

Original Article

Rapid bedside testing for septic arthritis: evaluating cost-effective diagnostic toolsPranav Rajasekharan¹, Atmananda Hegde¹, Prajwal Mane¹, Chethan Shetty¹, Rishit Anand²¹ Department of Orthopedics, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, India² Under-Graduate MBBS Student, Kasturba Medical College Mangalore, Manipal Academy of Higher Education, Manipal, India**Abstract**

Introduction: Diagnosing septic arthritis through synovial fluid culture and analysis can be time-consuming, and the limited accessibility of these tests in primary and secondary healthcare centers restricts their utility in emergency situations. Therefore, there is a pressing need for an alternative, rapid, and reliable test to significantly reduce morbidity. This study aimed to evaluate the efficacy of leucocyte esterase (LE) and glucose reagent strip tests for the early diagnosis of septic arthritis.

Methodology: This cross-sectional study included 75 individuals presenting with atraumatic native joint effusion. Following arthrocentesis, bedside LE and glucose strip testing were performed, along with synovial fluid culture and analysis.

Results: Out of the 75 cases, 25 (33.3%) were diagnosed with septic arthritis based on standard diagnostic tests. The LE strip test showed a sensitivity of 92%, specificity of 70%, positive predictive value (PPV) of 60%, and negative predictive value (NPV) of 94%. The glucose strip test demonstrated a sensitivity of 88%, specificity of 76%, PPV of 67%, and NPV of 93%. Combining the two tests resulted in a sensitivity of 84%, specificity of 88%, PPV of 77.8%, and NPV of 91.7%. The overall diagnostic accuracy was 80% for the glucose strip test, 77.3% for the LE strip test, and 86.7% for the combined results.

Conclusions: The LE and glucose strip tests are cost-effective bedside assessments for the rapid diagnosis of septic arthritis. Combining the results from both strip tests yielded greater diagnostic accuracy than each one alone.

Key words: diagnostic accuracy; glucose; leucocyte esterase; septic arthritis; strip tests.

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Introduction

Septic arthritis is an orthopedic emergency caused by infection in native joints. It can occur in individuals of all age groups, but is most commonly observed in the elderly and children [1,2]. Various etiologies, including hematogenous spread, adjacent infections, trauma, and iatrogenic causes, contribute to its pathogenesis; and *Staphylococcus aureus* and *Streptococcus* are the most prevalent organisms [2]. The disease is rapidly progressive and can lead to irreversible damage and destruction of joints and surrounding structures. Therefore, early diagnosis and appropriate management are crucial to preventing severe structural and functional impairment in septic arthritis [1,2].

Clinical examination, laboratory assessments, and radiological evaluations, all play significant roles in the prompt diagnosis of joint infections. Numerous conditions, such as osteoarthritis, gout, rheumatoid arthritis, systemic lupus erythematosus, reactive arthritis, and tumors, can mimic the presentation of

septic arthritis [3]. Previous reviews indicate that clinical examination has variable sensitivity (23% to 100%) and specificity (3.5% to 100%) for diagnosing septic arthritis [4].

Current recommendations emphasize the importance of laboratory assessments in diagnosing septic arthritis [5,6]. The European Bone and Joint Infection Society (EBJIS) recommends synovial fluid evaluation, focusing on synovial leucocyte count and bacterial identification. Indicators of septic arthritis include the presence of purulent aspirate or drainage, more than 50,000 synovial white blood cells (WBC) per microliter, 90% polymorphonucleocytes (PMN), and microbial growth in synovial fluid [7]. Studies have shown that blood tests, including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), D-dimer, interleukin-6, and procalcitonin, exhibit variable sensitivity and specificity in diagnosing septic arthritis, and are recommended as adjunctive investigations [8–11]. Radiological assessments may also aid in

diagnosing septic arthritis and may be used for image-guided needle aspiration [12,13]. While various clinical and laboratory methods are currently available, each has its own advantages and limitations. One major drawback of the gold standard diagnostic method— isolating the causative organism—is that it is time-consuming, and can potentially delay critical decision-making and treatment. Consequently, alternate rapid investigative modalities, such as the synovial fluid lactate/glucose ratio and high-resolution thermal imaging, are being explored to enhance diagnostic efficacy [14]. Among these tests, leucocyte esterase (LE) and glucose strip tests have garnered particular interest.

LE is an enzyme that is released by leucocytes at the site of infection [15]. It has been used in urine dipstick tests for the diagnosis of urinary tract infections [16]. The test is cost-effective, rapid, and can be used at any level of healthcare facility [15,16]. Over the years, LE tests have been used in the diagnosis of cervicitis, vaginitis, and exudates associated with skeletal muscle infections [17–19]. Additionally, it has been used to identify septic arthritis through a colorimetric semi-quantitative technique [20–22]. However, a significant drawback of these tests is their inability to differentiate between neutrophil activities related to septic arthritis and those associated with other inflammatory diseases [20–22].

Under normal conditions, the concentration of glucose in synovial fluid closely resembles that in blood, with a maximum difference of up to 10 mg/dL [23]. Glucose levels in synovial fluid tend to decrease in cases of bacterial infection [24]. Previous studies have suggested that septic arthritis should be suspected if the glucose concentration in synovial fluid falls below 40 mg/dL [24]. Although a few studies have explored the use of colorimetric glucose strip tests for diagnosing

sepsis in joints, further research is needed.

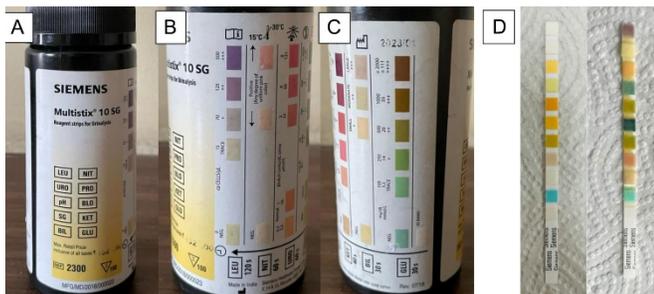
Our approach focused on addressing the gap in the availability of rapid diagnostic tools for septic arthritis. LE and glucose strip tests are quick, cost-effective, and accurate in diagnosing the condition, making them particularly useful in resource-limited settings. Our study aimed to evaluate the accuracy of these tests for the early diagnosis of septic arthritis, by comparing their results with synovial fluid culture and analysis. Current literature indicates that most of these tests exhibit suboptimal accuracy when diagnosing native septic arthritis on their own. This highlights the need for further studies across various geographical settings and research designs to better understand their role in diagnosing or ruling out native septic arthritis. Our study represents a step towards achieving this goal.

Methodology

The study was conducted at the Department of Orthopedics, Kasturba Medical College and its affiliated hospitals in Mangalore, Karnataka, India; from July 2022 to January 2024. It was a cross-sectional, analytical study. Informed consent was obtained from all participants, and approval was secured from the Scientific and Ethics Committee of the institution prior to the commencement of the study. The inclusion criteria comprised all individuals presenting with atraumatic native joint effusion. The exclusion criteria were individuals who had undergone replacement surgery of the affected joint, those who received antibiotic therapy before aspiration, patients with inadequate synovial fluid volume after aspiration, those with hemorrhagic synovial fluid even after centrifugation, cases where fluid specimen analysis was performed more than 6 hours after aspiration, and individuals with incomplete data. All patients provided informed consent before joint aspiration. After arthrocentesis, bedside tests for LE and glucose, along with synovial fluid analysis, were performed using a standard protocol. Culture sensitivity and relevant blood investigations were also performed. This was referenced from a study conducted in Germany by Kolbeck *et al.* [25].

If the synovial fluid was found to be hemorrhagic, it was centrifuged for 1 minute in an Eppendorf tube, and the resulting supernatant was used for strip testing. 300 μ L of fluid were pipetted onto test fields. LE and glucose test strips (SIEMENS Multistix 10 SG Reagent Strips, Berlin, Germany), typically used for urine analysis, were immersed in the fluids for 60 seconds. Changes in color on the testing strips were used to semi-quantitatively assess LE and glucose content (Figure 1).

Figure 1. Reagent strip box and strip test analysis.



A: Siemens Multistix 10 SG reagent strip box; **B:** color scale for leucocyte esterase (LE) test; **C:** color scale for glucose test; **D:** strip test before and after dipping into synovial fluid showing the change in color of the pad for LE and glucose tests (topmost and bottommost color pads respectively).

The LE scale ranged from (–), indicating 0 cells/uL; to (+++), indicating > 500 cells/uL. The glucose scale ranged from (–), indicating 0 mmol/L; to (++++), for ≥ 111 mmol/L. In the case of LE, scores of (–), (trace), and (+) were considered negative; while scores of (++) and (+++) were considered positive. In the case of glucose, a (–) or (trace) score denoted a decrease in glucose concentration in the synovial fluid (negative), whereas scores from (+) to (++++), were deemed positive.

Septic arthritis was diagnosed based on a combination of synovial fluid culture and analysis. Joint fluid was identified as septic under the following conditions: 1) a pathogen was isolated from the synovial fluid; 2) a pathogen was isolated from blood culture, accompanied by typical clinical symptoms of septic arthritis; 3) the synovial fluid was purulent with no crystals present; or 4) microbiological findings were negative, but the synovial fluid indicated WBC > 50,000/mm³ and PMN% > 90%, with no crystals present. The data obtained were recorded on the study proforma, and the combined data were analyzed using appropriate statistical tests.

Statistical analysis

The data were entered into MS Excel, and analyzed using IBM SPSS version 20 software (IBM Corp, Armonk, NY, USA). Qualitative data were measured using percentage and frequency, while quantitative data were analyzed using mean and standard deviation. The diagnostic abilities of 1) a positive (++ or +++) LE test, 2) a negative (–) glucose test, and 3) the combination of a positive (++ or +++) LE test and a negative (–) glucose test for detecting septic arthritis were evaluated. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+), negative likelihood ratio (LR–), and the

area under the receiver operating characteristic (ROC) curve (AUC) were calculated for each reagent test, along with the 95% confidence intervals (CIs).

Results

The study involved 75 participants aged between 3 and 88 years, with a mean age of 52.5 ± 22.2 years. The majority of participants (29.3%) were in the age group of 46–60 years. Of the participants, 50.7% (38) were male and 49.3% (37) were female. The most common co-morbidities observed included diabetes mellitus alone (14, 18.7%), diabetes mellitus combined with hypertension (12, 16%), hypertension alone (6, 8%), and ischemic heart disease (2, 2.7%). Notably, 41 individuals (54.7%) had no comorbidities. A total of 56 participants (74.7%) were without any addictive habits. Conversely, 12% (9) were active smokers, 4% (3) consumed alcohol, and 9.3% (7) both smoked and consumed alcohol. The majority of participants presented with atraumatic naive joint effusion in the left knee (39, 52%), followed by the right knee (32, 42.7%), left shoulder (2, 2.7%), right shoulder (1, 1.3%), and left hip (1, 1.3%).

Most cases of native atraumatic fluid effusion did not yield any organisms upon synovial fluid culture (51, 68.0%). The prevalent organisms identified were *Staphylococcus aureus* (16, 21.3%), Group B *Streptococcus* (4, 5.3%), *Streptococcus pneumoniae* (3, 4%), and *E. coli* (1, 1.3%).

The distribution of participants based on laboratory blood parameters is depicted in Table 1. Crystals were found in the synovial fluid of 22.7% (17) of participants. Blood culture was positive in only 1 case (1.3%), where *Staphylococcus aureus* was detected. Table 2 shows the laboratory parameters of synovial fluid in atraumatic fluid effusion

Upon evaluation, the final diagnoses included septic arthritis in 33.3% (25) of individuals, synovitis in 32% (24), pseudogout in 16% (12), reactive arthritis in 10.7% (8), gout in 6.6% (5), and rheumatoid arthritis in 1.3% (1).

LE test scores of (–), (trace), and (+) were deemed negative, while (++) and (+++) were considered positive (Table 3). Overall, 38 participants (50.7%) with atraumatic synovial fluid effusion tested positive

Table 1. Distribution of participants based on laboratory parameters of blood.

Laboratory parameter	n	%
Total leucocyte count (cells/cumm) (range: 6,543 to 20,099; mean: 11,291 + 3,296)		
4,500–11,000	25	33.3
> 11,000	50	66.7
C-reactive protein (mg/dL) (range: 4 to 245; mean: 72.0 + 48.0)		
< 0.3	–	–
0.3–1	–	–
1–10	74	98.7
> 10	1	1.3
Erythrocyte sedimentation rate (mm/hour) (range: 12 to 154; mean: 63.4 + 29.4)		
< 20	2	2.7
20–100	65	86.7
> 100	8	10.7

Table 2. Laboratory parameters of synovial fluid in atraumatic fluid effusion.

Laboratory parameter	Range	Mean + SD
Protein (g/L)	12–65	36.1 + 13.4
Glucose (mg/dL)	11–99	58.8 + 21.5
WBC	10,000–70,456	37492 + 16216
Polymorphonucleocyte (%)	10–99	55.7 + 27.5

WBC: white blood cells; SD: standard deviation.

Table 3. Distribution of cases based on leucocyte esterase (LE) strip test.

LE strip test result	n	%
-	14	18.7
Trace	7	9.3
+	16	21.3
++	25	33.3
+++	13	17.3

on the LE strip test and were thus suspected of having septic arthritis.

Glucose test scores of (-) and (trace) indicated a reduction in glucose concentration in the joint fluid, while scores of (+) to (+++++) were interpreted as positive (Table 4). The glucose strip test was positive in 54.7% (41) of cases and negative in 45.3% (34) of cases.

Among the 75 cases of atraumatic synovial fluid effusion, the standard diagnostic test identified 25 cases (33.3%) as septic arthritis, while the LE strip tests diagnosed 38 cases (50.7%), and the glucose strip tests identified 41 cases (54.7%) as septic arthritis (Figure 2).

The LE strip test effectively diagnosed septic arthritis (23, 92%), gout (2, 40%), synovitis (9, 37.5%), reactive arthritis (2, 25%), and pseudogout (2, 16.7%).

Higher negative results for glucose strip tests were noted in cases of septic arthritis (22, 88%) and in a single case of rheumatoid arthritis (1, 100%). In comparison, all cases of reactive arthritis (8, 100%) tested positive for glucose strip tests. Additionally, 10 cases (83.3%) of pseudogout, 4 cases (80%) of gout, and 16 cases (66.7%) of synovitis tested positive for the glucose strip test.

The positive and negative likelihood ratios for LE strip tests were 3.07 and 0.11, respectively; for glucose strip tests were 3.67 and 0.16 respectively; and for the combined tests were 7.00 and 0.18, respectively.

The study concluded that the LE strip test had a higher sensitivity (92%) than the glucose strip test

Figure 2. Comparison of diagnosis of septic arthritis based on culture, leucocyte esterase (LE) strip test, and glucose strip test.

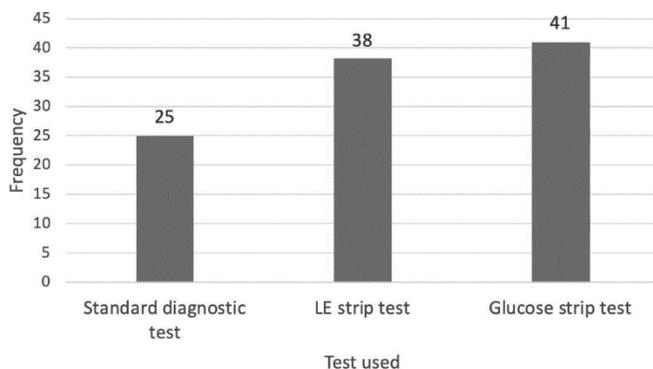
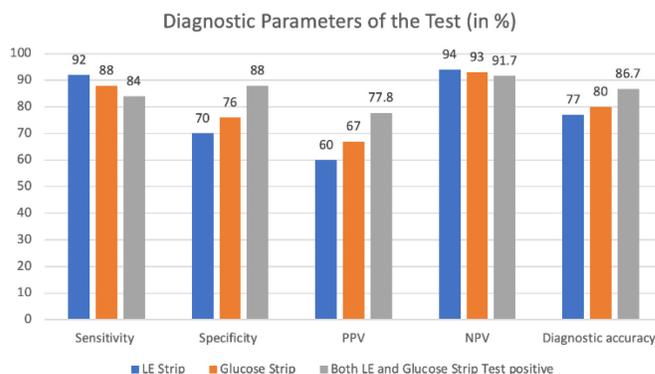


Table 4. Distribution of cases based on glucose strip test.

Glucose strip test	n	%
-	27	36.0
Trace	7	9.3
+	20	26.7
++	15	20.0
+++	6	8.0

(88%) and the combined test (84%). However, the combined test demonstrated a higher specificity (88%) compared to the LE (70%) and glucose strip tests (76%). The PPV was highest for the combined test (77.8%), whereas the NPV was highest for the LE strip tests (94%). Overall, the diagnostic accuracy was 77.3% for LE strip tests, 80% for glucose strip tests, and 86.7% for the combined tests (Tables 5, 6, 7; Figure 3).

Figure 3. Comparison of leucocyte esterase (LE) strip, Glucose strip, and combined screening tests.



PPV: positive predictive value; NPV: negative predictive value.

Table 5. Diagnostic accuracy of leucocyte esterase (LE) strip test in the diagnosis of septic arthritis.

LE strip test	Standard test		Total
	Positive	Negative	
Positive	23	15	38
Negative	2	35	37
Total	25	50	75

Table 6. Diagnostic accuracy of glucose strip test in the diagnosis of septic arthritis.

Glucose strip test	Standard test		Total
	Positive	Negative	
Positive (for septic arthritis)	22	12	34
Negative	3	38	41
Total	25	50	75

Table 7. Diagnostic accuracy of combined tests (glucose strip and leucocyte esterase (LE) strip test) in the diagnosis of septic arthritis.

Combined test (both)	Standard test		Total
	Positive	Negative	
Positive	21	6	27
Negative	4	44	48
Total	25	50	75

Discussion

A patient presenting with painful joint effusion requires a thorough assessment to establish differential diagnoses [1,2]. Early diagnosis and appropriate management of these cases are of utmost importance, especially in cases of suspected septic arthritis [3]. The gold standard for diagnosing septic arthritis is synovial fluid culture [3,4]. However, prior antibiotic coverage may alter the results. Other drawbacks of synovial fluid culture include biofilm formation, poor sample collection techniques, natural antibiotics in the synovial cavity, relatively higher cost, and delay in diagnosis [6,7]. Gram stain is an alternative for the early diagnosis of septic arthritis. However, Gbejuade *et al* noted that Gram stain showed poor correlation with synovial fluid culture in diagnosing septic arthritis, and recommended WBC count as a better investigation compared to Gram stain [8]. Stirling *et al.* noted that concomitant crystal arthritis may reduce the accuracy of Gram stain [9]. There is an ongoing effort to find a rapid, cost-effective and more accessible screening test for septic arthritis. LE and glucose strip tests are alternate tests studied worldwide.

Our study aimed to evaluate the combined accuracy of the LE and glucose strip tests in the early diagnosis of septic arthritis by comparing their results to synovial fluid analysis and culture. The current study included an equal distribution of participants across genders with a mean age of 52.5 ± 22.2 years. These results were in concordance with previous studies [10–12]. Hence, the study participants were representative of patients with septic arthritis worldwide.

Our study noted that the LE strip tests had a higher sensitivity (92%) and NPV (94.5%) in diagnosing septic arthritis. In addition, they demonstrated moderate specificity (70%) and PPV (60.5%) in diagnosing septic arthritis. The overall diagnostic accuracy was 77.3%. This was comparable to a previous study by Aslani *et al.* and Hassas *et al.* [13,14]. In contrast, moderate sensitivity and higher specificity were noted by McNabb *et al.* [16]. The reduced specificity in our study may be due to increased neutrophils and a subsequent rise in LE levels in other inflammatory conditions, a previously documented drawback of LE testing. Our evaluation showed that LE strip tests turned out to be positive in septic arthritis (92%), gout (40%), synovitis (37.5%), reactive arthritis (25%), and pseudogout (16.7%). Zhang *et al.* noted that inflammatory arthritis may lead to false positive results, leading to reduced specificity [17]. Our study is in concordance with these findings. A pilot study by Li *et al.* noted that centrifugation can reduce false positive results of LE

strip tests [18].

LE strip tests have other advantages as well. While antibiotic coverage may reduce the sensitivity of culture reports on septic arthritis, Aslani *et al.* noted that the strip test's sensitivity and PPV were higher among septic arthritis patients taking antibiotics, compared to those who were not. LE strip tests have also shown high sensitivity and specificity in cases of periprosthetic joint infection [19,20]. However, these patients were excluded from our study.

Our study noted lower sensitivity (88%), and NPV (92.5%); but higher specificity (76%) and PPV (66.7%) for glucose strip tests compared to LE strip tests in diagnosing native joint sepsis. Most previous studies have noted higher specificity compared to sensitivity for glucose strip tests in diagnosing septic arthritis [25,26], but our study noted lower specificity. We observed that synovitis (33% cases), gout (20% cases), and pseudogout (16.7% cases) also showed negative results (i.e., positive for the disease). Synovial fluid glucose levels may be reduced in both infection and inflammatory conditions due to metabolic activities of the neutrophils [23]. In addition, bacterial action reduces glucose levels in the fluid [23]. Further research is needed to ascertain the cause.

Our study noted that combining the tests improved the specificity (88%) and PPV (77.8%), while compromising on sensitivity (84%) and NPV (91.7%) (Table 7). The overall diagnostic accuracy improved, with LE strips at 77.3%, glucose strips at 80%, and combined tests at 86.7%. Previous studies have noted similar findings [25,26]. Table 8 compares the diagnostic accuracy of the LE strip test, glucose strip test, and combined strip test between our study and a previous study by Kolbeck *et al.* [25]. Research has indicated that delayed treatment is associated with disease progression and increased duration of hospital stay [26,27].

The findings of this study support the use of these strips for the early diagnosis of septic arthritis. These strips are rapid, cost-effective, portable, and readily available; making them a valuable resource for diagnosing septic arthritis—especially in settings where access to diagnostic resources is limited, which could potentially completely alter the clinical practice in such regions.

The results of our study, albeit promising, need to be correlated with clinical findings, and additional tests should be studied to improve the accuracy in diagnosing septic arthritis. Newer approaches like lactate/glucose ratio have been studied worldwide [28]. There is a need for research on these modalities to improve the

diagnostic accuracy of tests.

One of the limitations of this study was that it was a single center study which limits the generalizability of the results. Another limitation is that there can be operator variability in interpreting the colorimetric changes as it is a subjective analysis. Therefore, further large-scale, multi-centric studies are recommended, with a larger sample size, and future automation to standardize and strengthen the results, to advocate its use as a screening test in resource-limited settings.

Conclusions

LE and glucose strip tests proved to be rapid and cost-effective tools for diagnosing septic arthritis, particularly in resource-limited settings; thus, greatly reducing the associated morbidity by facilitating prompt management. It would also justify the early use of empirical broad-spectrum antibiotic therapy for septic arthritis. Figure 4 highlights the clinical utility of combined tests as demonstrated by the AUC scores and the relevance and accuracy of combined tests. The ROC curves emphasize the same increased accuracy of the combined test. The combined use of these tests (as demonstrated by the AUC-ROC curves shown in Figure 4) can enhance diagnostic accuracy, and warrants further validation through larger, multicenter studies.

Authors' contributions

PR: data curation, investigation, methodology, writing—original draft; AH: conceptualization, project administration, supervision, validation; PM: visualization, formal analysis; CS: resources, conceptualization; RA: writing—review and editing.

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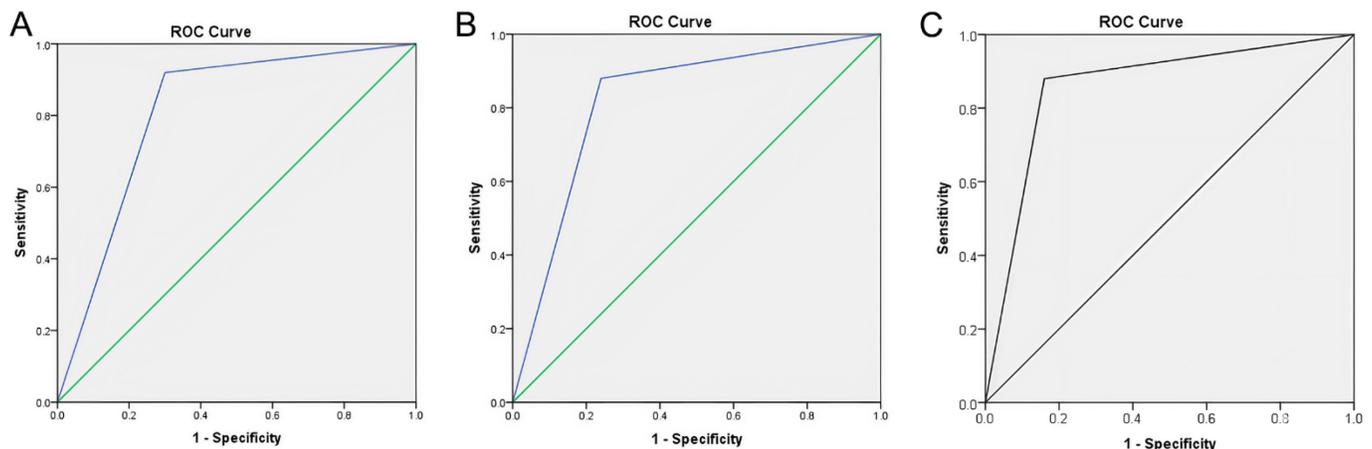
Conflict of interests

No conflict of interests is declared.

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Figure 4. Area under the receiver operating characteristic (AUC-ROC) curves comparing the diagnostic accuracy of **A:** LE strip test – 0.810 (0.709–0.911); **B:** glucose strip test – 0.820 (0.717–0.923); and **C:** combined strip tests – 0.860 (0.76–0.96) in the diagnosis of septic arthritis.



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