Amjad Abdulrahman Almayouf et al. Saudi J Er Med. 2025;6(1):317-325
DOI: 10.24911/SJEMed.72-1715381409

REVIEW ARTICLE

Diagnostic accuracy of rapid pediatric sepsis screening tools in the emergency department-a systematic review

Amjad Abdulrahman Almayouf[1], Mohammed Abdulrahman Aleid[2*], Abdullah Mohammed Alshushan[3], Amro Abdullah Alsultan[2]

ABSTRACT

Pediatric sepsis remains a significant cause of morbidity and mortality, necessitating efficient screening tools for early detection. This study addressed the evolving landscape of pediatric sepsis screening strategies, emphasizing the importance of nuanced approaches and technological advancements. With a focus on sensitivity, specificity, and positive predictive value, this study explored the performance of diverse screening tools and their impact on timely interventions. A systematic review was conducted using PubMed, Embase, and Cochrane Library, following defined inclusion criteria. Studies involving pediatric populations, sepsis screening, and reporting performance metrics were included. A two-step screening process, quality assessment, and data extraction were undertaken. The synthesis adopted a narrative approach, considering the anticipated heterogeneity in study designs, populations, and screening tools. Diverse screening tools exhibited variable outcomes. The current study findings underscored the complexity of balancing sensitivity and specificity, which is crucial for avoiding false positives and ensuring timely interventions. This study contributed to the ongoing discourse on pediatric sepsis screening by synthesizing evidence from diverse studies. The nuanced nature of pediatric sepsis demands tailored screening tools, and technological integration, which holds promise. Despite challenges and variances in tool performance, this study highlights the essential role of screening in early sepsis detection. Future research should prioritize refining tools, addressing limitations, and exploring novel technologies to enhance precision in pediatric sepsis screening.

Keywords: Systematic review, diagnostic accuracy, pediatric sepsis, screening tools, emergency department.

Introduction

Pediatric sepsis, a severe and potentially life-threatening condition arising from the body's extreme response to an infection, remains a critical concern in emergency medicine [1-3]. Unlike adult sepsis, its pediatric counterpart exhibits unique challenges in terms of recognition, diagnosis, and management [4-6]. Timely intervention is paramount, yet the subtleties in symptom presentation and the rapid progression of the condition necessitate effective screening tools for early detection [7].

Sepsis in children often begins with an infection, commonly bacterial, viral, or fungal, that triggers a systemic inflammatory response [8,9]. The cascade of events in sepsis can lead to organ dysfunction and failure [10,11]. Prompt identification is crucial, but the manifestations of sepsis in pediatric patients vary widely, making it a diagnostic challenge. Symptoms might include fever, rapid breathing, abnormal heart rate, altered mental status, and other nonspecific signs that can be subtle, especially in the early stages [12].

The management of pediatric sepsis involves a multidisciplinary approach, including timely administration of antibiotics, fluid resuscitation, and supportive care [13]. The urgency in initiating appropriate treatment underscores the need for efficient and accurate screening tools [13]. Rapid diagnosis and early intervention significantly improve outcomes, reducing morbidity and mortality associated with pediatric sepsis [14].

Correspondence to: Mohammed Abdulrahman Aleid
*Resident, Pediatric Emergency, Maternity and Children Hospital, Buraidah, Saudi Arabia.
Email: mohammedaleid141@gmail.com
Full list of author information is available at the end of the article.
Received: 10 May 2024 | **Accepted**: 14 July 2024

The prevalence of pediatric sepsis is a considerable public health concern. While exact figures vary globally, sepsis contributes significantly to pediatric morbidity and mortality. The World Health Organization recognizes sepsis as a major cause of death in infants and children worldwide [15]. The burden of sepsis underscores the importance of developing and implementing effective screening tools tailored to the pediatric population.

In the realm of pediatric emergency medicine, the development and validation of screening tools for rapid sepsis detection have become a focal point [7]. These tools aim to expedite the identification of septic cases, allowing for timely intervention and improved patient outcomes. The validation of such tools is critical to ensuring their accuracy and reliability in diverse clinical settings.

Our study enters this landscape, aspiring to contribute to the refinement of pediatric sepsis screening strategies. Recognizing the challenges posed by the subtle and varied presentation of sepsis in children. The current study focused on evaluating existing screening tools and their performance metrics. By understanding the strengths and limitations of these tools, it was aimed to provide insights that can inform clinical practice and guide future research in the quest for more effective and precise screening approaches.

As the intricacies of pediatric sepsis and the landscape of screening tools were delved, the current study aligns with the broader objective of enhancing early detection in emergency settings. The ultimate goal was to improve outcomes for pediatric patients with sepsis by refining screening methodologies, addressing challenges, and contributing to the ongoing evolution of pediatric sepsis management.

Subjects and Methods

The systematic study adopted a comprehensive methodology to assess and analyze various screening tools designed for the early detection of pediatric sepsis. A meticulous and systematic search strategy was employed to identify relevant studies from electronic databases. The databases included PubMed, Embase, and Cochrane Library. The search was conducted using a combination of keywords and medical subject headings (MeSHs) terms related to pediatric sepsis, screening tools, early detection, and performance metrics.

Inclusion criteria were defined to ensure the selection of studies directly relevant to the objectives of the systematic review. Studies eligible for inclusion encompassed those focused on pediatric populations, addressed sepsis screening, and reported performance metrics such as sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) or timely improvement or other outcomes. The search was limited to studies published in English, and the initial selection process included titles and abstracts.

The next phase involved a thorough examination of the full texts of potentially eligible studies. Each study was critically appraised for its methodology, data collection procedures, and relevance to the research questions. A data extraction tool was developed to systematically capture essential information from each selected study. The extracted data included details on the study objective, design, sample size, screening tools utilized, and reported performance metrics.

To ensure the reliability and validity of the systematic study, a two-step screening process was implemented. Initially, two independent reviewers conducted the title and abstract screening, and any discrepancies were resolved through discussion. Subsequently, the full-text screening was performed using the predefined inclusion and exclusion criteria.

The quality of the included studies was assessed using recognized appraisal tools appropriate for the respective study designs. This critical appraisal process aimed to ascertain the internal validity of the studies and identify potential biases. The results of the quality assessment were considered in the interpretation of the findings and synthesis of the evidence.

The systematic study adhered to the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines to ensure transparency and completeness in reporting. The methodology was developed with the overarching goal of synthesizing the available evidence on pediatric sepsis screening tools while considering the methodological rigor of the included studies.

Results

A total of 1,085 articles were identified through the comprehensive searches. However, 621 were deleted because of being duplicated resulting in 464 studies. Following a meticulous screening process, 13 articles were deemed suitable for inclusion in this review [16-28] (Figure 1).

General characteristics of included studies

This comprehensive review encompasses a spectrum of studies that delved into strategies for early detection of pediatric sepsis and their corresponding outcomes. Cruz et al. [16] aimed to implement an emergency department (ED) protocol for septic shock recognition and adherence to treatment guidelines in a prospective cohort study involving 167 patients, leading to earlier recognition of suspected sepsis and reduced intervention time [16]. Subsequently, Cruz et al. [17] conducted a retrospective study analyzing the performance of an automated triage tool, which identified abnormal heart rates consistent with septic shock in 39,697 visits, achieving an impressive sensitivity of 81% and specificity of 89% [17].

Sepanski et al. [18] took a unique approach, focusing on developing a screening tool for pediatric severe sepsis with improved predictive value. Their study, involving 7,402 children, reported an enhancement in PPV to 48.7% [18]. Balamuth et al. [20] contributed by comparing the effectiveness of physician judgment and an electronic algorithmic alert in a retrospective cohort study comprising 19,524 visits. They found that the algorithmic alert was more sensitive, while physician judgment was more specific [20]. The subsequent study

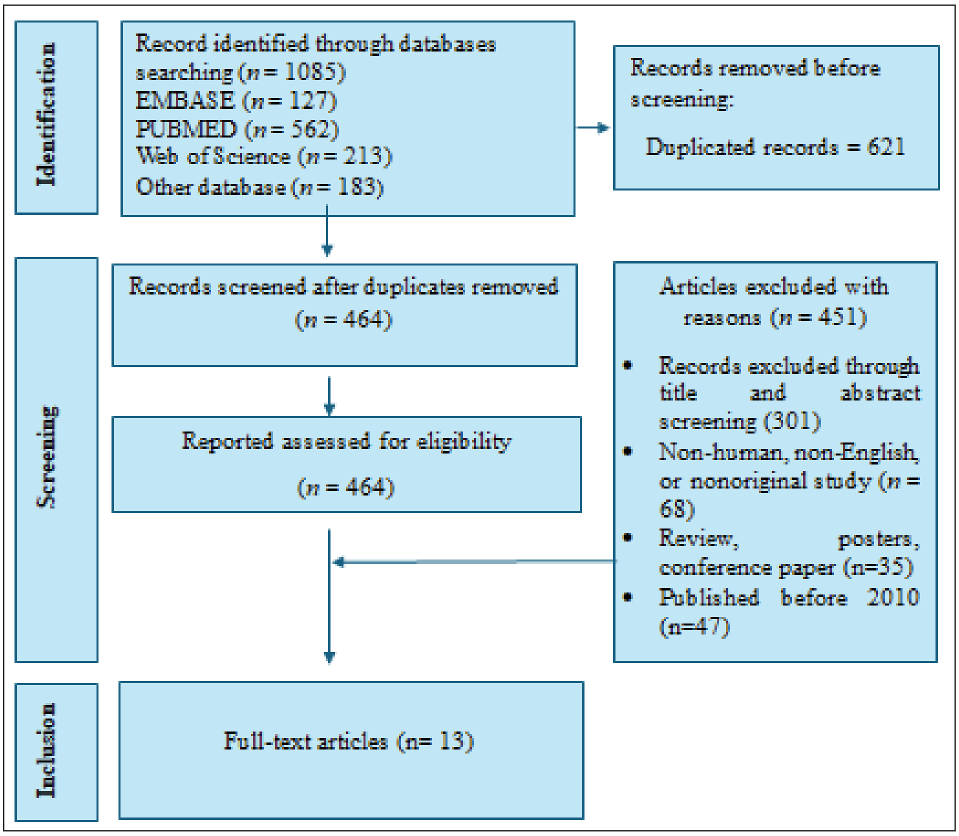

Figure 1. *The PRISMA figures showing the steps to choose the studies for systematic review.*

by Balamuth et al. [19] evaluated the performance of a sepsis recognition process, including an electronic sepsis alert and bedside assessment in a pediatric ED with 182,509 visits. The electronic sepsis alert demonstrated high sensitivity (86.2%) and specificity (99.1%) [19].

Lloyd et al. [21] conducted a prospective cohort study 2018, aiming to integrate a manual pediatric ED sepsis screening process into the electronic health record. Although specific sample size details were not provided, their electronic sepsis screening tool identified all patients flagged by the manual process earlier [21]. Eisenberg et al. [22] undertook a study in 29,010 encounters, creating and evaluating a continuous automated alert system embedded in the electronic health record for the detection of severe sepsis among pediatric inpatient and ED patients. Their final algorithm had 72% sensitivity, 91.8% specificity, 8.1% PPV, and 99.7% NPV [22].

Fesnak et al. [23] explored the timeliness of sepsis recognition and initial treatment in a retrospective study with 96,427 ED visits. Interestingly, they found no significant difference in the timeliness of care initiation in high-risk patients with sepsis [23]. Lee et al. [24] conducted a prospective study with an unspecified sample size, aiming to reduce the time to antibiotic administration in a dedicated children's hospital outpatient department in Mbarara, Uganda, utilizing a digital triage platform. The time for antibiotics was reduced from 51 to 44 minutes [24].

Scott et al. [25] derived and validated a model of the risk of septic shock among children with suspected sepsis, utilizing data known in the electronic health record, encompassing 2,464 visits. Their model exhibited an area under the curve (AUC) of 0.79 in the training set, 0.75 in the temporal test set, and 0.87 in the geographic test set [25]. Eisenberg et al. [26] conducted a retrospective and prospective study involving 122,221 ED encounters, comparing the performance and test characteristics of an automated sepsis abstract screening tool with a manual sepsis screen. The automated sepsis screening had higher sensitivity (84.6%) and specificity (95.1%) than the manual screening [26]. Finally, Ehwerhemuepha et al. [27] developed and validated an early warning system for sepsis in a retrospective cohort study involving 537,837 visits, exhibiting high area under the receiver operating characteristic curves (AUROCs) for death, severe sepsis, non-severe sepsis, and bacteremia [27].

Sepanski et al. [28] introduced a retrospective and prospective study involving 35,586 ED visits, creating a predictive tool for electronic alert systems to identify potential sepsis in children presenting to the ED. Their tool demonstrated 77% sensitivity for identifying gold standard sepsis and 22.5% PPV for high severity of illness (SOI) outcomes [28] (Table 1).

Characteristics of rapid pediatric sepsis screening tools

A multitude of screening tools was employed across these studies, each designed with unique parameters and activation criteria. Cruz et al. [16] utilized a computerized triage system with abnormal vital signs.

Table 1. General characteristics of included studies.

Study	Year	Objective	Study design	Sample size	Key findings
Cruz et al .[16]	2011	Implement an ED protocol for septic shock recognition and adherence to treatment guidelines.	Prospective cohort study.	167 patients	Earlier recognition of suspected sepsis, reduced intervention time.
Cruz et al. [17]	2012	Create and analyze the performance of an automated triage tool for identifying abnormal heart rates consistent with septic shock.	Retrospective study	39,697 visits	81% sensitivity and 89% specificity in identifying patients with shock.
Sepanski et al. [18]	2014	Develop a screening tool for pediatric severe sepsis with improved predictive value.		7,402 children	Positive predictive value improved to 48.7%.
Balamuth et al. [19]	2017	Evaluate the performance of a sepsis recognition process including an electronic sepsis alert and bedside assessment in a pediatric ED.	Prospective cohort study.	182,509 visits	Electronic sepsis alert had 86.2% sensitivity and 99.1% specificity.
Balamuth et al. [20]	2015	Compare the effectiveness of physician judgment and an electronic algorithmic alert in identifying pediatric patients with severe sepsis/ septic shock.	Retrospective cohort study	19,524 visits	Algorithmic alerts are more sensitive, and physician judgment is more specific.
Lloyd et al. 2018 [21]	2018	Integrate a manual pediatric emergency department sepsis screening process into the electronic health record.	Prospective cohort study.	Not provided	The electronic sepsis screening tool identified 100% of patients flagged by the manual process earlier.
Eisenberg et al. [22]	2019	Create and evaluate a continuous automated alert system embedded in the electronic health record for the detection of severe sepsis among pediatric inpatient and emergency department patients.		29,010 encounters	The automated algorithm had 72% sensitivity, 91.8% specificity, 8.1% PPV, and 99.7% NPV.
Fesnak et al. [23]	2020	Compare timeliness of sepsis recognition and initial treatment in patients with and without high-risk comorbid conditions.	Retrospective study	96,427 ED visits	Timeliness of care initiation was not different in high-risk patients with sepsis.
Lee et al. [24]	2020	Reduce time to antibiotic administration in a dedicated children's hospital outpatient department in Mbarara, Uganda.	Prospective study	Not provided	Time to antibiotics was reduced from 51 to 44 minutes with a digital triage platform.
Scott et al. [25]	2019	Derive and validate a model of risk of septic shock among children with suspected sepsis using data known in the electronic health record.		2,464 visits	The model had an AUC of 0.79 in the training set, 0.75 in the temporal test set, and 0.87 in the geographic test set.
Eisenberg et al. [26]	2021	Compare the performance and test characteristics of an automated sepsis abstract screening tool with that of a manual sepsis screen in patients presenting to a pediatric emergency department (ED).	Retrospective and Prospective	122,221 ED encounters	Automated sepsis screening had higher sensitivity (84.6%) and specificity (95.1%) than manual screening.
Ehwerhemuepha et al. [27]	2021	Develop and validate an early warning system for sepsis based on a predictive model of critical decompensation.	Retrospective cohort study.	537,837 visits	The model had high AUROCs for death, severe sepsis, non-severe sepsis, and bacteremia.
Sepanski et al. [28]	2020	Create a predictive tool for electronic alert systems to identify potential sepsis in children presenting to the emergency department.	Retrospective and Prospective	35,586 ED visits	The tool had 77% sensitivity for identifying gold standard sepsis and 22.5% PPV for high SOI outcomes.

Cruz et al. [17] introduced a computerized best-practice alert (BPA) triage system with corrected heart rate for temperature and alarm on tachycardia. Sepanski et al. [18] implemented an electronic medical record with age-specific thresholds for abnormal heart rate and respiratory rate [18]. Balamuth et al. [20] employed an electronic algorithmic alert. Balamuth et al. [19] utilized an electronic sepsis alert system with specific criteria, including elevated pulse rate or hypotension, concern for infection, abnormal capillary refill, abnormal mental status, or high-risk condition [19]. Lloyd et al. [21] integrated a manual pediatric ED sepsis screening process into the electronic health record.

Eisenberg et al. [22] developed an automated electronic health records (EHR)-based alert system, Fesnak et al. [23] used an electronic sepsis alert system with age-specific criteria, and Lee et al. [24] implemented a digital triage platform considering clinical signs, symptoms, and vital signs. Scott et al. [25] utilized routine electronic health record data without specifying a particular system. Eisenberg et al. [26] employed an automated sepsis abstract screening tool, and Ehwerhemuepha et al. [27]

Table 2. Characteristics of rapid pediatric sepsis screening tools.

Study	Triage system	Screening parameters	Activation criteria	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Cruz et al. [16]	Computerized triage system	Abnormal vital signs	Toxic appearance or high risk for invasive infection	Not provided	Not provided	Not provided	Not provided
Cruz et al. [17]	Computerized best-practice alert (BPA) triage system	Corrected heart rate for temperature, alarmed on tachycardia	Ill appearance or medical comorbidities predisposing to sepsis	81%	89%	4%	99.9%
Sepanski et al. [18]	Electronic medical record	Age-specific thresholds for abnormal heart rate and respiratory rate	Identification of SS cases based on ICCPS parameters	Not provided	Not provided	48.7%	Not provided
Balamuth et al. [20]	Electronic algorithmic alert	Not provided	Potential sepsis identified by the ED clinical team	92.1%	83.4%	Not provided	Not provided
Balamuth et al. [19]	Electronic sepsis alert	Elevated pulse rate or hypotension, concern for infection, abnormal capillary refill, abnormal mental status, or high-risk condition	Positive electronic sepsis alert or clinical concern	86.2%	99.1%	25.4%	100%
Lloyd et al. 2018 [21]	Electronic health record	Mapped criteria from manual screening tool to standard documentation	Scores meeting predefined sepsis risk threshold	Not provided	Not provided	Not provided	Not provided
Eisenberg et al. [22]	Automated EHR-based alert system	Not provided	Not provided	72%	91.8%	8.1%	99.7%
Fesnak et al. [23]	Electronic sepsis alert	Age-specific tachycardia or hypotension, concern for infection, abnormal capillary refill, abnormal mental status, or high-risk condition	Positive sepsis alert or clinical concern	Not provided	Not provided	Not provided	Not provided
Lee et al. [24]	Digital triage platform	Clinical signs, symptoms, and vital signs	Emergency triggers and predictive risk algorithms	Not provided	Not provided	Not provided	Not provided
Scott et al. [25]	Not provided	Routine electronic health record data	Not provided	82%	48%	90%	Not provided
Eisenberg et al. [26]	Automated sepsis abstract screening	Not provided	Development of severe sepsis or septic shock within 24 hours	84.6%	95.1%	3.7%	99.9%
Ehwerhemuepha et al. [27]	Predictive model	Triage vital signs, previous diagnoses, medications, and healthcare utilizations within 6 months of the index ED visit.	Development of severe sepsis, death, positive bacteremia	Not provided	Not provided	Not provided	Not provided
Sepanski et al. [28]	Electronic health record-based tool	New standards for normal/abnormal vital signs based on data from ~1.2 million children at 169 hospitals	Continuous monitoring during ED visits	77%	Not provided	22.5%	Not provided

devised a predictive model considering triage vital signs, previous diagnoses, medications, and healthcare utilizations within 6 months of the index ED visit. Sepanski et al. [28] introduced an electronic health record-based tool using new standards for normal/abnormal vital signs based on data from approximately 1.2 million children at 169 hospitals, with continuous monitoring during ED visits (Table 2).

Results of rapid pediatric sepsis screening tools

These diverse screening tools yielded varied outcomes in terms of sensitivity, specificity, PPV, NPV, and other relevant measures. Cruz et al. [16] observed a significant decrease in median time from triage to the first bolus and antibiotics post-protocol initiation. Cruz et al. [17] reported a sensitivity of 81% and specificity of 89% for their BPA-automated sensitive triage tool. Sepanski et al. [18] achieved an improved PPV of 48.7% for their screening tool. Balamuth et al. [20] found the algorithmic alert to be more sensitive than physician judgment. Balamuth et al. [19] reported high sensitivity (86.2%) and specificity (99.1%) for their electronic sepsis alert. Lloyd et al. [21] successfully identified 100% of patients flagged by the manual process earlier with their electronic sepsis screening tool. Eisenberg et al. [22] developed a

Table 3. *Results of rapid pediatric sepsis screening tools.*

Study	Outcome measures	Results
Cruz et al. [16]	Time from triage to first bolus and antibiotics	Median time decreased significantly post-protocol initiation.
Cruz et al. [17]	Sensitivity, specificity, positive, and negative predictive values for shock identification	BPA-automated sensitive triage tool had 81% sensitivity and 89% specificity.
Sepanski et al. [18]	Positive predictive value	The final tool's positive predictive value improved to 48.7%.
Balamuth et al. [20]	Sensitivity, specificity, positive, and negative predictive values for severe sepsis/septic shock identification	Algorithmic alerts are more sensitive, and physician judgment is more specific.
Balamuth et al. [19]	Sensitivity, specificity, positive, and negative predictive values for severe sepsis detection	Electronic sepsis alert alone had 86.2% sensitivity and 99.1% specificity.
Lloyd et al. [21]	Performance of the electronic sepsis screening tool	The automated tool identified 100% of patients flagged by the manual process on average 68 minutes earlier.
Eisenberg et al. [22]	Algorithm's appropriate detection of severe sepsis	The final algorithm alerted in 9.0% of encounters with 72% sensitivity, and 91.8% specificity.
Fesnak et al. [23]	Timeliness of sepsis recognition and initial treatment	No difference in timeliness of care initiation in high-risk patients with sepsis.
Lee et al. [24]	Time from triage to antibiotic administration	Time to antibiotics was reduced from 51 to 44 minutes with the digital triage platform.
Scott et al. [25]	Risk of septic shock at hospital arrival	The model had an AUC of 0.79 in the training set, 0.75 in the temporal test set, and 0.87 in the geographic test set.
Eisenberg et al. [26]	Performance and test characteristics of automated sepsis screening	Automated screening had higher sensitivity (84.6%) and specificity (95.1%) than manual screening.
Ehwerhemuepha et al. [27]	Early warning system for sepsis	The model had high AUROCs for death, severe sepsis, non-severe sepsis, and bacteremia.
Sepanski et al. [28]	Predictive tool for electronic alert systems to identify potential sepsis	The tool had 77% sensitivity for identifying gold standard sepsis and 22.5% PPV for high SOI outcomes.

continuous automated alert system with 72% sensitivity, 91.8% specificity, 8.1% PPV, and 99.7% NPV. Fesnak et al. [23] found no significant difference in the timeliness of care initiation in high-risk patients with sepsis. Lee et al. [24] reduced the time from triage to antibiotic administration from 51 to 44 minutes with their digital triage platform. Scott et al. [25] derived and validated a model with an AUC of 0.79 in the training set, 0.75 in the temporal test set, and 0.87 in the geographic test set for the risk of septic shock. Eisenberg et al. [26] observed higher sensitivity (84.6%) and specificity (95.1%) for their automated sepsis abstract screening compared to manual screening. Ehwerhemuepha et al. [27] developed a predictive model with high AUROCs for death, severe sepsis, non-severe sepsis, and bacteremia. Finally, Sepanski et al. [28] introduced a predictive tool with 77% sensitivity for identifying gold standard sepsis and 22.5% PPV for high SOI outcomes. In terms of sensitivity, the highest performers included the automated triage tool developed by Balamuth et al. [19] and the automated sepsis abstract screening tool from Eisenberg et al. [26], both achieving sensitivities of 86.2% and 84.6%, respectively. These tools demonstrated a remarkable ability to identify potential cases of pediatric sepsis, offering a valuable edge in early detection. For specificity, the computerized BPA triage system designed by Cruz et al. [17] and the routine electronic health record data-based model by Scott et al. [25] stood out with specificities of 89% and 48%, respectively. While the BPA system showcased high specificity, Scott et al.'s [25] model achieved balanced accuracy, emphasizing the importance of specificity in avoiding false positives. Considering PPV, the electronic sepsis alert developed by Balamuth et al. [19] led with a PPV of 25.4%, indicating its efficacy in predicting severe outcomes. Additionally, Sepanski et al.'s [18] screening tool demonstrated an improved PPV of 48.7%, emphasizing its ability to reliably predict pediatric severe sepsis. The NPV is a crucial metric, particularly in ruling out cases [18]. Eisenberg et al.'s [22] continuous automated alert system achieved an outstanding NPV of 99.7%, showcasing its robustness in correctly identifying non-septic cases [22]. The BPA-automated sensitive triage tool by Cruz et al. [17] also exhibited a high NPV of 99.9% (Table 3).

Discussion

The exploration of various rapid pediatric sepsis screening tools across the studies has provided valuable insights into their effectiveness, emphasizing the multifaceted nature of early detection strategies in pediatric populations. The diverse array of tools, each with its unique approach and parameters, has contributed to the growing body of knowledge surrounding pediatric sepsis detection.

Variability in sensitivity and specificity

The studies presented a notable range in sensitivity and specificity, crucial metrics in evaluating the performance of sepsis screening tools. Balamuth et al. and Eisenberg et al. [19,26] emerged as top performers, and showcased sensitivities of 86.2% and 84.6%, respectively. Balamuth et al. [19] employed an electronic sepsis alert system that included specific criteria such as elevated pulse rate or hypotension, concern for infection, abnormal capillary refill, abnormal mental status, or high-risk condition [19]. This comprehensive set of parameters allowed for sensitive identification of potential pediatric sepsis cases, enabling early detection and intervention. Similarly, Eisenberg et al. [26] implemented an automated sepsis abstract screening tool in their study, which outperformed manual screening with higher sensitivity and specificity. The tool's capacity to accurately detect cases of sepsis contributed to its commendable performance.

On the contrary, Cruz et al. and Scott et al. [17,25] highlighted the significance of specificity in their studies, with specificities of 89% and 48%, respectively. Cruz et al. [17] utilized a computerized BPA triage system in their approach, focusing on corrected heart rate for temperature and alarming on tachycardia as activation criteria. The emphasis on specific vital sign parameters contributed to the tool's high specificity, ensuring a reduced likelihood of false positives. Scott et al. [25], in their routine electronic health record data-based model, also prioritized specificity with an emphasis on routine data parameters [25]. However, the lower specificity observed in Scott et al.'s [25] model might suggest a trade-off with sensitivity.

The success of Balamuth et al.'s [19] electronic sepsis alert and Eisenberg et al.'s [26] automated sepsis abstract screening tool could be attributed to the inclusivity of various clinical parameters, allowing for a more comprehensive evaluation of sepsis risk. The consideration of multiple clinical indicators, such as vital signs, infection concerns, and high-risk conditions, likely contributed to the tools' ability to accurately identify cases of pediatric sepsis [7,29-31]. In contrast, Cruz et al.'s [17] BPA triage system and Scott et al.'s [25] routine electronic health record data-based model, while achieving high specificity, might have employed more specific activation criteria, potentially leading to a trade-off with sensitivity. The stringent focus on particular parameters might have limited the tools' ability to capture all instances of sepsis, especially in cases where atypical presentations occur [32,33].

These findings emphasize the delicate balance between sensitivity and specificity in the design of sepsis screening tools. The choice of parameters and activation criteria significantly influences a tool's performance, and it is crucial to tailor these criteria based on the specific objectives and characteristics of the target population. The consideration of various clinical indicators in the tools used by Balamuth et al. and Eisenberg et al. [19,26] exemplifies a holistic approach that could be more suitable for the diverse and dynamic nature of pediatric sepsis presentations. Future developments in sepsis screening tools should carefully weigh the trade-offs between sensitivity and specificity, aiming for a balanced approach that maximizes early detection without compromising accuracy.

Positive predictive value and negative predictive value

PPV and NPV play pivotal roles in understanding the predictive capabilities of screening tools [34]. Balamuth et al. [19] presented a noteworthy PPV of 25.4%, indicating its efficacy in predicting severe outcomes. Additionally, Sepanski et al.'s [18] screening tool exhibited an improved PPV of 48.7%, underlining its reliability in predicting pediatric severe sepsis. Eisenberg et al.'s [22] continuous automated alert system achieved an outstanding NPV of 99.7%, showcasing its robustness in correctly identifying non-septic cases. The high NPV is particularly crucial in ruling out cases and preventing unnecessary interventions [35,36].

Impact on timeliness of care

Time is of the essence in pediatric sepsis, and several studies assessed the impact of screening tools on the timeliness of care initiation [29,37,38]. Cruz et al. [16] observed a significant decrease in median time from triage to the first bolus and antibiotics post-protocol initiation. However, Fesnak et al. [23] found no significant difference in the timeliness of care initiation in high-risk patients with sepsis, indicating that not all screening tools might result in a notable improvement in time to treatment initiation. Lee et al. [24] demonstrated a reduction in the time from triage to antibiotic administration from 51 to 44 minutes with their digital triage platform, highlighting the potential of technological interventions in enhancing timely care.

Model derivation and validation

Scott et al. [25] and Ehwerhemuepha et al. [27] focused on deriving and validating predictive models for sepsis risk assessment. Scott et al.'s [25] model exhibited AUCs of 0.79, 0.75, and 0.87 in the training set, temporal test set, and geographic test set, respectively, providing a reliable risk assessment for the likelihood of septic shock. Ehwerhemuepha et al.'s [27] model demonstrated a high AUROCs for death, severe sepsis, non-severe sepsis, and bacteremia, offering a comprehensive early warning system. These models hold promise for enhancing risk prediction and early intervention.

Integration of EHR and automation

The integration of EHR and automation in screening tools, as seen in studies by Cruz et al. [16], Lloyd et al. [21], Eisenberg et al. [22], and Eisenberg et al. [26], showcased advancements in leveraging technology for efficient and accurate detection. Automation, as demonstrated by Eisenberg et al. [22], with a continuous automated alert system, revealed a balance in sensitivity and specificity, emphasizing the potential of automated approaches in enhancing the accuracy and efficiency of sepsis screening.

Despite the advancements presented in these studies, it is essential to acknowledge certain limitations. Sample sizes varied across studies, and some did not provide specific sample details, potentially impacting the generalizability of the findings. Additionally, the retrospective nature of some studies might introduce biases or limitations in data collection. Future research should focus on larger, diverse populations and prospective designs to enhance the robustness of the findings. Furthermore, external validation of predictive models in different healthcare settings would contribute to their generalizability.

Conclusion

The studies collectively underscore the progress in developing and evaluating rapid pediatric sepsis screening tools. The variability in sensitivity, specificity, PPV, and NPV among different tools highlights the need for a tailored approach based on the specific healthcare setting and population. The integration of technology, predictive modeling, and automated alerts holds promise for improving early detection and timely intervention in pediatric sepsis. As advancements continue, ongoing research and collaboration are imperative to refine existing tools and develop new strategies, ultimately enhancing outcomes for pediatric patients at risk of sepsis.

List of Abbreviations

AUC	Area under the curve
AUROCs	Area under the receiver operating characteristic curves
BPA	Best-practice alert
ED	Emergency department
EHR	Electronic health records
NPV	Negative predictive value
PPV	Positive predictive value
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SOI	Severity of illness

Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.

Funding

None.

Consent to participate

Not required.

Ethical approval

Not required.

Author details

Amjad Abdulrahman Almayouf[1], Mohammed Abdulrahman Aleid[2], Abdullah Mohammed Alshushan[3], Amro Abdullah Alsultan[4]

1. Consultant, Pediatric Emergency, Maternity and Children Hospital, Buraidah, Saudi Arabia
2. Resident, Pediatric Emergency, Maternity and Children Hospital, Buraidah, Saudi Arabia
3. Fellow, Pediatric Emergency, Maternity and Children Hospital, Buraidah, Saudi Arabia

References

1. Randolph AG, McCulloh RJ. Pediatric sepsis. Virulence. 2014;5(1):179–89. https://doi.org/10.4161/viru.27045
2. O'Reilly HD, Menon K. Sepsis in paediatrics. BJA Educ. 2021;21(2):51–8. https://doi.org/10.1016/j.bjae.2020.09.004
3. Harley A, Schlapbach LJ, Johnston ANB, Massey D. Challenges in the recognition and management of paediatric sepsis - The journey. Australas Emerg Care. 2022;25(1):23–9. https://doi.org/10.1016/j.auec.2021.03.006
4. Vonrosenstiel N, Vonrosenstiel I, Adam D. Management of sepsis and septic shock in infants and children. Pediatr Drugs. 2001;3(1):9–27. https://doi.org/10.2165/00128072-200103010-00002
5. Wheeler DS, Wong HR, Zingarelli B. Pediatric Sepsis–Part I:"Children are not small adults!". Open Inflamm J. 2011;4(1):4–15. https://doi.org/10.2174/1875041901104010004
6. Hotchkiss RS, Moldawer LL, Opal SM, Reinhart K, Turnbull IR, Vincent J-L. Sepsis and septic shock. Nat Rev Dis Primers. 2016;2(1):16045. https://doi.org/10.1038/nrdp.2016.45
7. Miranda M, Nadel S. Pediatric Sepsis: a summary of current definitions and management recommendations. Curr Pediatr Rep. 2023;11(2):29–39. https://doi.org/10.1007/s40124-023-00286-3
8. Peshimam N, Nadel S. Sepsis in children: state-of-the-art treatment. Therap Adv Infect Dis. 2021;8:204993612110553. https://doi.org/10.1177/20499361211055332
9. Ebrahim GJ. Sepsis, septic shock, and the systemic inflammatory response syndrome. J Trop Pediatr. 2011;57(2):77–9. https://doi.org/10.1093/tropej/fmr022
10. Caraballo C, Jaimes F. Organ dysfunction in sepsis: an ominous trajectory from infection to death. Yale J Biol Med. 2019;92(4):629–40. http://www.ncbi.nlm.nih.gov/pubmed/31866778
11. Silva E, Passos RDH, Ferri MB, de Figueiredo LFP. Sepsis: from bench to bedside. Clinics. 2008;63(1):109–20. https://doi.org/10.1590/S1807-59322008000100019
12. Nijman RG, Jorgensen R, Levin M, Herberg J, Maconochie IK. Management of children with fever at risk for pediatric sepsis: a prospective study in pediatric emergency care. Front Pediatr. 2020;8:548154. https://doi.org/10.3389/fped.2020.548154
13. Kawasaki T. Update on pediatric sepsis: a review. J Inten Care. 2017;5(1):47. https://doi.org/10.1186/s40560-017-0240-1
14. Miranda M, Nadel S. Septic shock: early rapid recognition and ongoing management. Pediatr Child Health (Oxford). 2023;33(5):134–43. https://doi.org/10.1016/j.paed.2023.02.003
15. de Souza D, Machado F. Epidemiology of pediatric septic shock. J Pediatr Inten Care. 2019;08(01):003–10. https://doi.org/10.1055/s-0038-1676634
16. Cruz AT, Perry AM, Williams EA, Graf JM, Wuestner ER, Patel B. Implementation of goal-directed therapy for children with suspected sepsis in the emergency department. Pediatrics. 2011;127(3):e758–66. https://doi.org/10.1542/peds.2010-2895
17. Cruz AT, Williams EA, Graf JM. Test characteristics of an automated age- and temperature-adjusted tachycardia alert in pediatric septic shock. Pediatr Emerg Care. 2012;28(9):889–94. https://doi.org/10.1097/PEC.0b013e318267a78a
18. Sepanski RJ, Godambe SA, Mangum CD, Bovat CS, Zaritsky AL, Shah SH. Designing a pediatric severe sepsis screening tool. Front Pediatr. 2014;2:56. https://doi.org/10.3389/fped.2014.00056
19. Balamuth F, Alpern ER, Abbadessa MK. Improving recognition of pediatric severe sepsis in the emergency department: contributions of a vital sign–based electronic alert and bedside clinician identification. Ann Emerg

Med. 2017;70(6):759–68.e2. https://doi.org/10.1016/j.annemergmed.2017.03.019

20. Balamuth F, Alpern ER, Grundmeier RW. Comparison of two sepsis recognition methods in a pediatric emergency department. Acad Emerg Med. 2015;22(11):1298–306. https://doi.org/10.1111/acem.12814
21. Lloyd J, Ahrens E, Clark D, Dachenhaus T, Nuss K. Automating a manual sepsis screening tool in a pediatric emergency department. Appl Clin Inform. 2018;09(04):803–8. https://doi.org/10.1055/s-0038-1675211
22. Eisenberg M, Madden K, Christianson JR, Melendez E, Harper MB. Performance of an automated screening algorithm for early detection of pediatric severe sepsis*. Pediatr Crit Care Med. 2019;20(12):e516–23. https://doi.org/10.1097/PCC.0000000000002101
23. Fesnak S, Abbadessa MK, Hayes K. Sepsis in complex patients in the emergency department. Pediatr Emerg Care. 2020;36(2):63–5. https://doi.org/10.1097/PEC.0000000000002038
24. Lee V, Dunsmuir D, Businge S. Evaluation of a digital triage platform in Uganda: a quality improvement initiative to reduce the time to antibiotic administration. PLoS One. 2020;15(10):e0240092. https://doi.org/10.1371/journal.pone.0240092
25. Scott HF, Colborn KL, Sevick CJ. Development and validation of a predictive model of the risk of pediatric septic shock using data known at the time of hospital arrival. J Pediatr. 2020;217:145–51. https://doi.org/10.1016/j.jpeds.2019.09.079
26. Eisenberg M, Freiman E, Capraro A, Madden K, Monuteaux MC, Hudgins J, et al. Comparison of manual and automated sepsis screening tools in a pediatric emergency department. Pediatrics. 2021;147(2):e2020022590. https://doi.org/10.1542/peds.2020-022590
27. Ehwerhemuepha L, Heyming T, Marano R. Development and validation of an early warning tool for sepsis and decompensation in children during emergency department triage. Sci Rep. 2021;11(1):8578. https://doi.org/10.1038/s41598-021-87595-z
28. Sepanski RJ, Zaritsky AL, Godambe SA. Identifying children at high risk for infection-related decompensation using a predictive emergency department-based electronic assessment tool. Diagnosis. 2021;8(4):458–68. https://doi.org/10.1515/dx-2020-0030
29. Cruz AT, Lane RD, Balamuth F. Updates on pediatric sepsis. J Am Coll Emerg Phys Open. 2020;1(5):981–93. https://doi.org/10.1002/emp2.12173
30. Oruganti S, Evans J, Cromarty T, Javaid A, Roland D. Identification of sepsis in paediatric emergency departments: a scoping review. Acta Paediatr. 2022;111(12):2262–77. https://doi.org/10.1111/apa.16536
31. Umberger R, Indranoi C, Simpson M, Jensen R, Shamiyeh J, Yende S. Enhanced screening and research data collection via automated EHR data capture and early identification of sepsis. SAGE Open Nurs. 2019;5:237796081985097. https://doi.org/10.1177/2377960819850972
32. Duncan CF, Youngstein T, Kirrane MD, Lonsdale DO. Diagnostic challenges in sepsis. Curr Infect Dis Rep. 2021;23(12):22. https://doi.org/10.1007/s11908-021-00765-y
33. De Oliveira H, Prodel M, Lamarsalle L. “Bow-tie” optimal pathway discovery analysis of sepsis hospital admissions using the Hospital Episode Statistics database in England. JAMIA Open. 2020;3(3):439–48. https://doi.org/10.1093/jamiaopen/ooaa039
34. Steinberg DM, Fine J, Chappell R. Sample size for positive and negative predictive value in diagnostic research using case–control designs. Biostatistics. 2009;10(1):94–105. https://doi.org/10.1093/biostatistics/kxn018
35. Trevethan R. Sensitivity, specificity, and predictive values: foundations, pliabilities, and pitfalls in research and practice. Front Public Health. 2017;5:307. https://doi.org/10.3389/fpubh.2017.00307
36. Loh TP, Lord SJ, Bell K. Setting minimum clinical performance specifications for tests based on disease prevalence and minimum acceptable positive and negative predictive values: practical considerations applied to COVID-19 testing. Clin Biochem. 2021;88:18–22. https://doi.org/10.1016/j.clinbiochem.2020.11.003
37. Eisenberg MA, Balamuth F. Pediatric sepsis screening in US hospitals. Pediatr Res. 2022;91(2):351–8. https://doi.org/10.1038/s41390-021-01708-y
38. Sever Z, Schlapbach LJ, Gilholm P, Jessup M, Phillips N, George S, et al. Impact of parental and healthcare professional concern on the diagnosis of pediatric sepsis: a diagnostic accuracy study. Front Pediatr. 2023;11:1140121. https://doi.org/10.3389/fped.2023.1140121