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Diagnostic Accuracy Of Different Clinicopathological Parameters In The Differentiation Of Septic Versus Aseptic Mono-Arthritis In The Pediatric Age Group

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Abstract

Objective: Determining the diagnostic accuracy of various clinicopathological parameters in differentiating Septic Arthritis versus Aseptic Inflammatory Arthritis in the paediatric age group.

Methods: A cross-sectional study took place at the Department of Orthopedics, Nawaz Sharif Medical College, University of Gujrat, Gujrat, from February 2023 to July 2024. 150 children aged 10-160 months, of either gender, presented for the first episode of acute monoarthritis lasting for less than a week were included and categorized into two groups. Group A included children with confirmed diagnosis of SA and Group B included children diagnosed with aseptic inflammatory arthritis. Body temperature and serum inflammatory markers were measured. Receiver operating characteristic curves were made to discover the optimum diagnostic cut-off values of the parameters. The areas under the curves were then estimated to juxtapose the overall predictive accuracy for SA.

Results: 49.33% of patients had SA and 50.67% had Aseptic Inflammatory Arthritis. All clinicopathological parameters including body temperature, TLC, ANC, NP, ESR, and CRP exhibited significantly higher values in Group A than in Group B ($p<0.01$). TLC had a considerable discriminatory power in distinguishing SA from aseptic inflammatory arthritis followed by ESR, CRP, NP, body temperature and ANC.

Conclusion: In conclusion, these clinicopathological parameters can be used for the prompt diagnosis of SA to start the treatment and prevent the progression of the disease.

Keywords: Acute Monoarthritis, Septic Arthritis, TLC, C-reactive protein.

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Introduction

Childhood arthritis is estimated to occur in 1 per 1000 children globally with monoarthritis accounting for the majority of the cases.1 Although acute monoarthritis is the most common manifestation of SA in children, it can also be a clinical feature of aseptic inflammatory arthritis including juvenile idiopathic arthritis (JIA), transient synovitis, reactive arthritis, and other inflammatory disorders.2 In a recent study conducted to determine the aetiology of acute monoarthritis, 56.1% of patients had SA, 10.2% had JIA, and 33.7% had no definitive cause.3 Acute monoarthritis typically occurs in larger joints including the hip, knee, and ankle. Bacteremia is the main cause of SA in children.4 It is a medical emergency and results in irreversible damage to the joint.

The overall incidence of SA ranges from 4 to 37 per 100,000 children in high-income countries.3,5 Thereby, it is crucial to discern Septic Arthritis from Aseptic Inflammatory Arthritis in children with acute monoarthritis, particularly because of the different treatment approaches and prognosis of both conditions.2,6,7

As SA rapidly progresses and is associated with poor prognosis and increased mortality rates, it requires prompt diagnosis and adequate clinical and/or surgical management to avoid grave complications and irreversible injury to the joint.5 On the other hand, non-infectious or Aseptic Inflammatory Arthritis is usually managed using non-steroidal anti-inflammatory medications, glucocorticoids, and anti-rheumatic drugs.8 However, SA in children is a major diagnostic challenge to healthcare providers, with the unavailability of a single test to promptly and correctly diagnose the disease.9

Clinicians mainly diagnose SA based on clinical characteristics and laboratory tests.10 Synovial fluid culture is the only definitive method but it is not readily available and may provide false negative results.10 Inflammatory markers such as total leucocyte count (TLC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), absolute neutrophil count (ANC), neutrophil percentage (NP), and absolute platelet count (APC) provide quick and accurate results.9 However, limited literature is available regarding the diagnostic accuracy of these parameters in the differentiation of septic from aseptic arthritis in children. So, the current study was intended to determine the diagnostic performance of various clinicopathological parameters in the differentiation of Septic Arthritis versus Aseptic Arthritis in the paediatric population.

Methodology

Department of Orthopaedics Nawaz Sharif Medical College, University of Gujrat from Feb 2023 till July 2024. A total of 150 children, aged 10 months to 160 months, of either gender, presented for the first episode of acute monoarthritis lasting for less than a week were included. These patients were referred from different departments i.e., emergency, pediatrics, and pathology, of the same hospital. The study excluded children with known sepsis, known secondary arthritis, associated osteomyelitis, history of previous anti-inflammatory treatment, underlying immunosuppressive disorders such as cancer, AIDS, chronic renal failure, and drug-induced immunosuppression. After obtaining authorization from the ethical committee (REC # 219) and permission from parents/guardians, 150 patients were included and further categorized into two groups: Group A and Group B. Group A included children with a confirmed diagnosis of SA based on positive synovial fluid culture or a positive synovial fluid gram-staining.[11] Whereas, Group B included children diagnosed with Non-Specific Inflammatory Arthritis, typically considered as sudden onset, non-traumatic, and non-specific inflammatory signs. Both groups underwent detailed physical examinations and laboratory tests. Body temperature (°C) was estimated using a tympanic thermometer. Inflammatory markers including TLC (/mm³), ESR (mm/h), CRP (mg/L), ANP (/mm³), NP (%), and APC (10^9/L) were also measured. Data was analyzed using SPSS version 25. Descriptive data was exhibited as means, standard deviations, frequencies, and percentages. A comparison of demographic and clinicopathological parameters was performed using a chi-square test and independent sample t-test. Receiver operating characteristic (ROC) curves were made to discover the optimum diagnostic cut-off values of the parameters. The areas under the curves (AUCs) were then estimated to juxtapose the overall predictive accuracy for Septic Arthritis. The interpretation of AUC was made as follows: ≥0.9 = excellent; 0.8 - <0.9 = considerable; 0.7 – <0.8 = fair; and 0.6 - <0.7=poor discriminatory power.[12]

Results

The current study included 150 patients. Figure 1 exhibits the aetiology of acute monoarthritis in children. 49.33% of patients had Septic Arthritis, confirmed by positive synovial fluid culture or a positive synovial fluid gram-staining. While 50.67% of patients had Aseptic Inflammatory Arthritis.

Table 1: Baseline demographic and clinical features of patients in both groups (n=150)

Parameters		Total	Group A n (%)	Group B n (%)	p-value
Mean age (months)| mean ± S.D		82.31±46.64	81.04±39.32	83.55±53.04	0.743[a]
Gender	Male n (%)	72(48.0)	35(47.3)	37(48.7)	0.865[b]
	Female n (%)	78(52.0)	39(52.7)	39(51.3)	
Side involved	Right n (%)	81(54.0)	42(56.8)	39(51.3)	0.504[b]
	Left n (%)	69(46.0)	32(43.2)	37(48.7)	
Joint involved	Knee n (%)	35(23.3)	20(27.0)	15(19.7)	0.303[b]
	Hip n (%)	28(18.8)	9(12.2)	19(25.0)	
	Ankle n (%)	35(23.3)	17(23.0)	18(23.7)	
	Shoulder n (%)	17(11.3)	10(13.5)	7(9.2)	
	Elbow n (%)	35(23.3)	18(24.3)	17(22.4)	

Table 1: n = number of patients; % = percentage of patients; [a] = independent t-test was applied; [b] = chi-square test was used; p≤0.05 was significant.

Baseline demographic and clinical features are shown in Table 1. The mean age of patients in Group A was 81.04±39.32 months, whereas, it was 83.55±53.04 months in Group B. There were 47.3% male and 52.7% female patients in Group A. Group B consisted of 48.7% male and 51.3% female patients. The right side was involved in 56.8% of the patients in Group A and 51.3% of the patients in Group B. 43.2% and 48.7% of patients had left-side involvement in Group A and Group B, respectively. The knee joint was the most commonly affected joint in Group A (27.0%) and the hip joint was the most commonly affected in Group B (25.0%). There was no noteworthy difference in terms of the location of the affected joints between the two groups (p=0.303).

The comparison of clinicopathological parameters between the two groups is presented in Table 2. All factors exhibited a considerable variation between the two groups, except for APC. Mean body temperature was substantially higher in Group A than in Group B, p = 0. <0.001. Laboratory parameters including TLC, ANC, NP, ESR, and CRP showed substantially higher values in Group A than in Group B (p<0.01).

Table 2: Comparison of clinicopathological findings between two groups

Clinicopathological parameters	Group A (mean±S.D.)	Group B (mean±S.D.)	p-value*
Body temperature (°C)	38.50±0.71	37.76±1.22	<0.001
TLC (/mm^3)	127621.20±78312.91	40903.39±41704.09	<0.001
ANC (/mm^3)	7932.64±4341.24	5848.89±4688.12	0.005
NP (%)	45.95±20.93	31.78±16.46	<0.001
APC (10^9/L)	410.47±157.25	426.34±152.97	0.532
ESR (mm/h)	75.30±40.60	42.32±29.20	<0.001
CRP (mg/L)	99.50±53.92	59.53±46.33	<0.001

*Table 2: S.D. = Standard deviation; °C = degree Celsius; TLC = total leucocyte count; ANC = Absolute neutrophil count; NP = neutrophil percentage; APC = Absolute platelet count; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; /mm^3 = per cubic millimeter; % = percentage; L =liter; mm/h = millimeter per hour; mg/L = milligram per liter; * = independent t-test was applied and p≤0.05 was significant.*

Substantial clinicopathological parameters with p-values less than 0.05 in the univariate analysis were considered for ROC analysis. TLC demonstrated considerable discriminatory power in discerning septic arthritis from aseptic inflammatory arthritis based on the ROC-AUC values, as shown in Figure 2 and Table 3. CRP, ESR, and NP showed fair discriminatory power whereas, body temperature and ANC had poor discriminatory power. The area under the curve for body temperature at a cut-off value of 37.2°C was 0.664 [95% CI 0.557, 0.751]; for TLC at a cut-off value of 12150/mm^3, it was 0.844[95% CI 0.785, 0.904]; for ANC at a cut-off value of 6300/mm^3, it was 0.660 [95% CI 0.572, 0.748]; for NP at a cut-off value 66%, it was 0.703 [95% CI 0.621; 0.785], for CRP at a cut-off value 64 mg/L, it was 0.717 [95% CI 0.636, 0.798]; and for ESR at a cut-off value at 54 mm/h, AUC was 0.739 [95% CI 0.660, 0.817], as shown in Table 3.

Table 3: Receiver operating characteristics curve analysis of clinicopathological parameters of Acute Monoarthritis

Clinicopathological parameters	Cut off	AUC	95% CI		S.E.	p-value
			Lower	Upper		
Body temperature (°C)	37.2	0.664	0.557	0.751	0.044	0.001
TLC (/mm^3)	12150	0.844	0.785	0.904	0.030	0.000
ANC (/mm^3)	6300	0.660	0.572	0.748	0.045	0.001
NP (%)	66	0.703	0.621	0.785	0.042	0.000
CRP (mg/L)	64	0.717	0.636	0.798	0.041	0.000
ESR (mm/h)	54	0.739	0.660	0.817	0.040	0.000

Table 3: AUC = area under curve CI = Confidence interval; S.E. = standard error; °C = degree Celsius; TLC = total leucocyte count; ANC = Absolute neutrophil count; NP = neutrophil percentage; APC = Absolute platelet count; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein.

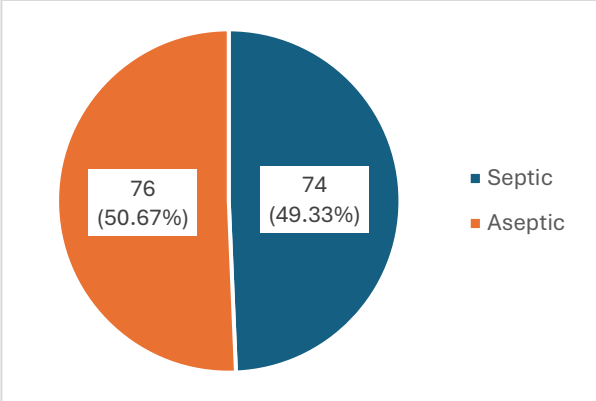

Figure 1: Etiology of Acute Monoarthritis in children

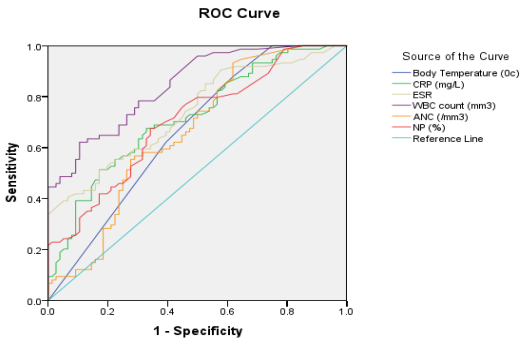

Figure 2: Receiver operating characteristics curve for clinicopathological parameters

Discussion

Discerning Septic Arthritis from Aseptic Inflammatory Arthritis is of crucial importance in children with acute monoarthritis, particularly because treatment approaches and prognosis of these conditions are considerably varied.[2,8,13] However, SA in children is a major diagnostic challenge, with the unavailability of a single test to quickly and appropriately diagnose the disease.[9] Synovial fluid culture or gram-staining are definitive methods of distinguishing septic from aseptic arthritis.[14-16] But these tests take a lot of time and often provide false-negative results.[17] Hence, there is a need for easily administered tests that provide accurate and timely results to start the treatment of this irreversible condition. So, the present study took place to determine the diagnostic performance of various clinicopathological parameters in the differentiation of Septic Arthritis versus Aseptic Arthritis in the paediatric population.

In the present study, TLC exhibited considerable discriminatory power (AUC = 0.844) in discerning SA from aseptic inflammatory arthritis based on the ROC-AUC values. A study by Nyaaba et al. reported a considerable AUC of 0.86 in predicting the diagnosis of SA[18], similar to the findings of this study. In a study by Demirel et al., TLC exhibited fair discriminatory power (AUC = 0.754).[9] In another study, WBCs in serum were substantially higher in patients with SA as compared to those with JIA ($p = 0.01$).[3] Darraj et al. also stated that patients with SA had markedly raised TLC.[5] In a French study, it was found that there was no substantial difference in white blood cell (WBC) count in blood between patients with SA and JIA ($p = 0.53$) [6], contrary to the findings of the current study. However, WBCs were markedly raised in synovial fluid among patients with SA ($p<0.001$).[6]

In the present study, CRP, ESR, and NP showed fair discriminatory power whereas, body temperature and ANC had poor discriminatory power. These findings are comparable to the findings of a study conducted in Korea. In that study, significant differences were observed in TLC, body temperature, CRP, and ESR between patients with SA and transient synovitis.[19] In another study by Kocher et al., history of fever, raised ESR and WBC levels were independent predictors of SA.[20] Similarly, Bayram et al. also documented elevated CRP as an independent predictor of SA.[21] Clever et al. reported that CRP > 20 mg/L was an independent factor in distinguishing SA from transient synovitis ($p<0.001$),[22] similar to the findings of the current study.

This study also has some limitations. First was the cross-sectional nature of this study. Secondly, the sample size was not enough as compared to the disease burden. Finally, the selection of children from a single centre limits the generalizability of these findings.

Conclusions

In conclusion, the outcomes of the current study revealed that TLC had considerable discriminatory power in distinguishing septic arthritis from aseptic inflammatory arthritis followed by ESR, CRP, NP, body temperature and ANC. These parameters can be used for the initial diagnosis of septic arthritis to start the treatment and prevent the progression of the disease. Future studies with bigger sample sizes are needed to ascertain the findings of the current study.

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- Experimentation/Study Conduction
W.H, M.Z.S, N.G, W.P - Analysis/Interpretation/Discussion
W.A, M.Z.S, N.G - Manuscript Writing
W.H, R.R.A, W.P - Critical Review

All authors approved the final version to be published & agreed to be accountable for all aspects of the work.