ATATÜRK ÜNİVERSİTESİ YAYINLARI
ATATURK UNIVERSITY PUBLICATIONS

Systematic Review *Sistematik Derleme* DOI: 10.17049/jnursology.1524051

Automated Alerts Systems for Pediatric Sepsis Patients: A Systematic Review

Pediatrik Sepsis Hastaları için Otomatik Uyarı Sistemleri: Sistematik Bir Derleme

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ABSTRACT

Objective: Pediatric sepsis is difficult to identify due to subtle symptoms, and early aggressive management is crucial to prevent septic shock. Artificial intelligence can improve sepsis detection by triggering alerts based on patient data. No systematic review has yet discussed AI use for pediatric sepsis screening. This study aims to answer: "What tools alert healthcare providers to the onset of sepsis in pediatric patients in hospitals?"

Methods: The study protocol was registered with PROSPERO (CRD42023467930). We searched PubMed, ProQuest, ScienceDirect, Scopus, and EBSCO, focusing on pediatric hospital settings using tools for early sepsis detection, excluding studies on non-sepsis patients, and limiting inclusion to English literature reviews without a publication year restriction. The Joanna Briggs Institute (JBI) Appraisal Tool evaluated study quality, and findings were synthesized qualitatively.

Results: Out of 16 articles, four tools for automatic sepsis alerts in pediatrics were identified: Electronic Medical Records (EMR), Electronic Health Records (EHR), The Electronic Alert System (EAS), and The Newborn Cry Diagnostic System (NCDS). EHR is the most commonly used. These tools require various data, such as vital signs, lab results, skin condition, capillary refill, and even a baby's cry.

Conclusion: Automated sepsis alerts in pediatrics enhance diagnostic accuracy, expedite decision-making, and decrease sepsis-related mortality. Limitations include language restrictions and the inability to assess each tool's effectiveness or identify the optimal sepsis detection algorithm, underscoring the need for further research, including a meta-analysis.

Keywords: Pediatrics, sepsis, artificial intelligence.

ÖZ

Amaç: Pediatrik sepsis, belirtilerinin belirsizliği nedeniyle tanınması zor bir durumdur ve septik şoku önlemek için erken ve yoğun tedavi hayati önem taşır. Yapay zeka, hasta verilerine dayanarak uyarılar oluşturarak sepsis tespitini iyileştirebilir. Ancak, pediatrik sepsis taramasında yapay zeka kullanımını ele alan sistematik bir inceleme bulunmamaktadır. Bu çalışmanın araştırma sorusu: "Hastane ortamında pediatrik hastalarda sepsisin başlangıcını sağlık çalışanlarına bildirmek için hangi araçlar kullanılmaktadır?"

Yöntemler: Çalışma protokolü, PROSPERO numarası CRD42023467930 ile kaydedilmiştir. PubMed, ProQuest, ScienceDirect, Scopus ve EBSCO veritabanlarında, pediatrik hastane ortamında sepsisin erken tespiti için kullanılan araçlara odaklanarak arama yapılmıştır. Sepsis gelişmeyen hastaları içeren çalışmalar hariç tutulmuş, yalnızca İngilizce derleme makaleler dahil edilmiştir. Çalışma kalitesi, Joanna Briggs Institute (JBI) Değerlendirme Aracı ile değerlendirilmiş ve bulgular niteliksel olarak sentezlenmiştir.

Bulgular: Toplam 16 makaleden, pediatrik sepsis için otomatik uyarı sağlayabilecek 4 araç belirlenmiştir: Elektronik Tıbbi Kayıtlar (EMR), Elektronik Sağlık Kayıtları (EHR), Elektronik Uyarı Sistemi (EAS) ve Yenidoğan Ağlama Teşhis Sistemi (NCDS). En sık kullanılan araç EHR'dir. Bu sistemler, hayati belirtiler, laboratuvar sonuçları, cilt durumu ve bebeğin ağlaması gibi çeşitli verilere ihtiyaç duyar.

Sonuç: Otomatik uyarı sistemleri, tanı doğruluğunu artırır, karar verme sürecini hızlandırır ve çocuklarda sepsisle ilişkili ölüm oranlarını azaltır. Dil sınırlamaları ve araçların etkinliğini değerlendirme konusundaki yetersizlikler, daha fazla araştırmaya ihtiyaç olduğunu göstermektedir.

Anahtar Kelimeler: Pediatri, sepsis, yapay zeka.

Geliş Tarihi/Received	29.07.2024
Revizyon Talebi/Revision Requested	22.10.2024
Son Revizyon/Last Revision	23.11.2024
Kabul Tarihi/Accepted	16.12.2024
Yayın Tarihi/Publication Date	13.03.2025

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Cite this article: Dewi DDSA, Suprihatiningsih S, Soselisa AH, Cealy FR, Nuha MU, Sandi NC, Royani T, Pertiwi AAP, Masdar M. Automated Alerts Systems for Pediatric Sepsis Patients: A Systematic Review. *J Nursology*. 2025;28(2):206-214. doi: 10.17049/jnursology.1524051

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INTRODUCTION

Lately, clinical and health research has found that sepsis has remained the key cause of pediatric mortality in hospitals.[1] Sepsis can be defined as a systemic infection associated with some organ dysfunction, caused by a dysregulated host response to the infection.[2,3] In general, the fundamental difference in the condition of pediatrics sepsis lies in the difficulty of recognition or signs of symptoms.[4] Globally, sepsis causes mortality and morbidity in pediatrics or children, with around 22 cases of pediatric sepsis per 100,000 person-years and around 1.3 million cases of neonatal sepsis per 100,000 live births per year.[5,6] Recent studies found that in developed countries, the pediatric mortality caused by sepsis is up to 50%, whereas in high-income countries, 3–7% of pediatrics with sepsis die, with mortality rates increasing up to 20% in the Pediatric Intensive Care Unit (PICU).[7]

Sepsis conditions should be threatened by aggressive management to improve outcomes and prevent sepsis shock.[8] Unfortunately, until now the treatment of sepsis in children is still based on guidelines for the treatment of sepsis in adults.[9] This complex condition in pediatrics can be reduced by early diagnosis and timely intervention with antibiotics, vasoactive medications, and resuscitation.[10] Early diagnosis of sepsis in pediatrics has been studied. Alerts based on clinical physiologic data embedded in an electronic health record system have been studied as potential methods to facilitate sepsis recognition in pediatrics.[11] Artificial intelligence can be included to potentially activate the sepsis alert based on the patient's data on the Electronic Health Records (EHR).[12] Besides that, any tools and machine learning can also be the tools for sepsis alert used for pediatrics in hospitals.[13,14]

AIM

This systematic review is used to learn about any tools used to alert to sepsis conditions in pediatrics in the hospital setting. We will see the data used for automated alert systems in the hospital to diagnose sepsis in pediatric patients accurately, support sepsis treatment and management, and analyze patient outcomes after the tools were used.

METHODS

Type of Study

The type of this study is a systematic review using PRISMA Guidelines.[15] Figure 1 shows the PRISMA flow diagram of the study. We used PICO's (patient, intervention, comparison, outcome) framework to clearly define the research question of this study with population (pediatrics with sepsis), Intervention (artificial intelligence), Comparison (none), and Outcome (decision support systems). The study protocol was registered in PROSPERO with the number CRD42023467930.

Search Strategies

We searched PubMed, ProQuest, ScienceDirect, Scopus, and EBSCO on December 02, 2024, with no time restriction. We comprehensively searched the database to identify informatics tools used for early sepsis detection in pediatrics. We searched using keywords that were developed based on our questions with the MeSH Term (pediatrics) AND (early diagnosis OR early warning score OR decision support systems, clinical OR machine learning OR artificial intelligence) AND (sepsis OR neonatal sepsis), the search strategies can be seen in the supplementary data 1. We exported all identified records to the Rayyan.ai program, which was used to screen the articles and determine which studies to include or exclude in the review. We also conducted hand searches in Google Scholar by reviewing related references from articles that met the inclusion criteria, using the same keywords, with the last update on May 19, 2024.

Eligibility Criteria

In this review, the inclusion criteria of the studies were: (1) pediatric only populations (< 18 years old), male and female, (2) Neonatal Intensive Care Unit (NICU), PICU, or emergency setting, (3) tools to detect sepsis or screening or early warning, (4) Patients with undetected sepsis, protocols, reviews, ongoing clinical trials, meta-analyses, conference posters or proceedings, and letters to the editor were all excluded. (5) Only full-text articles with English language.

Data Extraction

Seven authors (DDSAD, S, TR, MUN, NCS, FRC, AHS) were independent reviewers and did screening with Rayyan.ai data management. All the included studies were extracted to sheets individually by AHS, S, DDSAD, FRC, NCS. A formal discussion was conducted to discuss the different perspectives on the data collection and extraction done by the reviewer. The extracted final data of the study were (author's name, year of publication, title, country, study methods, unit/department, tools, data screening, result, and quality assessment). Table 1 summarizes the 16 studies that use and compare the effectiveness of manual and electronic sepsis alerts in pediatrics.

Quality Assessment

After the included study was agreed upon by all authors, two primary reviewers (NCS, MM and TR) used the

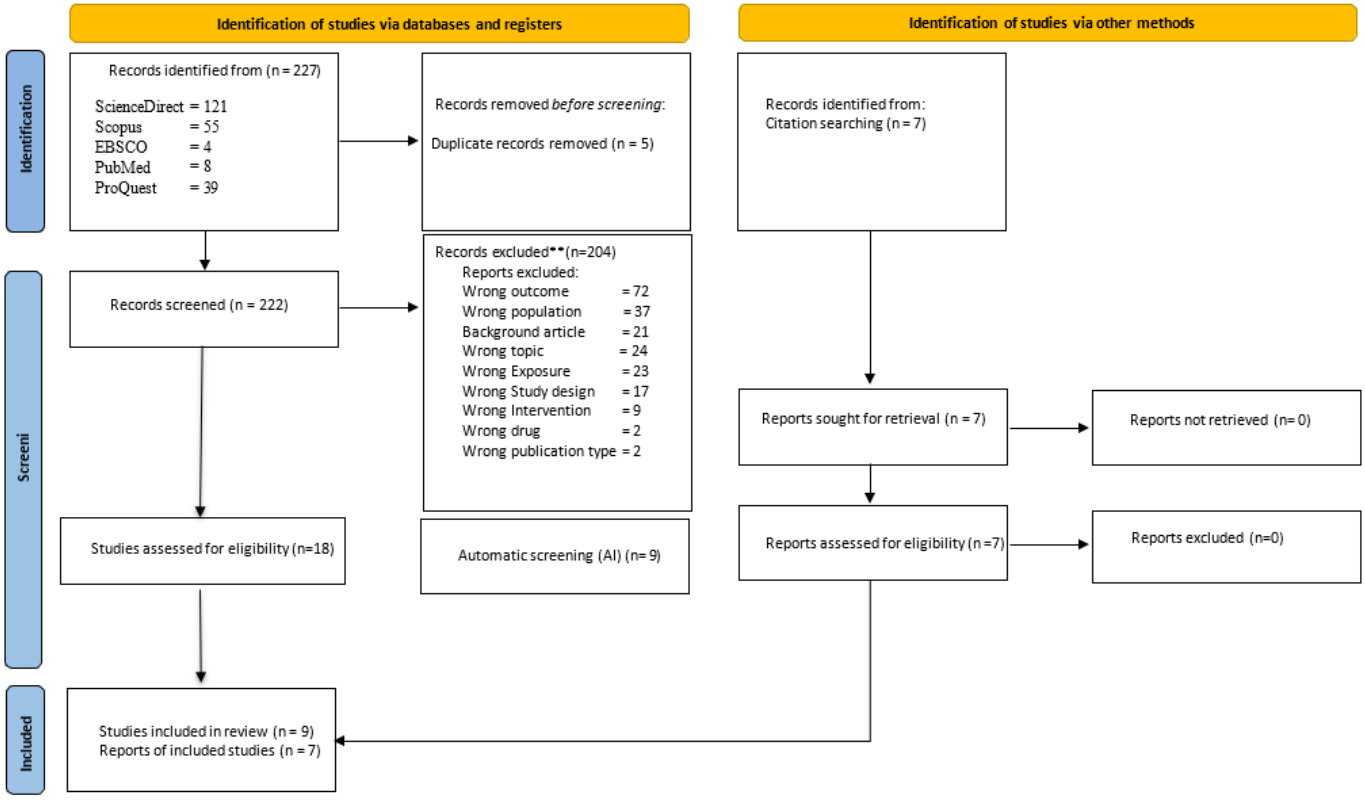

Figure 1. PRISMA Flow Diagram

methodological quality assessment using Joanna Briggs Institute (JBI) for 14 cohort studies and two quasi-experimental. The critical appraisal tools provided by JBI aid in evaluating the reliability, applicability, and outcome of published studies. Two primary reviewers (NCS and TR) independently scored each of the cohort and experimental studies, obtaining a final decision to include the study. Differences between analysts were settled by other commentators (AHS, S, DDSAD, FRC, NCS, AAPP, MM), and the outcomes were reached through mutual agreement. Based on the assessment results, articles included in this study must meet the minimum standards for article assessment more than 50%.

RESULTS

Study Quality

Based on the results of the article quality analysis, 10 articles were very good and met all points in the quality assessment tools with JBI. One article was 91% complete, two article were 82% complete, one article was 73% complete, one article was 64% complete, and one article was 54% complete. Data on quality appraisal is included and can be seen in Table 1.

Characteristics of Included Studies

Early detection of sepsis is significant for handling sepsis, mainly in severe sepsis. Since 2014, according to the article we found, efforts have been made to detect early severe sepsis in children. The use of EHR, Electronic Medical Records (EMR), Electronic Alert System (EAS), and Newborn Cry Diagnostic System (NCDS), based on the journals we found above, is used in countries that have advanced technology such as the United States of America (USA) and the states of the USA. The average number of samples using the EHR was 1,214 participants, the average using the EMR instrument was 44,579 participants, the EAS was 48,197 participants, and the NCDS was 53 participants (Table 1).

Use of EHR for Sepsis Detection in Pediatric

EHR is More Effective

In seven articles that use EHR with automated screening tools, the focus of these studies is comparing automatic and manual screening tools, automatic screening tools are faster,[16–21] more accurate,[17,19,20] more just accurate[16] and more thoroughly, specificity 91.8%, sensitivity 72%[22], so it is more effective. By detecting sepsis more quickly in children, sepsis control can be carried out more quickly, so that septic shock can be prevented.

EHR is More Comprehensive

Apart from being more effective, this automatic screening tool from the HER can be used in both the

Table 1. Overview Characteristics of Included Study

No	Author's name Year	Country	Study methods	Unit	Tools	Data Screening	Result	Quality Assessment
1	Lloyd et al.[16], 2018	United State of America	Cohort Study	ED	EHR	Tachycardia, Tachypnea, Temperature abnormality, Skin abnormality, Capillary refill abnormality, High-risk condition, Concern for infection/ temperature abnormality, Hypotension, Pulse abnormality	As accurate as manual screening Identifies 68 minutes faster than manual	91%
2	Eisenberg et al.[18], 2021a	United State of America	Cohort Study	ICU & ED	EHR	Temperature, white blood cells, heart rate, respiratory rate	Detect sepsis with greater accuracy Identify sepsis 59 minutes faster than manual	100%
3	Depinet et al.[21], 2022	United State of America	Cohort Study	ICU & ED	EHR	Fever/ hipotermia, hypertension, Tachycardia, Tachypnea, skin turgor, mental status, pulse, skin	Rate of administration of antibiotics for 60 minutes (47% fulfilled 50% fulfilled)	100%
4	Le et al.[19], 2019	United State of America	Retrospective Cohort Study	ICU & ED	EHR	Age, blood pressure, heart rate, oxygen saturation, Glasgow Coma Scale (GCS) status, white blood cells.	Can recognize sepsis early and more accurately	100%
5	Dewan et al.[20], 2020	United State of America	A prospective cohort study	PICU	EHR	Body temperature, blood test	Faster and more precise sepsis screening	73%
6	Eisenberg, et al.[22], 2019	United State of America	Retrospective cohort study	ICU & ED	EHR	Vital signs (body temperature, heart race, respiratory rate)	Can detect sepsis more quickly and accurately (91.8% specificity and 72% sensitivity)	54%
7	Eisenberg et al.[17], 2021b	United State of America	Retrospective cohort study	Pediatric ED	Automated Sepsis Screening Tools	Body temperature, leucocyte count, heart rate, respiratory rate, cardiac dysfunction, one or more organ dysfunction	The tool can detect sepsis more quickly and thoroughly (sensitivity increased from 64% to 84.6%)	100%
8	Tabaie et al.[13], 2021	United States of America	Retrospective Cohort Study	Inpatient	EMR	Blood test	Can predict the onset of sepsis in children with a central venous line 8 hours before the clinical team takes blood cultures.	100%
9	Sepanski et al.[23], 2014	United States of America	Retrospective Cohort Study	ICU & ED	EMR	Blood test and vital signs	The average time for application of the screening tool before revision took 10.3 (before revision) and 11.1 hours (after revision).	100%
10	Stinson et al.[25], 2019	United State of America	Retrospective Cohort Study	Inpatient & ED	EMR	Vital sign, capillary refill, mental status and abnormalities of pulses and skin condition	Implementation of an EMR-based sepsis recognition tool resulted in a diagnostic or therapeutic intervention with a management time of 24.4 minutes.	82%

Table 1. Overview Characteristics of Included Study (Continued)

No	Author's name Year	Country	Study methods	Unit	Tools	Data Screening	Result	Quality Assessment
11	Xiang et al.[24], 2021	China	A single center retrospective study	Hospital	EMR	Vital signs and blood test and laboratory data (c-reactive, protein level, and neutrophil count)	Existing tools for detecting septic shock are Extreme Gradient Boosting (XGBoost), Septic shock early warning (SSEW), and pediatric Sequential Organ Failure Score (pSofa). AI-SSEW has proven to be more effective and accurate in detecting septic shock in children.	100%
12	Balamuth et al.[11], 2017	United State of America	Cohort Prospective Study	ED	Electronic Alert Improves Pediatric Sepsis Recognition	Tachycardia or hypotension, fever or hypothermia or risk for infection.	Electronic sepsis alert implementation increased ED sepsis detection from 83% to 96%	100%
13	Kamaleswaran et al.[12], 2018	United State of America	Observational cohort study	PICU	Electronic Screening Algorithm Alert	Pulse, oxygen saturation (SpO2) and blood pressure (systole and diastole)	Effectively detect severe sepsis 8 hours faster than an algorithm using real-time electronic screening.	82%
14	Gibbs et al.[26], 2021	United State of America	Experiment Study	Hospital	Electronic sepsis alerts	Temperature, blood pressure, respiratory, pulse, capillary refill, skin appearance, high of consciousness, high risk condition, fluid bolus	There was a decrease in the sepsis mortality rate in children after implementing the use of Electronic Sepsis Alert, namely at 3 days 2.53 compared to 0% and 30 days 3.8 compared to 1.3%.	100%
15	Alturki et al.[27], 2022	Saudi Arabia.	Retrospective cohort study	PICU	EAS	Vital sign, initial laboratory values, time to start antibiotics, need for inotropic support and laboratory result	Application of EAS sepsis can detect sepsis. The median time to receive antibiotics from EAS triggers was shorter at 39 minutes (23%).	64%
16	Matikolaie & Tadj[14], 2022	Canada	Experiment study	Hospital	NCDS	Identify sick infants from healthy ones includes cleft palate, hearing disorder, hyperbilirubinemia, autism, asphyxia, hypothyroidism, and respiratory distress Identify the reason the baby cry, mother's gestational age, baby's weight, Apgar score, gender, baby's age, type of disease.	Using Support Vector Machine (SVM), which counteracts the baby's crying signal called Cry Audio Signal (CAS). The best F-score value with 86% on expiratory data. Quadratic discriminant produces the best F Score with 83.90% for inspiration.	100%

EAS; Electronic Alert System, ED; Emergency Department, EHR; Electronic Health Record, EMR; Electronic Medical Record, ICU; Intensive Care Unit, NCDS; Newborn Cry Diagnostic System PICU; Pediatric Intensive Care Unit,

Pediatric Emergency Department (PED), Intensive Care Unit (ICU)/ PICU, both special children's hospitals and general hospitals. The dataset included in the EHR is data found after the nurse or doctor has carried out an assessment. The data screened for early detection of sepsis varies from article to article, including tachycardia, tachypnea, temperature abnormality, skin abnormality, capillary refill abnormality, high-risk condition, concern for infection/ temperature abnormality, Hypotension/ hypertension, pulse abnormality, white blood cells, mental status, Age, blood pressure, oxygen saturation, Glasgow Coma Scale (GCS) status and one or more organ dysfunction.

EHR is More Recommended and Widely Used

Of the 16 articles we reviewed, EHRs were most used to facilitate automated screening tools. The dataset in the EHR that is needed to detect early sepsis is general data that is documented based on the results of the nurse/doctor's assessment.

Use of EMR for Sepsis Detection in Pediatric

The results of 4 journals using EMR show that 3 journals use blood culture measurements, with blood tests,[13] with blood tests and vital signs,[23] and blood test and laboratory data (c-reactive, protein level, and neutrophil count)[24] while one journal uses measurements of vital signs, capillary refill, mental status, and abnormalities of pulses, and skin condition[25]. Seven of the four studies, three of them showed the effectiveness of using blood culture in detecting sepsis within a time span of 4 to 24 hours.

Use of EAS for Sepsis Detection in Pediatric

Tachycardia or hypotension, fever or hypothermia or risk for infection.[11] EAS uses pulse, Spo2, blood pressure (systole and diastole).[12] A sepsis score calculated using the parameters vital signs, heart rate, blood pressure, respiratory rate and temperature, skin perfusion characteristics, capillary refill, pulse quality, neurological assessment, and history or presence of high-risk conditions,[26] vital signs at hospital admission, initial laboratory values, start time for antibiotics, need for inotropic support.[27] The results of four journals show that this measurement is effective in detecting sepsis quickly with a sensitivity of more than 80%.

Use of NCDS for Sepsis Detection in Pediatric

The results of the systematic review carried out show that there is a unique variation that is used as a type of non-invasive tool used to detect sepsis. The NCDS uses a Support Vector Machine (SVM), which counteracts the baby's crying signal called the Cry Audio Signal (CAS).[14] This research conducted in Canada used the well-known MFCC (Mel Frequency Cepstral Coefficients) features and prosodic features of slope, rhythm, and intensity including SVM, decision trees, and discriminant analysis. Research conducted before, found that babies suffering from septic disease cried differently compared to healthy babies through this experiment. In an effort to detect sepsis, NCDS also requires other data such as the baby's health condition and the presence of disorders (hearing, respiratory, cleft lip, cleft palate), reasons for the baby's crying, birth weight, APGAR (Appearance, Pulse, Grimace, Activity, Respiration) score, gender, age, type of disease, and age. maternal pregnancy.[14] NCDS has been used successfully in efforts to recognize sepsis only in newborns. However, various difficulties were expressed, such as differences in the rhythm of babies' cries for different needs.[14]

Data Used for Automatic Sepsis Alert

The use of data in sepsis screening for pediatric patients is very dependent on the algorithm used and specified in the selected tools. Various variations are found depending on the tools used.

Data Used for the EHR

Electronic Health Records were developed and used as a sepsis screening tool or for early detection of sepsis in pediatrics. Some of the data used include vital signs such as tachycardia/ heart rate,[16–19,21,22] blood pressure,[16,19,22] tachypnea/ respiratory rate,[16–18,21,22] pulse abnormality,[16,21] Body temperature/ Temperature abnormality,[16–18,20–22] skin/ skin turgor/ skin abnormality,[16,21] capillary refill/ abnormality capillary refill,[16] high risk condition,[16] white blood cells,[17–19] and mental status/ GCS status,[19,21] blood test,[20] and cardiac dysfunction or more organ dysfunction.[18]

Data Used for EMR

Electronic Medical Records were also developed and used as a tool in developing pediatric sepsis screening in hospitals. It has been reported that several data are used to detect the incidence of sepsis in children, including blood tests,[13,23,24] vital signs,[23–25] capillary refill time,[25] mental status,[25] skin condition,[25] blood test and laboratory data.[24]

Data Used for EAS

The Electronic Alert System is a system that was built and developed to become a tool in pediatric sepsis screening, with the data needed, namely vital signs such as pulse,[11,12,26,27] oxygen saturation,[12,27] blood pressure,[12,26,27] temperature,[26,27] respiratory,[26,27] capillary refill time,[26] skin appearance,[26] initial laboratory values such as fluid bolus,[26,27] high of consciousness,[26] needs for inotropic support and laboratory result,[27] time to start antibiotics,[27] and risk for infection.[11]

Data Used for NCDS

The NCDS is a diagnostic system developed by several researchers. The use of Machine Learning to detect newborn babies' cries is called SVM, which counteracts the baby's crying signal called CAS. This tool identifies babies with a cleft palate, hearing disorders, hyperbilirubinemia, autism, asphyxia, hypothyroidism, and respiratory distress. Identify the cause of the baby's crying, namely the mother's gestational age, baby's weight, APGAR score, gender, the baby's age, and type of disease.[14]

DISCUSSION

Impact of Automatic Sepsis Alert

The results of this systematic review have had a very significant impact on reducing the severity of sepsis in pediatrics through early detection of sepsis in children in hospitals in several countries. The positive impact is detecting sepsis earlier,[12,13,16–20,22] being more accurate,[11,12,17–20,22,24,27] carrying out earlier treatment and administering more effective antibiotics to reduce the number of deaths caused by sepsis in pediatrics.[21,26] These results are in line with other systematic reviews that state that the main advantages of using an automatic alerting system in the management of sepsis include reducing the death rate with better sepsis management including faster and more effective administration of antibiotics.[28,29] Good management of sepsis was revealed as one of the advantages of using automatic sepsis alerts which were stated in other studies to be effective in speeding up sepsis detection compared to manual methods.[29,30] In its use, the automatic system alert is very dependent on the type, data used (algorithm) and sensitivity of the tool in optimizing the work of the automatic sepsis alert in detecting sepsis events in hospitals.[31]

This systematic review produces the important point that it turns out that the development of EHRs to increase sepsis screening is more effective and is more widely used in various countries.[16–21] Other research was found in line with these findings, where EHR management was suggested to be better in alerts, governance, alert metrics, initiating alert management programs, evaluating alert systems, and optimizing existing alerts to improve patient care and reduce the burden of vigilance on health workers.[32] The use of EHR in practice can maintain and harmonize the relationship between the environment, human resources, workflow, policies, culture, and others so that its development will increase patient safety.[33,34] Other research was conducted focusing on the use of EHRs in improving patient safety in treatment rooms in general, with the results of the review showing that the use of EHRs is easy to modify as a support system for improving pediatric patient safety.[35]

However, the application of EHR for developing automatic alerts in the clinical realm still has many limitations. A qualitative study shows good and positive adaptation in the use of EHR for health workers, however various improvements and further development of EHR are needed to increase the effectiveness of EHR use to improve patient safety.[34] Literature studies show various limitations of using EHR, including lack of harmony, problems in patient matching, the possibility of algorithm manipulation, increasing the burden on health workers, and still limited data on security and privacy concerns.[36] Developments related to the use of EHR really need to be carried out to determine various set points in automatic alerts.[37]

Limitations of the study

This review has limitations, including the use of language, which is limited to English, and does not look further into the complete effectiveness of using each tool. Another limitation of this research is the inability to conclude an optimal algorithm for determining and detecting sepsis in children, so a meta-analysis needs to be carried out to answer and explain this. We still include the Critical Appraisal results of 55-65%, because this systematic review aims to carry out an in-depth investigation regarding the use of tools to detect sepsis in pediatric patients.

There are four tools developed for automatic sepsis alert for pediatric patients, namely EHR, EMR, EAS, and one study that uses NCDS. Three of the four tools have several indicators in common, namely vital signs such as body temperature, heart rate, blood pressure and breathing. One of the four tools uses a baby's cry as an indicator in detecting sepsis for children.

Etik Komite Onayı: PROSPERO (Date: 09/10/2023, number: CRD42023467930) kaydı yapılmıştır.
Bilgilendirilmiş Onam: Çalışmaya katılan öğrencilerin bilgilendirilmiş yazılı onamları alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Yazar Katkıları: Fikir- DDSAD; Tasarım – DDSAD ve S; Denetleme – AAPP ve MM; Kaynaklar-; Malzemeler – DDSAD, S, AHS, FRC, MUN, NCS, TR; Veri Toplanması ve/veya İşleme – DDSAD, AHS, FRC, MUN, NCS, TR; Analiz ve/veya Yorumlama – DDSAD, S, AHS, FRC; Literatür Taraması- S ve AHS; Makale Yazımı – DDSAD, AAPP, MM; Eleştirel İnceleme- AAPP ve MM.
Teşekkür: Yazarlar Gadjah Mada Üniversitesi Tıp, Halk Sağlığı ve Hemşirelik Fakültesi, Hemşirelik Yüksek Lisans Programı'na ve özellikle Hemşirelik Yüksek Lisans Programı Başkanı Sri Hartini, S.Kep., Ns., M.Kes., Ph.D, için tasarımı sırasında yaptıkları yararlı katkılar için teşekkür eder.
Çıkar Çatışması: Yazarlar, çıkar çatışması olmadığını beyan etmiştir.
Finansal Destek: Yazarlar, bu çalışma için finansal destek almadığını beyan etmiştir.

Ethics Committee Approval: Registered number approval was obtain from PROSPERO (Date: 09/10/2023, number: CRD42023467930)
Informed Consent: Informed written consent was taken from the students participating in the study.
Peer-review: Externally peer-reviewed.
Author Contributions: Concept- DDSAD; Design – DDSAD and S; Supervision – AAPP and MM; Resources-; Materials – DDSAD, S, AHS, FRC, MUN, NCS, TR; Data Collection and/or Processing – DDSAD, AHS, FRC, MUN, NCS, TR; Analysis and/or Interpretation – DDSAD, S, AHS, FRC; Literature Search – S and AHS; Writing Manuscript – DDSAD, AAPP, MM; Critical Review – AAPP and MM.
Acknowledgments: The authors would like to thank to the Master of Nursing Program, Faculty of Medicine, Public Health, and Nursing, Universitas Gadjah Mada and a special thanks goes to Sri Hartini, S.Kep., Ns., M.Kes., Ph.D. as Head of Master of Nursing Study Program, Universitas Gadjah Mada for the useful discussion during protocol design.
Conflict of Interest: The authors have no conflicts of interest to declare.
Financial Disclosure: The authors declared that this study has received no financial support.

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