidity rates resulting in irreversible joint function loss in up to 50% of patients. Delays in diagnosis and treatment can lead to severe joint destruction, restricted range of motion, and deformities.[4] Early differentiation between acute bacterial septic arthritis and non-septic arthritis poses challenges and impacts treatment decisions. Traditional signs of infection such as fever, constitutional symptoms, and joint warmth, redness, and swelling can overlap with other causes of acute inflammatory non-septic arthritis, such as crystal-induced arthritis. Gram stain of synovial fluid is only diagnostic in 50-60% of cases of acute bacterial septic arthritis, while culture yields higher but delayed results (3-5 days), potentially delaying antibiotic initiation.[5-6] Procalcitonin, a protein encoded by the CALC-I gene on chromosome 11, is typically undetectable or low (<0.1 ng/mL) in healthy individuals but rises in response to inflammation and bacterial infections, distinguishing it from viral infections. Elevated serum procalcitonin levels are associated with severe bacterial infections, sepsis, septic shock, and multiple organ failure. However, its diagnostic performance in localized infections has been reported as suboptimal, influenced by non-infectious triggers like surgical trauma, Kawasaki disease, and adult-onset Still's disease.[7] This study aimed to evaluate the clinical utility of serum procalcitonin in distinguishing early between acute bacterial septic arthritis and acute inflammatory non-septic arthritis, complementing clinical signs and symptoms.

MATERIALS AND METHODS

Study Setting and Duration

This cross-sectional study was conducted at ASMC Lalitpur between January 2024 and June 2024. The research enrolled 100 patients, all adults over 18 years old, who presented with arthritis in at least one joint lasting less than 14 days. Diagnosis of septic arthritis followed the Newman criteria, requiring:

1. Isolation of an organism from the joint,
2. Isolation of an organism from another site,
3. Absence of isolated organisms but supporting evidence such as histological or radiological signs of infection, or turbid joint fluid upon aspiration.
4. Patients were excluded from the study if they met any of the following criteria: (i) recent major surgery, burns, or use of antibiotics within the past 5 days; (ii) presence of multiple organ failure, thyroid cancer, or bone fractures; (iii) concurrent diagnosis of both acute bacterial septic arthritis and acute inflammatory non-septic arthritis; and (iv) presence of other simultaneous infections.

Clinical Evaluation

Baseline patient characteristics were comprehensively documented, encompassing age, sex, body mass index (BMI), presence of fever and chills, underlying medical conditions, history of recent antibiotic use, history of prosthetic joints, intravenous drug use (IVDU) history, prior immunosuppressive drug use, history of intra-articular steroid injections, current smoking status, current alcohol consumption, history of herbal medication use, onset of arthritis symptoms, and number of affected joints. All patients underwent thorough physical examinations conducted by physicians. Parameters such as body temperature, pain intensity accessed via visual analog scale (VAS, 0–10 cm), number of affected joints, and presence of tophi were recorded. Sepsis was defined according to the systemic inflammatory response syndrome (SIRS) criteria, which include:

1. Body temperature <36°C or >38°C,
2. Heart rate >90 beats/min,
3. Respiratory rate >20 breaths/min or arterial partial pressure of carbon dioxide <4.3 kPa (32 mmHg),
4. Leukocyte count <4000 cells/μL or >12,000 cells/μL, or presence of >10% immature neutrophils (band forms).

Methods

All patients underwent complete blood count (CBC), urine analysis (UA), and blood cultures. Arthrocentesis was performed on all patients, and synovial fluid samples were analyzed for synovial cell count, cultured for microorganisms, and examined for crystals using polarized light microscopy A total of 100 patients with fever, limping, and suspicion of osteomyelitis or septic arthritis, were prospectively studied. Venous blood samples were collected on admission, before initiation of intravenous antibiotic treatment, for culture and determination of leukocyte count, ESR, CRP, and PCT.

Basic Laboratory

All patients underwent complete blood count (CBC), and blood cultures. Arthrocentesis was performed on all patients, and synovial fluid samples were analyzed for synovial cell count, cultured for microorganisms, and examined for crystals using polarized light microscopy. Under strict aseptic conditions, 5 ml of venous blood was taken for CBC,ESR, and for biomarkers for blood culture, 1 ml was placed on brain heart infusion (BHI) broth. After clotting for 30 minutes and centrifuging for 15 minutes at 1000 × g, the remaining 2 ml was discarded, and the serum was stored at −20°C for CRP, hs-CRP, and PCT analysis. To detect microbial growth, 1 ml of blood was incubated with 10 ml of BHI broth aerobically at 37°C. Turbidity was checked after 18–24 hours. Positive Gram stains from turbid samples were subcultured on MacConkey and blood agar, incubated at 37°C, and identified using conventional biotyping

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techniques from our department. Serum samples in batches were further analyzed for PCT and hs-CRP by ELISA and CRP by latex agglutination. CRP was detected using a latex agglutination kit (Recombigen Laboratories, New Delhi) per the manufacturer's instructions. Serum levels of procalcitonin, high-sensitivity C-reactive protein (hs-CRP), and erythrocyte sedimentation rate (ESR) were measured in all patients. hs-CRP was assessed using a particle-enhanced immune-turbidimetric assay from Roche Diagnostics GmbH, Mannheim, Germany. Procalcitonin concentration was determined via electro-chemiluminescence immunoassay (ECLIA) using equipment from Roche Diagnostics GmbH, with a detection limit of 0.02 ng/mL.

Assay of Procalcitonin

Serum procalcitonin concentration was measured using the electro-chemiluminescence immunoassay (ECLIA) method (Roche Diagnostics GmbH) with a detection limit of 0.02 ng/mL.

Statistical Analysis

Continuous variables were presented as mean ± standard deviation, while categorical variables were compared using the Chi-square test. Student's t-test was employed for normally distributed continuous variables, whereas the Mann–Whitney test was used for non-normally distributed variables, as determined by the Shapiro–Wilk test. All statistical tests used were two-tailed, with a significance level set at $P < 0.01$. To evaluate the diagnostic performance of serum procalcitonin levels, hs-CRP, ESR, and synovial fluid white blood cell count for early detection of acute bacterial septic arthritis, Sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy were assessed using a 2 × 2 contingency table. A P-value < 0.05 indicated statistical significance for all analyses.

RESULTS

One hundred patients were enrolled in the study, with approximately 36 diagnosed with acute bacterial septic arthritis and 64 with acute inflammatory non-septic arthritis. Common pathogens identified in the septic arthritis group included Staphylococcus aureus and Streptococcus group B, with other pathogens including Streptococcus bovis, Streptococcus viridans, Campylobacter fetus, and Neisseria gonorrhoeae. In approximately eight cases, specific organisms were not isolated; however, these patients met the diagnostic criteria for septic arthritis according to Newman's criteria due to purulent synovial fluid and rapid radiographic progression consistent with septic arthritis, responding well to antibiotic therapy. In the acute inflammatory non-septic arthritis group, patients presented with conditions such as gout, pseudogout, flares of ankylosing spondylitis, reactive arthritis, and rheumatoid arthritis exacerbations. Patients diagnosed with acute bacterial septic arthritis were notably younger compared to those with acute inflammatory non-septic arthritis (mean ± SD = 56.96 ± 17.01 years vs. 66.42 ± 16.7 years, $P = 0.02$). Additionally, individuals in the septic arthritis group exhibited higher body temperatures (mean ± SD = 38.27 ± 0.74°C vs. 37.21 ± 0.69°C, $P < 0.001$), a greater incidence of chills (50% vs. 10%, $P < 0.001$), and more frequent sepsis syndrome (39% vs. 2%, $P < 0.001$) compared to those with non-septic arthritis. Tophi were exclusively found in the non-septic arthritis group. However, there were no significant differences observed between the groups in terms of gender.

Here's the proportional breakdown of the pathogens in the septic arthritis group (rounded to the nearest whole numbers):

- Staphylococcus aureus: 9
- Streptococcus group B: 14
- Streptococcus bovis: 1
- Streptococcus viridans: 1
- Campylobacter fetus: 1
- Neisseria gonorrhoeae: 1
- No specific organisms isolated: 8

And for the acute inflammatory non-septic arthritis group (rounded to the nearest whole numbers):

- Gout: 31
- Pseudogout: 18
- Flares of ankylosing spondylitis: 1
- Reactive arthritis: 5
- Rheumatoid arthritis exacerbations: 8

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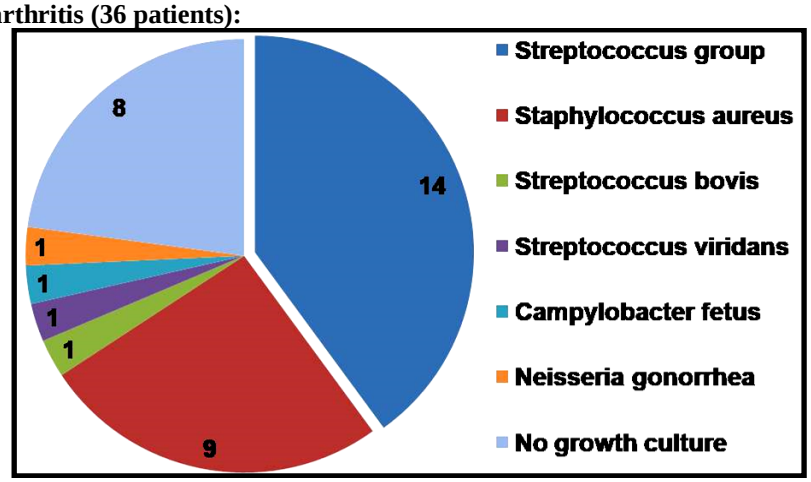
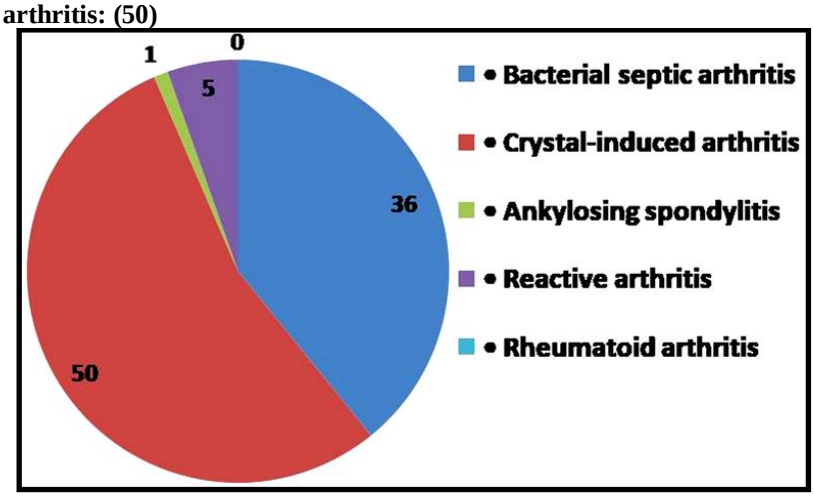
The study involved 100 patients with the following diagnoses:
Bacterial septic arthritis (36 patients):



Streptococcus group B: 14
Staphylococcus aureus: 9
Streptococcus bovis ;1
Streptococcus viridans: 1
Campylobacter fetus: 1
Neisseria gonorrhea: 1
No growth culture: 8

Crystal-induced arthritis: (50)



Gout: 31, Pseudogout: 18, Both gout and pseudogout: 1

- **Ankylosing spondylitis: 1**
- **Reactive arthritis: 5**
- **Rheumatoid arthritis: 8**

Total: 100 patients.

Sensitivity, Specificity, and Positive Predictive Value of PCT, CRP, ESR, and WBC

Marker	Sensitivity (%)	Specificity (%)	Positive Predictive Value (%)
PCT ≥ 0.5 ng/mL	59.3	86	75.3
hs-CRP > 10 mg/dL	78.2	19	51.4
CRP > 50 mg/dL	56	61	61.9
ESR ≥ 20 mm/h	65	52.3	60
WBC > 15 × 10^9/L	39.1	66.6	56.2

Explanation according to your results

- **PCT ≥ 0.5 ng/mL**: The sensitivity for diagnosing bacterial septic arthritis was 59.3%, the specificity was 86%, and the positive predictive value was 75.3%. ROC curve analysis demonstrated good diagnostic performance with an area under the curve (AUC) of 0.78 (95% CI 0.69–0.89).
- **CRP > 10 mg/dL**: The sensitivity was 78.2%, the specificity was 19%, and the positive predictive

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value was 51.4%. The AUC for hs-CRP was 0.67 (95% CI 0.55–0.79).

- **CRP > 50 mg/dL**: The sensitivity was 56%, the specificity was 61%, and the positive predictive value was 61.9%.
- **ESR ≥ 20 mm/h**: The sensitivity was 95%, the specificity was 19%, and the positive predictive value was 56.4%.
- **ESR > 40 mm/h**: The sensitivity was 65%, the specificity was 52.3%, and the positive predictive value was 60%.
- **WBC > 15 × 10^9/L**: The sensitivity was 39.1%, the specificity was 66.6%, and the positive predictive value was 56.2%).

Serum procalcitonin (PCT ≥ 0.5 ng/mL) and inflammatory markers like CRP and ESR show varied sensitivity, specificity, and predictive values for diagnosing bacterial septic arthritis, with PCT demonstrating the highest specificity and moderate sensitivity. These values reflect the diagnostic accuracy of each marker in identifying acute bacterial septic arthritis among patients presenting with acute arthritis symptoms.

DISCUSSION

In our study involving 100 patients, 36 were diagnosed with acute bacterial septic arthritis, primarily caused by pathogens such as Staphylococcus aureus and Streptococcus group B. Another 64 patients presented with acute inflammatory non-septic arthritis, including conditions like gout and rheumatoid arthritis. Serum procalcitonin (PCT) ≥ 0.5 ng/mL demonstrated 59.3% sensitivity, 86% specificity, and a 75.3% positive predictive value for diagnosing septic arthritis. C-reactive protein (CRP) > 10 mg/dL exhibited 78.2% sensitivity but only 19% specificity. Erythrocyte sedimentation rate (ESR) ≥ 20 mm/h showed 95% sensitivity and 19% specificity. White blood cell count (WBC) > 15 × 10^9/L displayed 39.1% sensitivity and 66.6% specificity. Our study highlighted serum procalcitonin as a promising marker for early differentiation between septic and non-septic arthritis. Consistent with prior research, we observed significantly higher serum procalcitonin levels in acute bacterial septic arthritis compared to acute inflammatory non-septic arthritis. While some studies reported no significant difference in procalcitonin levels between these groups, our findings underscored its potential utility. The optimal cut-off for diagnosing septic arthritis remains debated. In our study, using a 0.5 ng/mL cut-off was common, although a slightly higher cut-off of 0.66 ng/mL showed improved specificity (86%) with comparable sensitivity (59%). Recent meta-analyses suggested lower cut-offs (0.2-0.3 ng/mL) for higher sensitivity (up to 90%) without significantly affecting specificity. In evaluating other parameters like hs-CRP, ESR, and synovial fluid WBC, we found synovial fluid WBC to outperform serum procalcitonin in diagnosing septic arthritis, particularly when arthrocentesis was not feasible or synovial fluid WBC was unreliable due to prior antibiotic use or leukopenia. Nonetheless, serum procalcitonin's diagnostic performance was superior to synovial fluid procalcitonin. Despite its potential, serum procalcitonin elevation can occur in concurrent infections, thyroid cancer, post-major surgery, and septic shock, limiting its specificity as a biomarker for acute bacterial septic arthritis. Our study, complementing existing literature, demonstrated that while hs-CRP elevation is observed in septic arthritis, serum procalcitonin offers superior diagnostic capability for identifying acute bacterial septic arthritis. Three studies investigated the role of synovial fluid procalcitonin in diagnosing acute bacterial septic arthritis. They observed higher levels in septic arthritis patients compared to those with non-septic arthritis, such as rheumatoid arthritis, osteoarthritis, and crystal-induced arthritis. However, serum procalcitonin proved more effective than synovial fluid procalcitonin for diagnosing septic arthritis.[8,9,10] We also assessed other parameters, including hs-CRP, ESR, and synovial fluid WBC, which are known to aid in the diagnosis of septic arthritis. This is consistent with findings from previous studies.[11] Our findings indicated that synovial fluid WBC outperformed serum procalcitonin slightly in diagnosing septic arthritis. Therefore, in cases where arthrocentesis is impractical or synovial fluid WBC results are unreliable due to factors like prior antibiotic use or leukopenia, serum procalcitonin could serve as a valuable diagnostic tool. However, elevated serum procalcitonin levels in patients with concurrent infections such as thyroid cancer, post-major surgery, or septic shock may limit its specificity as a biomarker for acute bacterial septic arthritis. Our study, along with previous research, showed that hs-CRP levels are elevated in septic arthritis patients; nevertheless, serum procalcitonin demonstrated superior performance in diagnosing acute bacterial septic arthritis.[12,13] ESR did not show significant differences between patients with and without septic arthritis and should not be relied upon as a diagnostic tool for this condition. Procalcitonin has been shown to be valuable in diagnosing bloodstream infections, septic shock, bacteremia, community-acquired pneumonia, and hospital-acquired pneumonia.[14,15,16] Antibiotics treatment is strongly encouraged in communities that acquire pneumonia if procalcitonin level is greater than 0.5 ng/mL.[17] Procalcitonin holds promise as a potentially valuable biomarker for diagnosing acute bacterial septic arthritis. Its rapid availability allows for its use alongside other clinical data to distinguish between acute bacterial septic arthritis and non-septic inflammatory arthritis, even before synovial culture results are obtained. However, the cost-effectiveness of utilizing procalcitonin as a diagnostic tool for acute bacterial septic arthritis has not been studied and warrants investigation in future research.

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CONCLUSION

Serum procalcitonin (PCT≥0.5 ng/mL) and inflammatory markers like CRP and ESR show varied sensitivity, specificity, and predictive values for diagnosing bacterial septic arthritis, with PCT demonstrating the highest specificity and moderate sensitivity

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