

## Does the use of parameters derived from complete blood count increase the accuracy of septic arthritis diagnosis in adult patients?

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**The diagnosis of septic arthritis can be challenging and any delay in treatment can cause important disabilities. This study aimed to evaluate several ratios obtained from routine blood tests for possible use in the diagnosis of septic arthritis. Adult patients operated with the diagnosis of septic arthritis were retrospectively evaluated. 34 patients were found to be eligible for inclusion. The control group comprised 40 age-matched knee osteoarthritis patients without infection. Neutrophil-lymphocyte, monocyte-lymphocyte, platelet-lymphocyte, and platelet count-mean platelet volume ratios were calculated, and receiver operating characteristics (ROC) curve analysis was performed to determine the sensitivity, specificity, and area under curve (AUC) values of all parameters. Affected joints in the septic arthritis group included 22 knees, 6 hips, 4 shoulders, and 2 elbows. All evaluated parameters were significantly different between the groups ( $p < 0.001$ ). AUC value representing diagnostic performance was 97.3 when CRP and ESR values were used but increased to 98.6 when neutrophil/lymphocyte ratio was added and increased to 100 when all analyzed parameters were included. Analyzed parameters were found to increase the overall sensitivity and specificity of septic arthritis diagnosis when used together with CRP and ESR. Neutrophil/lymphocyte ratio was found as the most powerful predictor amongst the analyzed ratios and more significantly increased when joint culture was positive.**

**Keywords:** Septic arthritis, diagnosis, blood parameters, ratio, complete blood count.

### INTRODUCTION

Septic arthritis, which is one of the most common orthopedic infections, and also one of the most important orthopaedic emergencies needing urgent intervention, is difficult to diagnose and needs costly and long-term treatment<sup>1</sup>. The patient should be evaluated in all clinical, radiological, hematological, serological, and microbiological aspects for a definitive diagnosis. Urgent intervention should be performed to prevent serious morbidity when the doubt for septic arthritis is high<sup>2</sup>. However, the diagnosis is challenging especially in the adult population since accompanying diseases can mask the severity of clinical presentation and vague symptoms can prevent early diagnosis<sup>3-7</sup>.

There is no consensus on the definitive diagnosis algorithm of adult septic arthritis and the studies in the literature used various diagnostic criteria<sup>8</sup>.

Acute phase markers like CRP and ESR are mostly elevated but they are not able to verify the diagnosis definitely<sup>9</sup>. The search for new diagnostic markers continues and some other markers including leukocyte esterase and alpha-defensin are also in use but mostly for the diagnosis of periprosthetic infection and they are still questioned about their cost-effectiveness<sup>10</sup>. Comparing the relationship between blood parameters is an easy and cost-effective diagnostic method<sup>11</sup>. The use of different ratios obtained from complete blood counts (CBC) is widely analyzed in the literature to define new diagnostic tools for different pathologies including both infectious and non-infectious disorders<sup>12-14</sup>. This study aimed to evaluate the significance of several ratios obtained from routine complete blood tests in the diagnosis of adult septic arthritis, in search of a sensitive, specific and cost-effective parameter in the diagnosis of septic arthritis. We hypothesized that

blood parameter ratios exhibit significant differences in septic arthritis compared to non-septic joint conditions and can guide the definitive diagnosis.

### MATERIALS AND METHODS

The adult patients who underwent open or arthroscopic joint debridement due to septic arthritis of native major joints (hip, knee, ankle, shoulder, elbow or wrist) between 2014 and 2020 were retrospectively evaluated after the approval of local ethics committee. Patients were classified as having definite native joint septic arthritis if they presented with an acutely painful, swollen joint and systemic or local signs of infection, and fulfilled at least one of the following criteria:

1. Positive Gram stain or growth of a pathogenic organism from synovial fluid or intra-articular tissue culture; or
2. Synovial leukocyte count  $>100,000/\text{mm}^3$  with  $\geq 90\%$  polymorphonuclear cells in cases where cultures were negative<sup>8,15</sup>.

The higher synovial WBC threshold was used only for culture-negative patients, aiming to maximize diagnostic specificity in a retrospective dataset. Some guidelines accept lower synovial WBC thresholds (e.g.,  $>50,000/\text{mm}^3$  with  $\geq 75\text{--}90\%$  PMN), but also acknowledge substantial overlap with inflammatory arthropathies and trauma<sup>8,15</sup>.

The patients with hematological and immunosuppressive diseases, previous surgical intervention in another center, recent usage of drugs which can interfere with blood counts, and missing data were excluded. Out of 50 patients, 34 were found eligible (Figure 1). The control group included 40 patients who had no recent infection or chronic inflammatory condition and who had undergone surgical treatment for knee osteoarthritis.

Preoperative neutrophil, thrombocyte, mean platelet volume, lymphocyte, monocytes, CRP, ESR values were recorded and neutrophil/lymphocyte ratio, platelet/mean platelet volume ratio, platelet/lymphocyte ratio, and monocyte/lymphocyte ratios were calculated. Gram staining and culture results of the samples taken during surgery. CBC parameters (neutrophils, lymphocytes, monocytes, platelets), CRP, and ESR were obtained at the time of initial presentation to the orthopaedic service and prior to antibiotic administration. Two patients had missing value so they were excluded. Laboratory personnel processing CBC, CRP, and ESR measurements were part of the hospital's central laboratory and were blinded to the final diagnosis of septic arthritis vs osteoarthritis.

CRP and ESR were considered the baseline diagnostic markers reflecting routine clinical practice, the neutrophil-to-lymphocyte ratio was designated as

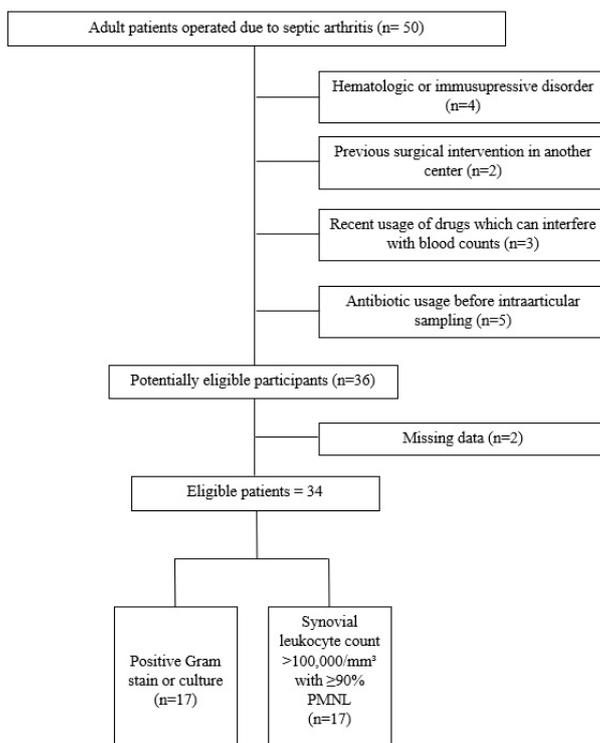


Fig. 1 — Flow chart of the included patients.

the primary CBC-derived parameter of interest based on prior literature, and all remaining hematologic ratios were treated as secondary exploratory indices.

Statistical comparisons between the groups were made with independent samples t-test. The optimal threshold value, specificity, and sensitivity of these ratios were determined statistically by the receiver operating characteristics (ROC) curve method. Logistic regression analysis was used to show the difference in sensitivity and specificity for diagnosis when combinations of analyzed parameters were utilized. A p-value of <0.05 was considered to be statistically significant.

## RESULTS

A total of 34 septic arthritis patients treated surgically between 2014-2020 were evaluated and compared with the values of control group comprised of 40 patients. There were 21 male and 13 female patients in septic arthritis group, while control group included 5 male and 35 female patients. The average age in septic arthritis group was 59.8, while it was 64.6 in control group ( $p=0.107$ ). No significant age difference was detected between the two groups (Table I). The most commonly isolated microorganism was *S. Aureus* (Table II). Cultures were negative in 17 patients (50%). More than one microorganism growth was

observed in 5 patients. Gram staining was positive in only 12 patients (35%). The most commonly involved joint was found to be knee joint with the rate of 65%, followed by hip (17%), shoulder (12%) and elbow (6%).

Average hospitalization of patients for septic arthritis was 16 days (1-48 days). Only 2 patients required reoperation. Underlying rheumatological disease was presented in 8 patients. A history of malignancy was present in 6 patients, chronic renal failure in 3 patients, chronic heart failure in 2 patients, and type 2 diabetes mellitus in 2 patients. Seven patients had a smoking history which was at least 15 packs/year.

The ratios of neutrophil/lymphocyte, platelet/lymphocyte, monocyte/lymphocyte, platelet/mean platelet volume, and CRP and ESR values were evaluated for the diagnosis of septic arthritis and analyzed statistically. Comparison of the values between case and control groups have been found statistically significant among all parameters ( $p<0.001$ ) (Table III).

The cut-off values with highest specificity and sensitivity for the diagnosis of septic arthritis for each parameter were as follows; the neutrophil/lymphocyte ratio of 2.3 (sensitivity: 94.1%, specificity; 80.0%), platelet/lymphocyte ratio of 135 (sensitivity: 79.4%, specificity 65.0%), monocyte/lymphocyte ratio of 0.30 (sensitivity: 76.5%, specificity: 82.5%), platelet/

**Table I.** — General characteristics of septic arthritis and control groups.

	Control group	Septic group	P value
Age	64.6±12.13	59.8±16.92	0.16
Gender	35 F, 5 M	13 F, 21 M	<0.01*
BMI (kg/m <sup>2</sup> )	28.01±4.16	26.54±7.2	0.27
* $p<0.01$ (BMI, body mass index; F, female; M, male).			

**Table II.** — Distribution of microorganisms grew in the culture of joint aspiration. Some cultures yielded more than one microorganism.

Microorganism	Number of patient
<i>Staphylococcus aureus</i>	10
<i>Escherichia coli</i>	3
<i>Staphylococcus epidermidis</i>	3
<i>Corynebacterium bacteria</i>	3
<i>Mycobacterium tuberculosis</i>	2
Coagulase-negative staphylococci	1
<i>Streptococcus dysgalactiae</i>	1
<i>Enterococcus faecalis</i>	1
Culture-negative	17

**Table III.** — Comparison of the control and septic arthritis groups according to the analyzed parameters.

Parameters	Group	Mean	Std. deviation	P-value
Neutrophil/lymphocyte	Septic	7.07	6.76	<0.001*
	Control	1.95	0.62	
Platelet/lymphocyte	Septic	317.67	262.87	<0.001*
	Control	135.29	52.41	
Monocyte/lymphocyte	Septic	0.71	0.65	<0.001*
	Control	0.23	0.07	
Platelet/mean platelet volume	Septic	44.75	18.53	<0.001*
	Control	31.63	12.49	
CRP	Septic	139.32	100.33	<0.001*
	Control	5.75	5.23	
ESR	Septic	85.84	30.97	<0.001*
	Control	19.23	12.38	

(\*p<0.001), (CRP, C-reactive protein; ESR, erythrocyte sedimentation rate).

mean platelet volume ratio of 40 (sensitivity: 61.8%, specificity: 87.5%) (Figure 2, Table IV). The best cut-off for CRP value was found as 10 mg/L with a sensitivity of 97.1% and specificity of 85.0%. When the cut-off value of 5 mg/L, which is the upper limit value used routinely, was taken as the threshold value, the sensitivity was found to be 100.0% and the specificity to be 60.0%. When the ESR cut-off value was taken as 35 mm/hr, the sensitivity was 97.1% and the specificity was 90.0%. While the sensitivity was found to be 94% and the specificity was found to be 92.5% with the ESR cut-off value of 40 mm/hr. However, the sensitivity was found 97.1% and specificity was found 60.0% when 20 mm/hr was taken as the cut-off value, which is the normal upper limit value for ESR which is used routinely in the laboratories.

After the logistic regression analyses, it was determined that if only CRP and ESR parameters were used in the diagnosis of septic arthritis, the area under curve, which represents diagnostic performance, was found to be 97.3%. If neutrophil/lymphocyte, monocytes/lymphocyte, thrombocyte/lymphocyte, and platelet/mean platelet volume ratios are added to these two parameters, the diagnostic performance was found to be 100%. If the neutrophil/lymphocyte value, which is the most significant among the 4 parameters investigated, is added, diagnostic performance was found to be 98.6%.

Calibration of the extended model (CRP + ESR + CBC ratios) is shown in Figure 3. The calibration curve demonstrated good overall agreement between predicted probabilities and observed frequencies of septic arthritis across deciles of risk.

A multivariable logistic regression including age, sex, CRP, and neutrophile-lymphocyte ratio was performed. Because of strong collinearity and quasi-separation when both CRP and ESR were included simultaneously, we constructed a parsimonious model with age, sex, CRP, and NLR. In this model: CRP remained a strong independent predictor (OR 10.2 per 10-mg/L increase; 95% CI 1.2–86.3; p=0.033). Neutrophile-lymphocyte ratio also showed a significant trend toward higher odds (OR 15.5 per 1-unit increase; 95% CI 0.47–504.1; p=0.032). Age and gender were not independently associated with septic arthritis in this model (p=0.09 and 0.60). A sensitivity analysis restricted to an age- and sex-balanced subset of patients was also performed (1:1 matching of septic arthritis and osteoarthritis patients within ±5 years and same sex). The effect estimates for CRP and neutrophile-lymphocyte ratio in this subset were similar in direction and magnitude, although with wider confidence intervals due to the smaller sample size.

We compared Model 2 (CRP + ESR + CBC ratios) with Model 1 (CRP + ESR) using categorical Net reclassification improvement (NRI) with clinically plausible risk thresholds of <10%, 10–50%, and >50% predicted probability of septic arthritis. The NRI for events (septic cases) was +0.03, while the NRI for non-events (controls) was –0.02, resulting in a total NRI of +0.01. In other words, the extended model correctly up-classified more septic cases but also incorrectly up-classified a few controls, leading to slight overall improvement in risk classification.

The values were also analyzed according to the presence of an accompanying disease and a positive culture in septic arthritis group. No statistical

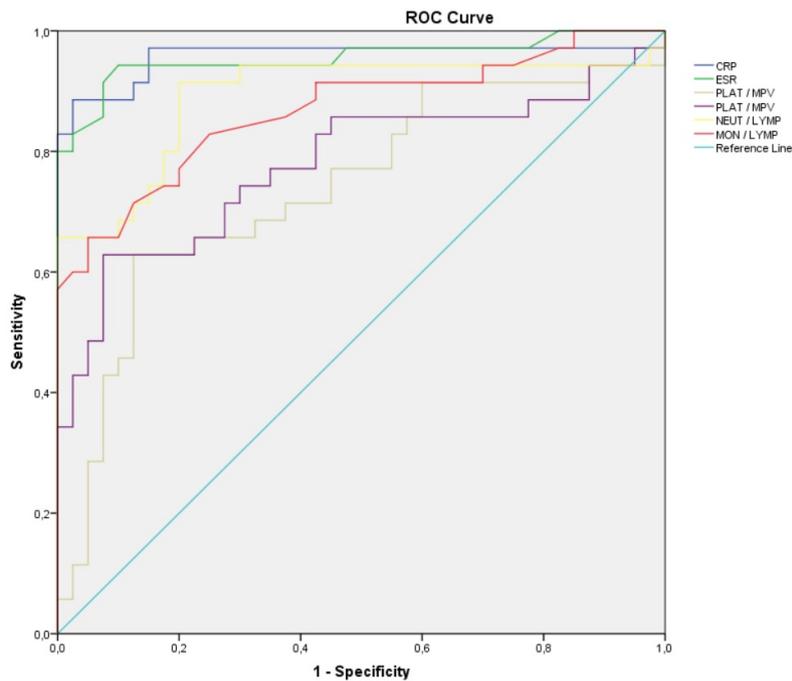


Fig. 2 — ROC (receiver operating characteristics) curve graph of all parameters analyzed. (NEUT, neutrophile; LYMP, lymphocyte; PLAT, platelet; LYMP, lymphocyte; MPV, mean platelet volume; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate).

Table IV. — The sensitivity, specificity and area under curve values for determined cut-off values.

Parameter	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Cut-off	AUC (95% CI)
NEUT/LYMP	94.1	80.0	79.5	91.4	2.3	91.8 (87.2-95.3)
PLAT/ LYMP	79.4	65.0	65.9	78.8	135.0	79.8 (72.1-85.6)
MON/ LYMP	76.5	82.5	78.8	80.5	0.3	88.9 (84.4-92.1)
PLAT/MPV	61.8	87.5	77.8	72.3	40.0	73.5 (65.7-78.1)
CRP (mg/L)	97.1	85.0	84.6	97.1	10.0	98.6 (94.2-99.8)
ESR (mm/hour)	97.1	90.0	89.2	97.3	35.0	97.7 (93.5-99.4)

(NEUT, neutrophile; LYMP, lymphocyte; PLAT, platelet; LYMP, lymphocyte; MPV, mean platelet volume; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PPV, positive predictive value; NPV, negative predictive value; AUC, area under curve).

difference was detected between patients with and without an accompanying disease in any parameter. However, the patients with a positive culture had significantly higher neutrophil/lymphocyte ratio and CRP values ( $p=0.036$ ,  $0.044$ , respectively) which might be explained by an increased bacterial load in patients with a positive culture (Table V).

## DISCUSSION

This study has shown that some ratios between the values of complete blood counts can aid the diagnosis of septic arthritis to some extent. Several studies also emphasized the importance of blood parameter ratios in literature. Tirumala et al investigated the utility of some parameters in the diagnosis of periprosthetic

infection. It was shown that monocyte/lymphocyte ratio had sensitivity and specificity of 81.6% and 78.3%, respectively when an optimal cut-off point of 0.44 was taken. In the same study platelet/lymphocyte ratio had a sensitivity of 78.2% and specificity of 82.5% when an optimal cut-off point of 234.13 was taken. Also, neutrophil/lymphocyte ratio had a sensitivity of 76.7% and specificity of 79.2% when 3.62 was taken as a cut-off value. In addition, platelet/mean platelet volume ratio had a sensitivity of 87.9% and specificity of 75.9% when 30.82 was taken as a cut-off point. When all 4 parameters at the respective cutoff points were considered, both sensitivity and specificity values were higher compared to sensitivity and specificity values of ESR except for the specificity of platelet/mean platelet volume ratio cut-off value. It was found

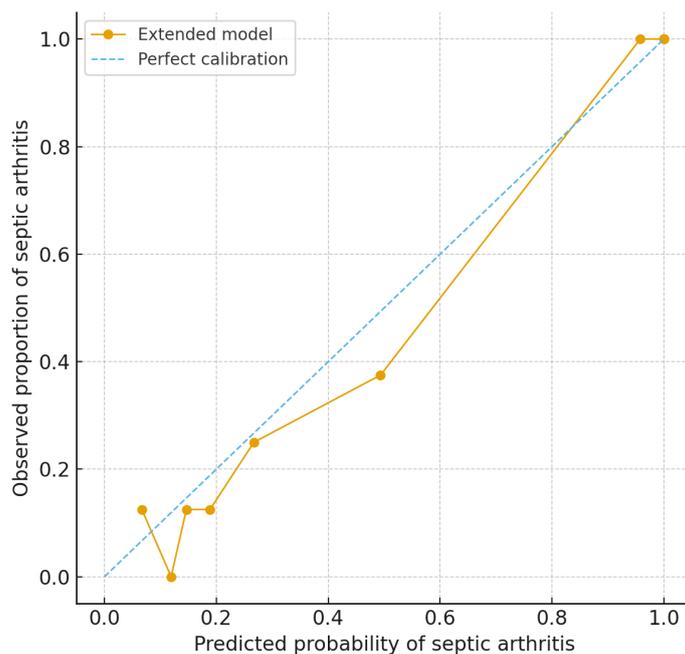


Fig. 3 — Calibration plot of the extended logistic regression model (CRP + ESR + CBC-derived ratios). The solid line represents the relationship between predicted probabilities of septic arthritis and the observed proportion of septic arthritis within deciles of predicted risk. The dashed diagonal line indicates perfect calibration (predicted = observed). The extended model showed good overall calibration with only minor deviations at intermediate risk levels.

Table V. — Comparison of the analyzed parameters according to culture results in septic arthritis.

Parameters	Culture	Mean	Std. deviation	P-value
Neutrophil/lymphocyte	Negative	4.66	3.58	0.036*
	Positive	9.47	8.30	
Platelet/lymphocyte	Negative	266.57	244.89	0.263
	Positive	368.75	277.48	
Monocyte/lymphocyte	Negative	0.51	0.40	0.086
	Positive	0.89	0.79	
Platelet/mean platelet volume	Negative	45.66	21.84	0.778
	Positive	43.83	15.13	
CRP	Negative	104.88	83.44	0.043*
	Positive	173.76	106.19	
ESR	Negative	92.04	35.31	0.249
	Positive	79.64	25.47	

(n=17) (\*p<0.05).

that platelet/mean platelet volume ratio had a higher sensitivity value compared to CRP, while monocyte/lymphocyte ratio, neutrophil/lymphocyte ratio, and platelet/lymphocyte ratio outperformed CRP in specificity. It was shown that the combination of CRP, ESR, and these 4 parameters significantly increase the specificity and sensitivity of periprosthetic infection diagnosis<sup>12</sup>. Our study also showed similar results

in septic arthritis patient group. However, the best diagnostic performance among blood parameter ratios belonged to neutrophil/lymphocyte ratio in our study. The reason behind this might be more severe clinical symptoms of septic arthritis compared to periprosthetic infection, causing a more aggressive immune response leading to more increased neutrophil number<sup>16-18</sup>. But this probability should be confirmed with other studies.

The results of our study should be interpreted alongside the growing literature on synovial and serum biomarkers in native septic arthritis, particularly the work of Varady et al<sup>19</sup>. and Massey et al<sup>20</sup>. Varady et al. showed in a large multi-institutional cohort that synovial fluid NLR (SF-NLR) has superior diagnostic accuracy compared with traditional synovial indices (SF-WBC and SF-%PMN), and that serum NLR independently predicts treatment failure and mortality, highlighting the potential of NLR as both a diagnostic and prognostic tool. Massey et al., on the other hand, used ROC analysis to redefine optimal synovial WBC cut-offs and demonstrated that prior antibiotic exposure markedly lowers the leukocyte threshold for diagnosing septic arthritis ( $\approx 33,000$  cells/ $\mu\text{L}$  in antibiotic-naïve patients vs  $\approx 16,000$  cells/ $\mu\text{L}$  after antibiotics, with corresponding neutrophil percentage cut-offs of 83% and 90%). Together, these studies emphasize both the limitations of the historical “50,000 cells/ $\mu\text{L}$  and 90% PMN” rule and the importance of accounting for antibiotic timing and alternative synovial indices such as NLR. Our work differs in that we focused primarily on serum-based inflammatory markers and CBC-derived ratios, directly comparing them with CRP and ESR, and we deliberately excluded patients who had received antibiotics before intra-articular sampling, then applied a very strict reference standard (culture positivity or WBC  $>100,000/\text{mm}^3$  with  $\geq 90\%$  PMN) to define definite infection. In this context, CRP and ESR remained the dominant diagnostic markers and CBC ratios added only modest incremental value, whereas Varady et al. found a larger advantage of NLR, particularly in synovial fluid. Collectively, these three studies suggest that synovial NLR and optimized synovial WBC thresholds may be especially informative at the joint level, while serum NLR and other CBC-derived ratios function mainly as adjunctive markers whose added value depends on the clinical setting, prior antibiotic exposure, and the strictness of the reference standard used.

Paziuk et al investigated the value of platelet/mean platelet volume ratio in the diagnosis of periprosthetic joint infection (PJI). The mean value of platelet/mean platelet volume ratio was found as 33.5 in the patients who had revision surgery as a result of PJI, while this value was obtained as 25.7 in aseptic revisions. Platelet/mean platelet volume ratio had a sensitivity of 48.1% and specificity of 80.9% when an optimal cutoff point of 31.7 was taken. The specificity value for the platelet/mean platelet volume ratio was greater than the specificity value for both ESR alone and CRP

alone according to ROC curve analysis. However, the diagnostic accuracy was significantly increased by using ESR, CRP and platelet/mean platelet volume ratio altogether<sup>11</sup>. But they didn't analyze the other ratios that we investigated. In our study we also found that combination of all values increases the diagnostic value.

In a retrospectively performed study, Şahin et al investigated the diagnostic value of platelet/mean platelet volume ratio in periprosthetic joint infection among the 62 patients who underwent hip or knee revision surgery between 2016 – 2019. It was shown that platelet/mean platelet volume ratio had poorer diagnostic performance compared to ESR and CRP<sup>21</sup>. We also found a poor diagnostic performance for platelet/mean platelet volume ratio in our study.

In the literature, there are studies about the relation between the blood parameters ratios and some orthopedic diseases other than infection. In a study performed by Gao et al, monocyte/lymphocyte ratio was compared between 205 patients with knee osteoarthritis and 120 patients without osteoarthritis. Monocyte/lymphocyte ratio was found significantly higher in patients with osteoarthritis compared to healthy controls. It was also found that an increase in the monocyte/lymphocyte ratio was higher than the increase in both neutrophil/lymphocyte and platelet/lymphocyte ratios<sup>22</sup>. In a study performed by Kaymaz et al, the impact of neutrophil/lymphocyte ratio on the prognosis of Legg- Calve- Perthes in pediatric patients was investigated. The ratio was found higher in patients with a poorer prognosis compared to both better prognosis and the normal control group<sup>23</sup>. In a study performed by Temiz et al, the mortality of elderly patients in the first year after hip fracture was analyzed according to the neutrophil/lymphocyte ratio level during hospitalization. Higher neutrophil/lymphocyte ratio results were found in the group with higher mortality<sup>24</sup>.

The diagnostic values of blood parameter ratios were also investigated in other specialties. Gasparyan et al. showed that the platelet/lymphocyte ratio can be used as an inflammation marker in rheumatological diseases<sup>13</sup>. It is emphasized that the platelet/lymphocyte ratio can be seriously affected in neoplastic diseases due to immunosuppression and predisposition to thrombosis. It can also be influenced by the presence of rheumatological pathologies and can provide information about the activation of rheumatological diseases when overlapping infection or organ failure exists. It was also reported that the platelet/lymphocyte ratio can help evaluate the

effectiveness of anti-rheumatological treatment and the presence of multisystem involvement<sup>13</sup>. In a meta-analysis study performed by Erre et al, it was also highlighted that neutrophil/lymphocyte ratio and platelet/lymphocyte ratio were significantly higher in the patients with rheumatoid arthritis compared to the control group<sup>25</sup>. Therefore, the patients with a rheumatological disease in our study might have significantly increased the neutrophil/lymphocyte and platelet/lymphocyte ratios in septic arthritis group, knowing the fact that the control group didn't include any rheumatological diseases. This can compromise the validity of our results which indicated higher neutrophil/lymphocyte and platelet/lymphocyte ratios in septic arthritis patients. However, when the meta-analysis by Erre et. al was evaluated, it was evident that the average values for neutrophil/lymphocyte (2.3-3.7) and platelet/lymphocyte (137-193) ratios in rheumatoid arthritis group were way lower than the average values of septic arthritis group in our patient series. The patients with an accompanying disease in our septic arthritis patient serie had an average neutrophil/lymphocyte ratio of 8.5 and platelet/lymphocyte ratio of 415, while the patients without an accompanying disease had an average neutrophil/lymphocyte ratio of 6.1 and platelet/lymphocyte ratio of 249. Our further analysis also showed that the patients in septic arthritis group showed no significant difference in any of the parameters when compared according to the presence of an accompanying disease ( $p=0.319-0.968$ ). However, our results should still be taken cautiously and further studies including only septic arthritis patients with rheumatological disorders should be conducted to validate our results and define more precise cut-off values for patients with rheumatological disorders.

Similarly, in a study, Jiangdong Xiang et al showed that monocyte/lymphocyte ratio drew higher increment than both neutrophil/lymphocyte and platelet/lymphocyte ratio in patients with ovarian cancer<sup>22</sup>. Meshaal et al found in a study that neutrophil/lymphocyte and platelet/lymphocyte ratios were higher in infective endocarditis patients with increased mortality. A marked correlation was found between neutrophil/lymphocyte ratio and fulminant sepsis and major arterial emboli<sup>14</sup>.

This study has several limitations. The retrospective design and low number of patients limit the power of the results. The case-control design and the use of elective osteoarthritis patients as controls introduce spectrum bias, as controls do not fully represent the diagnostic uncertainty encountered in acute

monoarthritis. Important demographic differences between groups, especially sex distribution, also raise the possibility of confounding, though multivariable adjustment did not identify sex as an independent predictor. The strict reference standard used, synovial WBC  $>100,000/\text{mm}^3$  with  $\geq 90\%$  PMN for culture-negative cases, may have led to optimistic accuracy estimates. Although internal bootstrap validation was performed, external validation in larger, prospective cohorts is required. Some guidelines accept lower synovial WBC thresholds (e.g.,  $>50,000/\text{mm}^3$  with  $\geq 75-90\%$  PMN), but also acknowledge substantial overlap with inflammatory arthropathies and trauma. The higher synovial WBC threshold in this study was used only for culture-negative patients, aiming to maximize diagnostic specificity in a retrospective dataset. We explicitly acknowledge that our stricter definition likely selected for more florid infections and may have increased the apparent diagnostic performance of inflammatory markers. Although hematological and immunosuppressive diseases were excluded, patients were not exempt from accompanying diseases including rheumatological diseases disturbing the homogeneity of the group and some drugs can interfere with hematologic parameters<sup>26</sup>. However, further analysis of the values according to presence of an accompanying disease didn't reveal a significant difference in septic arthritis group.

## CONCLUSIONS

Our study revealed that using neutrophil/lymphocyte, platelet/lymphocyte, monocyte/lymphocyte, platelet/mean platelet volume ratio may provide significant diagnostic value and increase the accurate diagnosis. According to ROC curve analysis, the most powerful parameter was neutrophil/lymphocyte ratio when a cut-off point of 2.3 was taken, and it also showed a more significant increase in patients with a positive joint culture. CBC ratios show reasonably good discrimination, but they provide only marginal incremental clinical utility beyond CRP and ESR in this dataset. They can primarily as adjunctive markers that may be helpful in equivocal cases rather than as primary diagnostic tests. Given the retrospective design, spectrum imbalance, and strict reference standard, our findings should be regarded as preliminary and hypothesis-generating. Prospective multicenter studies including the full range of acute monoarthritis presentations are required to validate these markers, establish external calibration, and refine clinically actionable thresholds.

*Conflict of interest:* None.

*Ethics approval:* This retrospective chart review study involving human participants was in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The Human Investigation Committee (IRB) of Istanbul University-Cerrahpasa approved this study.

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