Efficient management of neonatal sepsis diagnosis using predictive analytics methods: a scoping review

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Abstract

Neonatal sepsis is a critical and life-threatening condition that significantly contributes to the high rates of illness and death among newborns, particularly in Low and Middle Income Countries (LMICs). The complexity of diagnosing and treating neonatal sepsis arises from the unique physiological characteristics of newborns and the increasing challenge of antibiotic resistance. However, early diagnosis and prompt treatment are crucial in effectively managing this condition. Predictive analytics methods can potentially address the gaps in diagnosing and treating neonatal sepsis, especially in resource-constrained settings. This scoping review aims to comprehensively analyze the critical factors involved in neonatal sepsis diagnosis and the potential impact of utilizing predictive analytics models in its diagnosis and treatment. This paper reviews the literature to determine the critical factors in managing neonatal sepsis efficiently. It will also delve into the ability of predictive analytics methods to diagnose neonatal sepsis at an early stage, reduce the usage of antibiotics, and achieve cost savings in treatment, highlighting the overall efficiency of diagnosing and managing neonatal sepsis. The findings of this review could provide insight into the impact of predictive analytics methods for diagnosing and treating neonatal sepsis in hospitals in low-resource settings. The review reveals that the predictive analytics methods could lead to efficient management of neonatal sepsis through analysis of critical factors such as early diagnosis of neonatal sepsis at least 48 hours before clinical manifestation, reduction in antibiotic treatment by at least 33-97%, and reduction in cost of therapy by 4.1-50.4%.

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Introduction

Neonatal sepsis is a bacterial infection of the blood and cerebrospinal fluid that occurs in neonates. Early-Onset Sepsis (EOS) happens within the first seven days of life,[1] along with radiographic evidence of pneumonia.[2,3] Neonatal sepsis encompasses serious infections such as bacteremia, pneumonia, and meningitis, which manifest as very early-onset sepsis (within the first three days of life), early-onset sepsis (within the first week), and late-onset sepsis (after the first week until 28 days of life).[1,4]

The neonatal period, which spans the first 28 days of life, carries the highest daily risk of mortality, leading to significant morbidity and mortality in the neonatal intensive care unit (NICU),[5] particularly in Low and Middle Income Countries (LMICs).[6] Approximately 1 million newborns worldwide die from neonatal infections within the first 28 days of birth.[7] In developing countries, neonatal sepsis accounts for 30-50% of the 5 million total neonatal deaths each year.[8]

Diagnosing neonatal sepsis is challenging due to the frequent presence of noninfectious conditions that mimic sepsis, particularly in preterm infants, and the lack of optimal diagnostic tests.[9] Diagnostic challenges of neonatal sepsis are also attributed to the nonspecific nature of symptoms, making both diagnosis and treatment difficult. A blood culture test is the gold standard for diagnosing neonatal sepsis;[1] however, it takes between twenty-four and seventy-two hours to generate results and requires a well-equipped laboratory.[10]

Predictive analytics has sparked considerable interest in the healthcare industry due to its potential to revolutionize economies, particularly in delivering primary health services.[11] Predictive analytics in healthcare encompasses a wide range of medical and non-medical interventions to address health crises, bolster preparedness for future epidemics, and facilitate resilient recoveries during global health emergencies or disasters.[12] The application of predictive analytics methods, such as machine learning and artificial neural networks, has become an area of significant interest among researchers for the early detection and diagnosis of neonatal sepsis.[13] This has led to the development and publication of various statistical methods to predict the onset of sepsis in neonates. These methods play a crucial role in improving the timely identification of sepsis, thus contributing to better outcomes for affected newborns.

The current scoping review fills a significant gap in critical dimensions involved in managing neonatal sepsis. It addresses a research question on reducing the delay in diagnosing neonatal sepsis and making the diagnosis process efficient in improving healthcare in low-resource settings. The scoping review analyzes

dimensions including the early prediction of neonatal sepsis prior to symptom onset, decreased antibiotic utilization, and treatment costs, thereby providing a distinctive perspective that differentiates it from previous studies. Instead of examining each dimension separately, as previous studies have done, this review offers a comprehensive exploration of the most crucial dimensions, illuminating predictive analytics methods in this vital area of healthcare.

Ensuring the well-being of newborns in developing countries and around the world depends on giving proper attention to the essential aspects of diagnosing and treating neonatal sepsis.[14]

The core objective of the scoping review is to address the defined research question and analyze the impact of predictive analytics methods on early diagnosis and treatment, antibiotic usage reduction, and the overall cost of treatment.

The up-to-date review will benefit neonatal sepsis diagnosis and predictive analytics researchers. It offers a comprehensive understanding of the efficient management of neonatal sepsis using predictive analytics methods.

Materials and Methods

The databases (Scopus, Google Scholar, and PubMed) were searched to identify relevant literature published from 2014 to 2024. The search was focused on neonatal sepsis diagnosis, efficient management, predictive models, artificial intelligence, machine learning, diagnosis time, antibiotic usage, and treatment costs. The inclusion criteria were articles that applied predictive analytics techniques to guide diagnosis, reduce antibiotic usage, and reduce overall treatment costs. The focus was on the specific criteria of the ability to diagnose sepsis before the occurrence, the effect of applying predictive analytics techniques in reducing antibiotic usage, and the impact on the cost of treatment towards NICU stay, tests conducted, and overall cost of treatment for sepsis. This scoping review can significantly impact the neonatology and predictive analytics fields, and we are excited about its possibilities.

The scoping review was based on the Arksey and O'Malley framework and conducted in 5 steps: i) framing the research question; ii) identifying relevant literature; iii) selecting studies; iv) extracting, mapping, and charting the data; and v) summarizing the results.

The research concentrated on utilizing predictive analytics to diagnose neonatal sepsis and manage the condition in infants under 28 days old. The search criteria were independently applied according to the three essential dimensions: early diagnosis of neonatal sepsis, antibiotic reduction, and treatment cost. The inclusion criteria involved studies published in English and excluded review articles, letters, conference proceedings, and animal studies. Initially, the screening process involved reviewing titles and abstracts, thoroughly screening full-text articles, and extracting data. The extracted details included the author, journal, year of publication, type of neonatal sepsis, country of study, predictive methods utilized, the performance of predictive methods in early diagnosis of neonatal sepsis, and the impact of using predictive analytics calculators on antibiotic usage and cost of treatment. The quality of the study is ensured by considering the research articles published in reputed Scopus-indexed journals. The bias is eliminated through a selection of journals focusing on global research with validated results. The study also considered the implications of using predictive analytics methods for neonatal sepsis on the cost of NICU stay, treatment costs related to tests conducted to diagnose sepsis, and the overall cost of treatment through predictive analytics methods.

Out of the 17,269 records gathered from databases like Google Scholar, PubMed, and Scopus, 16,500 articles were identified as ineligible based on the inclusion and exclusion criteria of the literature review. Through further screening after identifying articles irrelevant to the study, 21 articles that met the inclusion criteria were included in the review. Detailed information on these included studies can be found in Tables 1, 2, and 3.

The studies included in the review were published between 2014 and 2024. Most studies investigating the impact of antibiotic usage and antimicrobial resistance utilized the Kaiser Permanente predictive tool. This tool is known for promptly predicting the occurrence of neonatal sepsis while analyzing specific clinical parameters.

Results

Impact of predictive analytics methods on the diagnosis of neonatal sepsis at an early stage

Neonatal sepsis can be managed by early diagnosis and treatment.[2] The gold standard diagnostic tool is a blood culture test that typically has a turnaround time for results of 2 to 3 days.[15] However, blood culture tests are sometimes inadequate, throw up

Table 1. Impact of predictive analytics on the diagnosis of neonatal sepsis.

SNo	Author	Year of publication	Types of sepsis	Diagnosis of sepsis through blood culture method Duration (hours)	Diagnosis of sepsis through predictive analytics method Duration (hours)						Algorithm
					-48	-24	-12	-8	-4	0	
1	Guzey *et al.*	2018	LONS	24		0.86					Random forest
2	Song *et al.*	2019	LONS	48-72	0.83	0.86	0.867	0.867	0.867 0.83	0.867	RF classifier Gradient boosting classifier Logistic regression
3	Cabrera *et al.*	2021	LONS	48				0.82	0.79		Logistic regression
4	Kaush *et al.*	2023	LONS	Not specified		0.83				0.83	XGBoost
5	Iqbal *et al.*	2024	EONS & LONS	Not specified		0.99					Random forest, bagging

EONS, early onset of sepsis; LONS, late onset of sepsis.

false negatives, and have not consistently demonstrated complete accuracy.[16] Moreover, in the absence of specific laboratory tests for neonatal sepsis and the inherent protean nature of the nonspecific symptoms, accurate clinical diagnosis of sepsis remains a challenge,[17,3] with delays in diagnosis and treatment as common issues[18] across the globe. Failure to quickly diagnose neonatal sepsis, primarily due to its indefinite signs and symptoms, makes the disease more lethal. Researchers have therefore emphasized the critical need for developing novel technology-based approaches, such as predictive analytics methods for the rapid prediction of neonatal sepsis,[19] which could diagnose as effectively or better than traditional blood culture testing methods. Table 1 summarizes several vital studies and approaches that highlight this potential.

The studies mentioned above collectively demonstrate how predictive analytics methods can enhance the diagnosis of neonatal sepsis, resulting in faster and more accurate identification of the condition before symptoms appear. In stark contrast to traditional diagnostic approaches, which often take more than 24 hours to provide conclusive results, predictive analytics methods have shown the capability to forecast the onset of sepsis at least 48 hours before the manifestation of clinical symptoms.

Impact of predictive analytics methods on antibiotic usage and antimicrobial resistance

Antibiotic resistance stems from poor infection control and overuse of antibiotics. While new strategies for antibiotic use are essential, prevention is the ultimate solution.[20] The growing occurrence of antibiotic resistance is now linked to higher neonatal mortality rates, posing a significant challenge to efforts aimed at decreasing global neonatal deaths. The issue of antibiotic resistance in newborns has been highlighted in recent research.[21] This problem is mainly caused by the increased and unnecessary use of antibiotics, posing a significant global challenge. According to the study by Laxminarayan *et al.*,[22] antibiotic resistance is primarily driven by microbial mutations resulting from antibiotic use, giving mutated strains a competitive advantage. LMICs have experienced a rise in antibiotic use due to higher incomes, increased hospitalization rates, and more hospital infections. NICUs in LMICs report significantly higher infection rates than those in the United States, raising concerns for healthcare practitioners and policymakers. Mani *et al.*[5] emphasize the need to address the overuse of antibiotics in infants receiving treatment to prevent antibiotic resistance and reduce healthcare costs. Tailored approaches specific to developing countries are crucial, as the varying pathogen profiles in regions like South Asia underscore the need for context-specific solutions.

Predictive analytics methods have proven effective in reducing antimicrobial usage in treating neonatal sepsis, addressing the challenge of rising microbial resistance due to prolonged use of empirical antibiotics. Predictive analytics can also help mitigate microbial resistance associated with protracted empirical antibiotic coverage. Among the predictive analytics methods, the Kaiser Permanente sepsis risk calculator (SRC) has significantly reduced antibiotic use in neonates.

Table 2 shows several studies that demonstrate the impact of these methods. Researchers have been exploring ways to improve the prediction and management of EOS in newborns, particularly those born at 34 weeks of gestation or later.

Table 2. Impact of predictive analytics on antibiotic usage.

SNo	Author	Year of publication	Country	Type of sepsis	Predictive analytics method	% reduction in antibiotic usage
1	Escobar *et al.*	2014	USA	EOS	Logistic regression	33
2	Shakib *et al.*	2015	USA	EOS	EOS calculator	88
3	Kerste *et al.*	2016	Netherlands	EOS	Kaiser risk calculator	50
4	Warren *et al.*	2016	USA	EOS	Kaiser risk calculator	75
5	Kuzniewicz *et al.*	2017	USA	EOS	Kaiser risk calculator	48
6	Mani *et al.*	2017	USA	EOS	Kaiser risk calculator	97
7	Beavers *et al.*	2018	USA	EOS	Kaiser risk calculator	59
8	Gievers *et al.*	2018	USA	EOS	SRS algorithm	91
9	Achten *et al.*	2019	USA	EOS	Kaiser risk calculator	48
10	Schmatz *et al.*	2020	USA	EOS	Kaiser risk calculator	68
11	Goel *et al.*	2022	UK	EOS	Sepsis risk calculator	46
12	Levi *et al.*	2023	Israel	EOS	Kaiser risk calculator	46
13	Leonardi *et al.*	2024	Belgium	EOS	Kaiser risk calculator	65

EOS, early onset of sepsis; SRS, sepsis risk score.

Table 3. Impact of predictive analytics on the cost of treatment.

No	Author	Year of publication	Diagnosis	Cost of treatment (in dollars) before implementation of sepsis risk calculator	Cost of treatment (in dollars) after implementation of sepsis risk calculator	% reduction in cost
1	Beavers *et al.*	2018	EOS	14700	7300	50.4
2	Achten *et al.*	2019	EOS	2653	2542	4.1
3	Guan *et al.*	2024	EOS	182491	97884	46.3

EOS, early onset of sepsis.

The studies above suggest that predictive analytics methods can significantly enhance treatment for neonatal sepsis and reduce unnecessary antibiotic use by at least 33-97%.

Impact of predictive analytics methods on the cost of treatment

The financial burden associated with treating neonatal sepsis arises from several factors. Key issues include the high costs of diagnostic testing, which stem from the challenges of achieving accurate diagnoses, unnecessary antibiotic administration, and the associated expenses. Extended stays in NICUs during the diagnostic and treatment phases also contribute significantly to these costs. Additionally, delays in diagnosis and the waiting period for culture test results directly affect the length of NICU stays, the frequency of laboratory tests, and the demand for medications during treatment. However, many studies suggest that implementing predictive analytics methods can reduce the overall costs of neonatal sepsis treatment, as indicated in Table 3. In summary, implementing the EOS calculator positively impacts antibiotic stewardship and demonstrates notable reductions in healthcare utilization and associated financial costs in late preterm and preterm newborns with suspected EOS by 4.1-50.4%.

Discussion and findings

Predictive analytics methods utilize advanced algorithms such as random forest, gradient boosting, XGBoost, and logistic regression, all of which have shown improved performance with an area under the curve (AUC) ranging from 0.82 to 0.87. For instance, a random forest algorithm with an AUC of 0.868 has been recognized as superior in predicting sepsis 24 hours before its onset.[23] Additionally, when non-invasive vital sign data is employed, a forward feature selection prediction model could detect clinical sepsis 48 hours in advance.[15] The AUC for this 48-hour prediction model was 0.861, while the onset detection model had an AUC of 0.868. These findings confirm that the Late Onset Neonatal Sepsis (LONS) production model based on machine learning can be safely implemented in clinical settings. Furthermore, a combination of electrocardiogram, respiration, and motion-based features allowed for predicting late-onset sepsis using logistic regression at least 5 hours before it occurred, achieving an AUC of 0.79.[24] Predictive algorithms that utilize heart rate (HR) and oxygen saturation (SpO2) data could also forecast an increased risk of sepsis before clinical diagnosis, achieving predictions up to 24 hours before blood culture results. The XGBoost predictive model demonstrated superior performance, with an AUC of 0.834 in the training dataset and 0.792 and 0.807 in the test datasets.[25] Lastly, bagging and random forest algorithms displayed comparable accuracy (98.4%) in predicting central nervous system (CNS) and central peritoneal sepsis (CPS). However, random forest outperformed the other algorithms with an accuracy of 98.4% and an ROC of 0.994 for forecasting outcomes.[13]

Combining maternal data with new neonatal clinical indicators and employing risk stratification algorithms could enhance the assessment and management of EOS in full-term and late-preterm infants. This approach may reduce the necessity for antibiotic treatment in 33% of newborns.[26] Utilizing the early EOS risk calculator and a clinical symptom assessment can safely reduce the number of newborns who require laboratory testing and decrease antibiotic usage by 88%.[27] Kerste *et al.*[28] conducted a study to evaluate the management of antibiotic use with the guidance of the sepsis calculator in newborns born at or after 34 weeks of gestation with suspected EOS. The study concluded that antibiotic use could be reduced by more than 50%. Similarly, Warren *et al.*[29] performed a study to assess the impact of implementing a neonatal early-onset sepsis calculator for neonates undergoing treatment for sepsis. Their conclusions indicate that the calculator holds the potential to substantially reduce the administration of antibiotics to newborns and lower the number of neonates requiring antibiotics at birth by as much as 75%. These findings have significant implications for improving the management and care of neonates at risk of sepsis. Kuzniewicz *et al.*[30] investigated the influence of neonatal EOS risk prediction models on sepsis evaluations and antibiotic utilization. They assessed the safety and efficacy of these models within an extensive integrated healthcare system. Their findings indicated that predictive algorithms, derived from a multivariable risk prediction model estimating the early onset of sepsis risk, led to a 48% decrease in the proportion of newborns receiving empirical antibiotic treatment. In a study by Money *et al.*,[31] the investigators conducted a comprehensive study to evaluate the effectiveness of implementing a protocol based on a neonatal early-onset sepsis calculator developed by Kaiser Permanente. The study aimed to determine whether this approach would safely reduce the use of antibiotics in newborns showing no signs of illness. The study concluded that utilizing the EOS calculator for managing sepsis could effectively mitigate the potential complications associated with antibiotic use in these cases, reducing antibiotic usage by 97%. Neonates born to mothers with chorioamnionitis face an elevated risk of EOS. In another study,[32] the authors observed that NICU admission rates declined from 91% to 37% after introducing the EOS risk calculator, and antibiotic administration rates decreased from 94% to 37%. Implementing the EOS risk calculator as part of the clinical evaluation of term and late preterm neonates positively impacted antibiotic usage. Gievers *et al.*[33] have developed and implemented an algorithm based on SRS (severity of illness score) designed explicitly for neonates exposed to chorioamnionitis. The targeted goal of the SRS algorithm is to reduce the unnecessary usage of antibiotics in this population. Their work has shown that the successful adoption of the SRS algorithm for chorioamnionitis-exposed neonates has led to a remarkable 91% decrease in antibiotic exposure. Their study also demonstrated the potential of the SRS algorithm to significantly reduce antibiotic usage in this vulnerable patient group while maintaining effective treatment protocols. Achten *et al.*[34] examined how using the neonatal EOS calculator to guide the management of EOS in newborns affected the administration of antibiotic therapy. They found that employing the neonatal EOS calculator led to a 48% decrease in empirical antibiotics for suspected EOS in newborns.

The primary objective of the investigation of a study conducted by Schmatz *et al.*[35] was to minimize the administration of antibiotics in asymptomatic neonates born at or after 35 weeks of gestational age to mothers with chorioamnionitis. This was achieved by implementing the Kaiser Permanente neonatal early-onset sepsis risk calculator. The study culminated in compelling evidence that the consistent utilization of the neonatal EOS calculator yielded a statistically significant reduction of 50% in antibiotic utilization. The research by Goel *et al.*[36] evaluated the influence of the SRC algorithm on managing EONS, particularly regarding antibiotic utilization and patient safety. Their multi-center study provides conclusive evidence that a cautious implementation of the SRC algorithm leads to a substantial 46% reduction in antibiotic usage for EONS while maintaining consistent morbidity and mortality levels. The investigation by Levi *et al.*[37] assessed the impact of employing the Kaiser Permanente early-onset sepsis cal-

culator on neonates regarding antibiotic utilization and duration of hospitalization. It was confirmed that employing the calculator yielded a 46% reduction in antibiotic therapy for suspected EOS, and this decrease was attained without an escalation in the occurrence of EOS. It concluded that the calculator represents a valuable decision-making instrument that can be judiciously applied with comprehensive clinical evaluation. Leonardi *et al.*[38] sought to determine the effectiveness of the SRC in decreasing antibiotic use. The findings indicated that the SRC could reduce the number of newborns receiving antibiotics by 64.5%. The neonatal early-onset sepsis calculator represents an innovative approach to antibiotic stewardship in newborns. Its implementation has shown promise in reducing empiric antibiotic usage for suspected EOS in neonates. The research mentioned above by Beavers *et al.*[32] studied the impact of using EOS calculators using predictive methods on treatment cost. They concluded that since the implementation of the EOS risk calculator, there has been a significant decrease in NICU admission rates for neonates born to mothers with chorioamnionitis, dropping from 91% to 37%. Additionally, there has been a noteworthy reduction in the number of blood cultures drawn and the administration of antibiotics in this patient population. Specifically, the rate of antibiotic administration decreased from 92% to 50%, while the number of blood cultures drawn decreased from 94% to 37%. Moreover, there have been substantial decreases in total charges, total bed charges, and length of stay, resulting in an overall 58% reduction in the cost of treatment. A study by Achten *et al.*[39] evaluated the impact of implementing the EOS calculator on healthcare utilization and financial costs associated with suspected sepsis. The findings indicate that implementing the EOS calculator significantly reduced EOS-related laboratory tests and antibiotic usage by at least 4.1%. Furthermore, there was a discernible decrease in the mean length of hospital stay and lower EOS-related financial costs following the implementation, particularly among term newborns. However, these benefits were less pronounced among preterm newborns. The research by Guan *et al.*[40] examined resource utilization and costs associated with three different screening approaches for EOS in infants born at 35 weeks of gestational age. The study concluded that the neonatal sepsis calculator and enhanced clinical observation methods show potential as superior options compared to categorical risk assessment. This is attributed to their potential to decrease the number of infants requiring intervention, reducing antibiotic exposure and associated costs by at least 46%.

Conclusions

This research article explores the practical application of predictive analytics techniques for efficiently managing neonatal sepsis diagnosis. The review demonstrates that these techniques have significant potential to accurately diagnose and treat sepsis before symptoms appear, which can significantly reduce antibiotic usage and lower costs associated with laboratory testing, NICU stays, and other related expenses. However, the current body of research lacks comprehensive studies focusing on how predictive analytics can assist healthcare providers in prescribing appropriate antibiotics for neonatal sepsis and other infectious diseases. This area is still in its early stages and requires further investigation to validate and generalize predictive techniques, ensuring their consistent and practical application in diagnosing and treating neonatal sepsis.

Predictive models for neonatal sepsis also encounter several limitations, particularly in low-resource settings. These challenges stem from the need for large, diverse datasets to train accurate models, which can be challenging. Significant computational power is also often required, which may not be readily available in such environments. These factors hinder the practical implementation of these models for identifying early signs of sepsis in newborns.

By advancing and standardizing predictive analytics methods, clinicians and healthcare professionals, especially in developing countries and low-resource settings, can receive substantial support in efficiently managing the diagnosis and treatment of neonatal sepsis.

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