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Review Article

AI-Driven Predictive Models for Early Detection of Pediatric Sepsis: A Systematic Review and Meta-Analysis

Achsa Sharon Shibu [1], Aadhira J [1], Mitra S [1], Muhammd Marzuq U A [1], Nickson P [1], Dhivya K *[2]

[1] Pharm. D Intern, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, Tamil Nadu, India

[2] Associate Professor, Department of Pharmacy Practice, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, Tamil Nadu, India

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For Correspondence:

Dhivya K, Associate Professor, Department of Pharmacy Practice, C.L. Baid Metha College of Pharmacy, Thoraipakkam, Chennai, Tamil Nadu, India.

Abstract

Background Pediatric sepsis continues to pose a major challenge in healthcare, compounded by delayed diagnosis and treatment resulting in poor outcomes. Artificial intelligence (AI) and machine learning (ML) continue to develop predictive models that can support the early identification of pediatric sepsis and assist with better patient outcomes. **Objective** This systematic review and meta-analysis evaluated AI-driven predictive models for identifying early pediatric sepsis and evaluated diagnostic accuracy, performance metrics, and clinical readiness. **Methods** Following PRISMA guidelines and registered in PROSPERO (CRD420251244587), we searched PubMed, Google Scholar, Cochrane, and Scopus for studies on AI models predicting pediatric sepsis. AUROC (Area Under the Receiver Operating Characteristic Curve) was the major performance metric, along with sensitivity, specificity, and accuracy. For statistical analysis, AUROC values were converted into Cohen's d to measure effect size, and upper and lower confidence intervals were determined. A forest plot was then generated, confirming the AI models' strong predictive performance with statistically significant results. **Results** This review contains 14 studies with a total of 96,764,476 pediatric patients. AI models improved the accuracy and the ease of detecting sepsis [average AUROC = 0.868 (86.8%)]. ML models were accurate for predicting and detecting sepsis, especially when real-time vital signs, laboratory tests and waveform data were analyzed together, which increased specificity and reliability of early detection. **Conclusion** AI models are superior to traditional clinical scoring systems in early detection of pediatric sepsis. Nevertheless, the field needs to overcome challenges with data heterogeneity, model interpretability, and clinical adoption. Future work should prioritize validation outside of the original data set, federated learning, and explanations of AI to improve their usability in clinical practice.

Keywords: Pediatric sepsis, artificial intelligence, machine learning, predictive analytics

INTRODUCTION

Sepsis is a life-threatening condition characterized by organ dysfunction resulting from a dysregulated host response to infection [1]. Sepsis continues to be a significant global health issue in pediatrics, particularly in pediatric intensive care units (PICUs), where it contributes substantially to morbidity and mortality. Early identification is critical; however, healthcare inequality, patient progress, and delays in recognition of septic infection in low- and middle-income countries can lead to worse outcomes [2]. The worldwide prevalence of pediatric sepsis is dependent upon local healthcare infrastructure and socioeconomic status. Children in high- and middle-income countries are more likely to have interventions available, while those in resource-poor settings experience higher rates of sepsis largely because of maternal infections, preterm births, and a lack of infection prevention measures [3].

Neonatal sepsis is still a major contributor to infant mortality and primarily due to perinatal risk factors such as maternal infection, premature birth, and lack of care around the time of birth. The most commonly implicated pathogens in neonatal sepsis involve gram-negative organisms such as Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa and gram-positive organisms such as Staphylococcus aureus and Streptococcus pneumoniae [4]. Recently, viral pathogens responsible for sepsis have emerged as significant contributors of serious illness in patients with conditions such as influenza, Respiratory Syncytial Virus, and Severe Acute Respiratory Syndrome Coronavirus 2 infection, Fungal organisms can also be thought of in patients with sepsis but primarily pose a risk in immunocompromised children or those undergoing chemotherapy or organ transplantation [5].

Recent developments in Artificial intelligence (AI)-based models and biomarker investigations have drastically improved early diagnosis and risk assessment. Machine learning (ML) algorithms incorporated into health records and laboratory data streamline diagnostic accuracy. Emerging biomarkers, such as microRNAs

(miRNAs), presepsin (sCD14-ST), and procalcitonin-to-albumin ratio, show promise in differentiating sepsis from other inflammatory conditions [6,7]. By integrating these biomarkers with AI-based models, further real-time risk assessment improvements are possible. However, AI-based sepsis-prediction models still face challenges. Biomarkers vary between populations, so larger studies are needed to make the results more reliable. Implementation in the clinical workflow comes with challenges, to [8]. Ethical issues such as data privacy, algorithmic bias, and model accessibility also need resolving. AI decision support systems, rapid pathogen identification, and compliance to evidence-based recommendations may provide strategies to optimize antibiotics and improve patient outcomes. Preventive measures such as improved maternal healthcare, screening of neonates for sepsis, and vaccination programs are vital in reducing pediatric sepsis mortality. Vaccination against Streptococcus pneumoniae, Haemophilus influenzae type B and Neisseria meningitidis decreases incidence of bacterial sepsis. Improving infection control protocols in (Neonatal Intensive Care unit) NICUs and PICUs is necessary to minimize hospital-acquired infections and improve sepsis care [9].

AI has revolutionized pediatric sepsis prediction by utilizing ML and deep learning (DL) models to analyze (Electronic health records) EHRs, biomarkers, and vital signs, enabling early intervention before sepsis escalates. These models fall into four primary categories: traditional ML models, deep learning models, hybrid models, and biomarker-integrated models [10]. Traditional ML algorithms like Random Forest (RF), Gradient Boosting Machines (GBM), and Support Vector Machines (SVM) effectively classify sepsis risk based on structured clinical data. Hybrid AI models combine ML and DL techniques to improve prediction accuracy while minimizing false positives. Ensemble learning models, integrating RF, neural networks, and XGBoost, offer enhanced specificity.

Models powered by AI enhance early detection, risk stratification and monitoring of pediatric sepsis. Machine learning models, specifically, artificial neural networks (ANNs) have been shown to outperform traditional approaches such as support vector machines (SVM) and logistic regression (LR), while producing very high accuracy levels. Predictive ML models that included common clinical variables (e.g., gestational age, birth weight, and inflammatory markers) had an increased accuracy when diagnosing neo-nates with infection [11]. Moreover, customized ML algorithms that incorporated electronic health record data were similarly shown to offer strong predictive performance relative to standard scoring systems such as the pediatric logistic organ dysfunction-2 (PELOD-2) score, and the systemic inflammatory response syndrome (SIRS) criteria [12,13]. Furthermore, deep learning models (e.g., long short-term memory (LSTM)) optimized the analysis of data in ICU settings, and AI models that combined clinical data with biomarkers improved the sensitivity and specificity of early detection of sepsis [14,15].

AI has demonstrated significant potential in the early detection and prediction of sepsis. By utilizing advanced ML algorithms and integrating diverse data sources, AI models can substantially improve the accuracy and timeliness of sepsis diagnosis. As these technologies evolve, their clinical implementation could lead to earlier interventions, better patient outcomes, and lower healthcare costs [16].

METHODOLOGY

A systematic review and meta-analysis were conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Literature Search

A comprehensive literature search was conducted across multiple electronic databases, including PubMed, Medline, Google scholar, Cochrane, and Scopus. The search strategy utilized both Medical Subject Headings (MeSH) terms and free-text keywords related to pediatric sepsis, artificial intelligence, machine learning, predictive analytics, vital signs, and laboratory results. An example search query might include terms such as:

- "Pediatric sepsis" OR "childhood sepsis"
- "Artificial intelligence" OR "AI" OR "machine learning"
- "Predictive model" OR "predictive analytics"

The search will focus on studies published in English from the inception of each database to the present. Additionally, references to the included studies will be manually screened to identify any other relevant articles.

Inclusion Criteria

- Studies that focus on pediatric populations (≤18 years old).
- Research that develops, validates, or tests AI-driven models for sepsis detection.
- Studies using vital signs and/or laboratory results as input variables for the AI model.
- Peer-reviewed articles or conference proceedings.
- Studies that report performance metrics such as sensitivity, specificity, accuracy, or area under the receiver operating characteristic curve (AUROC).

Exclusion Criteria

- Studies involving only adult populations.
- Non-AI-based models or heuristic algorithms.
- Studies lacking sufficient methodological detail or outcome data.
- Reviews, editorials, commentaries, or opinion pieces without original data.
- Articles not published in English.

Data extraction

Data from eligible studies were collected using a standardized extraction form. Key information to be gathered includes:

Study Characteristics

This includes details such as the author, year of publication, study design, and the setting of the study.

Population Characteristics

Information on the age range of participants, sample size, and clinical setting (e.g., emergency department, ICU).

Model Details

The type of AI model used (e.g., random forest, neural network) and the methods used for training and validation.

Outcome Measures

Performance metrics like sensitivity, specificity, accuracy, AUROC, and precision-recall curves were used, but our study mainly considered AUROC values.

Statistical Analysis

The AUROC serves as the primary performance metric as it quantifies how effectively the AI model separates septic from non-septic patients. This is especially relevant for imbalanced data where the positive (septic) cases are outnumbered compared to the negative (non-septic) cases. AUROC measures performance across all potential thresholds unlike sensitivity or specificity. This makes AUROC a more robust performance measure, since the score reflects the performance of the comparison across the relevant threshold space. AUROC adds the ability to compare different AI models easily with models having greater predictive accuracy having higher AUROC values. AUROC can help clinicians with earlier identification of sepsis cases while avoiding many false positives, which enhances patient treatment. The AI in this study were shown to perform very well with an average AUROC of 86.8%, which shows the encouraging performance from AI in the prediction of pediatric sepsis.

- AUROC values were converted into Cohen's d to measure effect size.
- Upper and lower confidence intervals (CI) were calculated.
- A forest plot was generated to visualize the predictive performance of AI models.

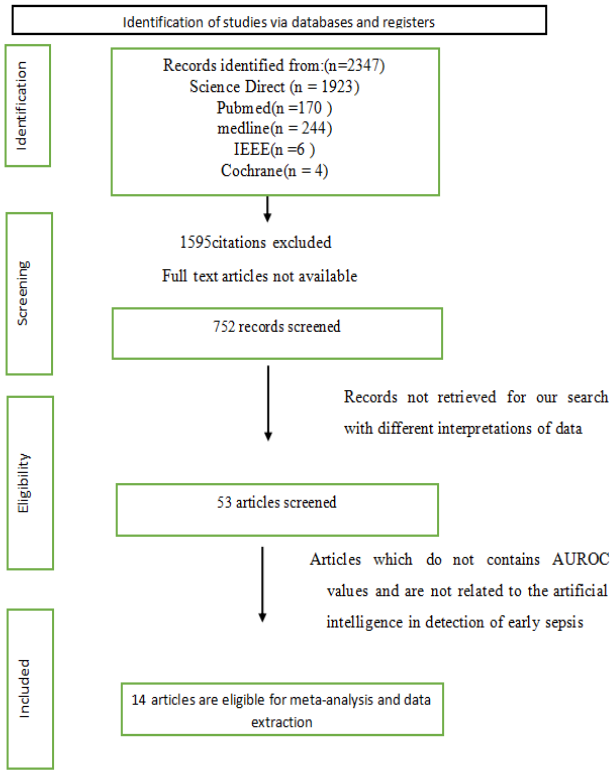

Figure 1: PRISMA

The Results should report actual screening numbers, such as records identified, duplicates removed, screened, full texts assessed, exclusions with reasons, and final studies included.

RESULTS

Results of the study showed that a meta-analysis across 14 studies contained 96,764,476 patients. Table 1 including the study number, title, authors, study design, year, and country. This summary is helpful for presenting comparative information across studies with regard to research methods utilized, publication trends, and composition across geographical locations.

Table 1: Study Characteristics

Study No	Title	Authors	Study design	Year	Country / Place
1.	Pediatric septic shock estimation using deep learning and electronic medical records [17]	Ji Weon Lee et al	Retrospective observational study	2010-2023	Seoul
2.	Pediatric Severe Sepsis Prediction Using Machine Learning [18]	Sidney Le et al	Retrospective set	2011-2016	California San Francisco

3.	Machine learning models for early sepsis recognition in the neonatal intensive care unit using readily available electronic health record data [19]	Aaron J et al	Retrospective case-control design	2019	Spain
4.	A Continuous Late-Onset Sepsis Prediction Algorithm for Preterm Infants Using Multi-Channel Physiological Signals From a Patient Monitor [20]	Zheng Peng et al	Quantitative study	2016-2018	Netherlands
5.	Cardiorespiratory signature of neonatal sepsis: development and validation of prediction models in 3 NICUs [21]	Sherry L et al	Multi-center cohort design	2023	United States
6.	Vital Sign-Based Detection of Sepsis in Neonates Using Machine Learning [22]	Antoine Honore et al	Single-center retrospective cohort study	2023	Sweden
7.	Using Machine Learning to Predict Invasive Bacterial Infections in Young Febrile Infants Visiting the Emergency Department [23]	I-Min Chiu et al	Retrospective study	2011-2018	Taiwan
8.	Machine Learning for Early Warning of Septic Shock in Children With Hematological Malignancies Accompanied by Fever or Neutropenia: A Single Center Retrospective Study [24]	Hansong Wang et al	Retrospective study	2021	China
9.	Effective diagnosis of sepsis in critically ill children using probabilistic graphical model [25]	Tuong Minh Nguyen et al	Retrospective study	2010-2019	China
10.	Prediction of Late-Onset Sepsis in Preterm Infants Using Monitoring Signals and Machine Learning [26]	Cabrera-Quiros, Laura et al	Retrospective study	2021	United States
11.	Medical decision support using machine learning for early detection of late-onset neonatal sepsis [27]	Subramani Mani et al	Retrospective cohort study	2014-2017	United States
12.	Development and clinical impact assessment of a machine-learning model for early prediction of late-onset sepsis [28]	Merel A.M. van den Berg et al	Retrospective cohort study	2023	Netherlands
13.	Identification of Pediatric Sepsis Subphenotypes for Enhanced Machine Learning Predictive Performance: A Latent Profile Analysis [29]	Tom Velez, Tony Wang et al	Retrospective study	2019	Washington, D.C.United States
14.	Deep Learning Model to Predict Serious Infection Among Children with Central Venous Lines [30]	Azade Tabaie et al	Retrospective cohort study	2013-2018	United States

Table 2 provides a summary of the AI models employed in each study and the respective interpretations. This summary allows for comparisons between different AI methodologies (e.g., random forest, logistic regression, neural networks), to identify the most efficacious methods for sepsis prediction.

Table 2: AI Model Used in the Included Studies

Study No	AI MODEL USED	CONCLUSION
1.	Artificial Neural Network	The deep learning model presented contributes to the early diagnosis of septic shock in children, decreasing diagnostic burden, providing certainty in clinical decision making, and giving an opportunity to safely initiate treatment rapidly, but must be validated externally in prospective studies to ensure clinical fidelity.
2.	Decision Trees	This algorithm uses artificial intelligence to continuously monitor electronic health records (EHRs) for possible signs of severe sepsis in pediatric inpatients. It

		analyzes real-time data, including vital signs, labs, and other clinical parameters, to identify subtle changes before symptoms present. Timely detection of possible sepsis allows for interventions for treatment through antibiotics, fluid resuscitation, and hospital resources, leading to better patient outcomes. Automating sepsis recognition decreases the manual workload, decreasing the time to a medical evaluation and intervention for established sepsis while minimizing false alarms.
3.	Logistic Regression, Decision Trees, Random Forests, Gradient Boosted Trees (XGBoost), Support Vector Machines (SVM), Neural Networks, k-Nearest Neighbors (k-NN), And Naïve Bayes.	ML algorithms can predict sepsis in NICU infants up to hours before clinical symptoms appear, potentially allowing for earlier intervention. More datasets and additional input features, such as continuous vital signs and biomarker trends, could enhance prediction. Nonetheless, substantial research and real-world prospective studies will be needed to validate models across populations. Future research should focus on model generalizability, reducing false positives, and integrating into the clinical workflow for optimizing neonatal care.
4.	Extreme Gradient Boosting (XGB), k-Nearest Neighbors (k-NN), Logistic Regression (LR), And Support Vector Machine (SVM).	This study shows that LOS in NICUs can be predicted using physiologic signals routinely measured in clinical practice. In addition to variables derived from cardiorespiratory waveforms, motion-based features added to predictive accuracy alongside ECG and chest impedance. The visualizations of the variables contributed significantly to the interpretability of the feature selection while further enhancing usability in a clinical practice. Next steps would be to validate the signal and model parameters with larger studies across multiple centers.
5.	Logistic Regression, a Neural Network, An Extreme Gradient Boosting Classifier Or Xgboost, And Random Forest	A cardiorespiratory early warning score predicts late-onset sepsis within 24 hours, outperforming heart rate or demographics alone.
6.	Naïve Bayes Classifier.	This algorithm can predict sepsis in NICU patients 24 hours before clinical suspicion on vital signs and demographics alone. We emphasize the need for standardized definitions of sepsis and to test the method prospectively. Clinical decision support systems have the potential of improving patient care, appropriateness of resources, and patient outcomes.
7.	Logistic Regression (LR), Support Vector Machine (SVM), And Extreme Gradient Boosting (XGBoost)	This study evaluated LR, SVM, and XGBoost for predicting IBIs in febrile infants. All outperformed traditional scoring, with SVM achieving optimal results using fewer features.
8.	Xgboost Algorithm	The SSEW model provides an accurate estimate of pediatric hematology-oncology patients' risk of septic shock up to 24 hours prior to its development, and enables intervention as needed. The model uses real-time clinical data to assess risk, identify at-risk patients, and help facilitate optimizing treatment pathways. However, the model warrants exploration of its performance and reliability in prospective studies in broader patient populations. Future studies should investigate additional accuracy and false alarm reduction, and working toward a model that would work in a clinical workflow would be ideal.
9.	Tree Augmented Naive Bayes (TAN)	PGM is a reliable diagnostic tool for pediatric sepsis, with lab tests aiding prediction and vital signs helping rule it out. Further validation with diverse datasets is needed.
10.	Logistic regressor, Naive Bayes, Nearest Mean Classifier	Routine monitoring data can predict sepsis, with ECG, respiration, and motion features identifying late-onset sepsis hours before clinical deterioration.
11.	Support Vector Machines (SVM), Artificial Neural Networks (ANN), Decision Trees, and Bayesian Networks	Routinely collected EHR data can effectively predict late-onset neonatal sepsis before clinical diagnosis. AI-driven decision support systems have the potential to enhance early detection, allowing for timely interventions and improved neonatal outcomes.
12.	Generalized Additive Models, Logistic Regression, And Xgboost	An ML algorithm was trained for early LOS detection, evaluated on prediction horizons and clinical impact. This study provides the most extensive retrospective simulation for LOS prediction to date.
13.	Latent Profile Analysis	LPA identified four pediatric sepsis subphenotypes, improving prediction for

		high-mortality cases. Larger studies are needed for validation.
14.	Bidirectional Long Short-Term Memory (LSTM) Network With Focal Loss and An Attention Mechanism to Predict the Onset of Psi	A deep learning model can predict CLABSI onset in hospitalized children 48 hours before specimen collection using EHR data.

Table 3 provides a summary of the AUROC values reported in each study, which describe the predictive performance of each of the AI models to discriminate septic from non-septic patients. AUROC values are the primary metric used to report model performance, with higher AUROC values reflecting better predictive performance.

The AUROC had a mean value of 86.8%, implying the AI models' overall high predictive efficiency towards early pediatric sepsis detection.

Table 3: AUROC Value

Study No	AUROC VALUE
1.	0.97
2.	0.916
3.	0.86
4.	0.88
5.	0.786
6.	0.82
7.	0.85
8.	0.93
9.	0.77
10.	0.79
11.	0.78
12.	0.73
13.	0.918
14.	0.993

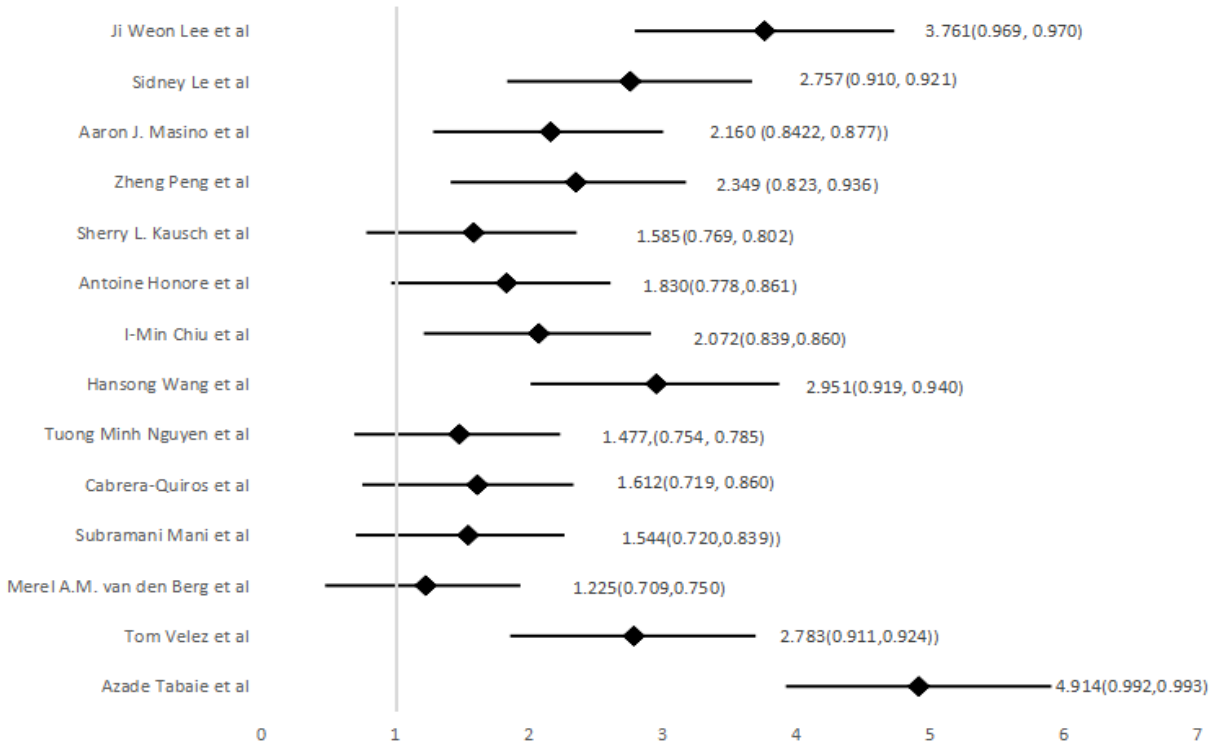

Figure 2: FOREST PLOTTING

DISCUSSION:

Artificial Intelligence has revolutionized healthcare by improving diagnostic accuracy, clinical workflows, and patient outcomes. Early sepsis detection is crucial in pediatrics, where rapid assessment reduces morbidity and mortality risks [31]. AI predictive models outperform traditional scoring systems, enabling earlier diagnosis and treatment initiation [33]. AI is also transforming radiology, pathology, genomics, and clinical decision-making. Deep learning detects abnormalities in MRI and CT scans, while natural language processing (NLP) extracts insights from electronic health records (EHR) for continuous diagnosis and personalized treatment [33].AI chatbots and virtual assistants improve patient access to medical advice, reducing the burden on healthcare professionals [34] .AI plays a key role in the pharmaceutical industry, driving advancements in drug discovery, pharmacovigilance, and precision medicine. Machine learning (ML) models predict drug interactions, optimize dosing strategies, and enhance medication safety [35]. Automation in life sciences and pharmaceutical manufacturing improves efficiency, reliability, and consistency while reducing human error [36]. These innovations enhance healthcare system performance and product quality.

In pediatric intensive care units (PICUs), AI models analyze real-time patient data, including vital signs and biomarkers, to detect sepsis before symptoms appear [37]. AI models outperform clinical scores such as Pediatric Logistic Organ Dysfunction-2 (PELOD-2) and Systemic Inflammatory Response Syndrome (SIRS) criteria by analyzing vast datasets for improved risk assessment [38,39]

A number of AI-based techniques have been effectively implemented for pediatric sepsis identification, including: Machine Learning (ML) techniques such as Random Forest, Gradient Boosting, and Support Vector Machines analyze structured clinical data to assess sepsis risk [40] . Deep Learning (DL) models like Recurrent Neural Networks (RNN), Long Short-Term Memory (LSTM), and transformer architectures detect physiological changes for early sepsis identification [41]. Explainable AI (XAI) methods such as SHAP (Shapley Additive Explanations) and LIME (Local Interpretable Model-Agnostic Explanations) provide transparency and information about the AI-model predictions so that clinicians can understand the rationale for AI-generated suggestions [42].

Although it holds significant promise, AI implementation in identification of pediatric sepsis faces a number of obstacles. Data security is a concern whenever AI models utilize large amounts of patient data for training purposes [43]. Another challenge is the "black box" nature of deep learning models, making it difficult for clinicians to interpret predictions [44]. Developing AI in clinical settings also requires upgrades to both infrastructure and training of clinicians while ensuring all models are validated against diverse patient populations [45]. While AI models can be very sensitive, but can have lower specificity producing false-alarms and unnecessary interventions increasing days in the hospital and healthcare utilization [46].

There are multiple important advantages to the use of AI for the detection of pediatric sepsis: Early Detection: AI has the potential to recognize sepsis several hours before clinical symptoms arise so that treatments may begin earlier and possibly improving chance of survival [47]. Automation and Efficiency: AI has the possibility to rapidly and effectively analyze large volumes of patient data, and trigger real-time alerts for those responsible for patient care [48]. Personalized Treatment Plans: AI generates individualized treatment plans based on patient specific risk factors, thereby improving clinical outcomes [49].

Although AI has many advantages, it still has limitations such as Lack of diverse pediatric data, which makes it difficult for AI models to generalize across populations, Variations in hospital protocols require continuous AI model updates and validation [50]. AI models demand high computational resources, posing challenges in resource-limited settings [51] and AI biases may exacerbate disparities in sepsis diagnosis, leading to inequitable healthcare outcomes [52].

AI models for pediatric sepsis detection have evolved from classical models to machine learning, hybrid models, and biomarker integration. Machine learning improves interpretability, deep learning analyzes complex datasets, hybrid models enhance predictive accuracy, and biomarker integration supports precision medicine. Challenges such as limited data availability, clinical validation barriers, and computational costs persist. Future research will refine AI models, integrate AI into clinical workflows, and standardize data to enhance early sepsis detection and optimize pediatric patient care [53].

CONCLUSION

AI-driven models aid early pediatric sepsis detection with an AUROC of 86.8%. The integration of real-time vital signs, biomarkers, and waveform data enhance predictive accuracy for timely, reliable diagnoses. While ML and DL improve predictions, challenges remain in validation, clinical adoption, and interpretation. Future research will develop resource-efficient, user-friendly AI algorithms to enhance patient outcomes. Efforts will also focus on standardizing AI in pediatric sepsis diagnosis and expanding its application to cancer patient care.

Author Contributions:

Achsa Sharon Shibu: Literature search, study screening and selection, data collection, data extraction, data analysis, interpretation of findings, preparation of tables and figures, manuscript writing, and review and editing.

Aadhira J: Conceptualization, literature search, study screening and selection, data collection, data extraction, data analysis, statistical analysis and meta-analysis, PRISMA flow diagram preparation, interpretation of results, and manuscript writing.

Mitra S.: Data collection, data extraction, data analysis, interpretation of findings, manuscript writing, and review and editing.

Muhammad Marzuq U A: Literature search, study screening, data collection, data extraction, data analysis, manuscript writing, and review and editing.

Nickson P: Literature search, study screening, data collection, data extraction, data analysis, manuscript writing, and review and editing.

Dhivya K: data analysis, and manuscript writing.

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