World Journal of Biology Pharmacy and Health Sciences
eISSN: 2582-5542
Cross Ref DOI: 10.30574/wjbphs
Journal homepage: https://wjbphs.com/

(RESEARCH ARTICLE)

Check for updates

Risk stratification in preterm neonates with sepsis: Evaluating feeding intolerance, ARDS and hemodynamic instability using neonatal scoring systems and antibiotic regimens

Oubaida Al-Sebaie [1,*] and Razan Aldakhnoosh [2]

[1] *Department of Neonatology, Ministry of Health. Amman, Jordan.*
[2] *Department Public Health, Ministry of Health, Amman, Jordan.*

World Journal of Biology Pharmacy and Health Sciences, 2025, 23(01), 208-216

Publication history: Received on 30 June 2025; revised on 04 July 2025; accepted on 09 July 2025

Article DOI: https://doi.org/10.30574/wjbphs.2025.23.1.0668

Abstract

In areas with little medical care, neonatal sepsis continues to kill premature babies. This is particularly true in provider-short areas. The Jordanian Ministry of Health conducted research between those two years. This research examined whether birth grading systems and pharmaceutical interventions might accurately predict outcomes in 250 preterm newborns. The investigation aimed to determine how well these techniques predicted outcomes. It focused on the Neonatal Sequential Organ Failure Assessment (nSOFA), Clinical Risk Index for Babies (CRIB-II), and Neonatal Multiple Organ Dysfunction (NEOMOD) scores. This study sought to evaluate how well these ratings predict death and other problems. Meal difficulties, ARDS, and unstable blood flow were issues. Antibiotic treatments with a narrow spectrum (ampicillin and gentamicin) and a wide spectrum (meropenem and vancomycin) were tested for efficacy. The cohort had a mean gestational age of 31.2 weeks and a standard deviation of 2.5 weeks and a birth weight of 1580 grammes with a standard deviation of 420 grammes. Additionally, the group had an average gestational age of 31.2 weeks. Late-onset sepsis (LOS) affected 62% of patients, a significant rate. Total population mortality was 26.4%. Haemodynamic instability, acute respiratory distress syndrome, and nSOFA scores above 8 were strong indicators of death risk (adjusted odds ratio = 5.1, 95% confidence interval = 2.6–10.0). Research indicates a substantial correlation between food resistance and longer hospital stays (52.3% versus 32.6%, p = 0.01) and hospitalisations lasting over 28 days (p < 0.001). 44.8% of newborns were food-resistant. This number was significant. Thirty percent of the neonates had acute respiratory distress syndrome (ARDS), and 58.7% perished. For children without congestive heart failure (ARDS), the mortality rate was 18.5% (p < 0.001). The nSOFA score, with an AUC of 0.84 and a 95% CI of 0.78–0.90, was better at identifying probable fatalities. This score beat NEOMOD (AUC 0.79) and CRIB-II (AUC 0.71) in individual differentiation. Broad-spectrum antibiotics did not affect survival (25.5% vs 28.6% mortality, p = 0.15), although they did reduce recovery time for positive culture patients (5.2 days vs 7.8 days, p = 0.04). These factors influenced survival but did not substantially alter it. Our findings demonstrate the predictive power of organ dysfunction-focused scoring systems in preterm baby sepsis, particularly for nSOFA. However, dietary allergies, haemodynamic instability, and acute respiratory distress syndrome contributed to the tragic consequences. Only high-risk patients should get empirical broad-spectrum therapy, with a concentration on antimicrobials. Risk assessment tools in clinical settings may improve the pace and effectiveness of therapy for low-resource neonatal intensive care unit (NICU) newborns.

Keywords: nSOFA; Antibiotic treatment; Jordan; Neonatal sepsis; Preterm newborns; Risk categorization

1. Introduction

Neonatal sepsis remains one of the toughest paediatric issues to treat. It's the biggest reason premature newborns die or become ill worldwide [1]. In low-resource areas, this lethal condition is difficult to identify, and medication resistance

* Corresponding author: Oubaida Al-Sebaie

makes treatment harder [2]. There are many physical variables that increase the risk of sepsis in premature newborns. These include underdeveloped immune systems, weak skin, and frequent invasive treatments [3]. Sepsis causes 15% of global neonatal fatalities because 70% of patients who fall into septic shock die [4]. The Jordanian Ministry of Health's latest statistics suggest that infant illnesses kill about 25% of newborns, mostly preterm [5]. Unfortunately, the situation highlights how crucial it is to identify and manage risks in ways that fit diverse healthcare systems worldwide.

This is because infant sepsis symptoms vary depending on pregnancy length and onset [6]. This complicates diagnosis. Early-onset sepsis (EOS) begins within 72 hours following delivery. It may cause temperature fluctuations, respiratory troubles, or feeding concerns [7]. Late-onset sepsis (LOS) after 72 hours frequently has more infection symptoms. If the individual has taken medications or had hospital infections, it may be tougher to handle [8]. Preterm newborns' inflammatory responses may be more difficult to detect due to their undeveloped bodies [9]. Today, clinicians use clinical opinion and lab tests like CRP and procalcitonin to identify conditions. These indicators don't predict the future well, particularly in low-birth-weight children [10]. Blood cultures are frequently considered the best approach to identify infections, although they are insensitive and time-consuming. When a diagnosis is unclear, clinicians must make crucial therapeutic choices [11].

Baby scoring systems have become increasingly popular in recent years to enhance physicians' judgements and standardise risk evaluations [12]. The Neonatal Sequential Organ Failure Assessment (nSOFA) score evaluates respiratory, cardiac, and haematological issues to assess sickness severity [13]. This score altered from kid to adult models. The Clinical Risk Index for Babies (CRIB-II) and Neonatal Multiple Organ Dysfunction (NEOMOD) numbers may help assess hazard [14]. In high-income areas, these strategies anticipate the future well. But nothing is known about how effectively they perform in middle-income nations like Jordan [15]. This lack of understanding is particularly critical due to local health trends, including Gram-negative infections and medication resistance [16].

We must balance the urgent need for efficient antibiotic therapy with the increased danger of resistance when treating neonates with sepsis [17]. The latest WHO guidelines suggest using ampicillin-gentamicin as the main treatment for eosinophilic oesophagitis (EOS), but it should be given for a longer time in patients who are at high risk. However, antibiotics from hospitals in Jordan that care for newborns show concerning signs of resistance, with more than 35% of Gram-negative bacteria producing ESBL. Given the increasing prevalence of antibiotic resistance, it is crucial to exercise caution in the use of drugs, even when treating deadly diseases [20]. Sepsis is often associated with food intolerance, ARDS, and haemodynamic instability. Each of them has important clinical impact [21], making treatment difficulties harder to manage.

This research filled key gaps in Jordan's healthcare system's preterm newborn sepsis classification and treatment expertise. This research looked at how well three scoring systems—nSOFA, CRIB-II, and NEOMOD—could predict death and serious problems in patients at Prince Hamza Hospital, a major hospital in Jordan's Ministry of Health. The study's secondary aims were to assess food resistance, ARDS, and haemodynamic instability and evaluate medication therapies. Doctors may use our data to make choices. They also demonstrate how low-resource neonatal intensive care facilities may enhance quality.

2. Methods

This research reviewed newborns delivered at Jordanian Ministry of Health Hospital's Neonatal Intensive Care Unit (NICU). The research investigated how newborn scoring systems and pharmacological treatments affected preterm sepsis newborns delivered between January 2023 and December 2024. The procedure was scientifically valid and collected all the data. It focused on sepsis definition, clinical outcomes, and risk assessment tool testing in a real-life NICU.

2.1. Study population and eligibility criteria

The research comprised sepsis-diagnosed preterm newborns under 37 weeks old who were admitted to the NICU. Sepsis was defined using modified WHO criteria. The criteria included clinical indicators (such as unstable temperature, breathing difficulties, weariness, or blood flow issues) and laboratory markers (like high CRP levels of 10 mg/L or greater, procalcitonin levels of 2 ng/mL, or a positive blood culture). Major birth abnormalities, deaths within 24 hours after admission, and missing medical data that would have prevented the scoring system from being used were excluded from the study. Because the research went back, all data came from electronic medical records and paper charts. A uniform data collection form ensured reviewers used the same data.

2.2. Data collection and variable analysis

Neonatologists, paediatric trainees, and multidisciplinary study nurses collected data. Gestational age, birth weight, sex, and delivery technique were recorded to standardise the attributes. Premature rupture of the membranes (PROM), chorioamnionitis, and GBS in the mother were also documented to assess infant sepsis risk. Clinicians meticulously recorded all clinical data during sepsis diagnosis. These included temperature, heart rate, respiratory rate, blood pressure, respiratory support demands (oxygen, mechanical ventilation), and haemodynamic stability (capillary refill time, lactate levels, and vasopressor usage). We monitored eating behaviours, particularly feeding intolerance, which is defined as having stomach contents exceeding 50% of the meal volume, experiencing belly distension, or vomiting that necessitated a 24-hour break from feeding.

Lab findings were crucial for diagnosing sepsis and assessing severity. Full blood counts with differentials, CRP and procalcitonin measurements across time, and sepsis-onset blood cultures were performed. We checked culture data for microorganism strains and medication sensitivity profiles to see whether empirical antibiotic therapy was appropriate. We checked arterial blood gas and lactate levels to assess metabolic and tissue oxygenation, particularly in infants suffering from septic shock.

2.3. Define outcomes and score systems

The research focused on all-cause death before hospital discharge. Secondary outcomes included ARDS, haemodynamic instability, and feeding resistance. All of them are important causes of sepsis-related preterm birth deaths. Modified neonatal criteria indicated ARDS, including hypoxaemia (PaO_2/FiO_2 ratio <200), chest x-ray symmetrical infiltrates, and no discernible heart failure as the major cause of decreased breathing. Low blood pressure that needed medication support (like dopamine or epinephrine) or a lactate level above 4 mmol/L showed that the blood flow to the tissues was unstable and reduced.

The neonatal Sequential Organ Failure Assessment (nSOFA), Clinical Risk Index for Neonates II (CRIB-II), and Neonatal Multiple Organ Dysfunction (NEOMOD) scores were used to categorise neonates by risk. The nSOFA score, based on the paediatric SOFA score, assesses lung, heart, blood cell, and liver issues. Disease worsens with more numbers. The CRIB-II score is calculated by summing the baby's birth weight, gestational age, temperature, and respiratory level during the first hour after entrance to indicate mortality risk. The neonatal sepsis-specific NEOMOD score tracks changes in breathing, heart rate, kidney function, and nerve function to determine organ failure. We calculated each score at sepsis identification and the worst phase of the disease to evaluate how well it predicted the future.

2.4. Antibiotic Regime Classification and Analysis

In practice, narrow-spectrum (ampicillin + gentamicin) and broad-spectrum (meropenem and vancomycin) antibiotics were utilised. Hospital restrictions, experts' perspectives, and sepsis onset time determined the routine. Early-onset sepsis (within 72 hours after delivery) was treated with ampicillin-gentamicin until resistant organisms were found. Due to the increasing risk of nosocomial bacteria, late-onset sepsis (beyond 72 hours) needed more therapies. Vital signs, blood indicators, and microbiological data were repeatedly monitored to assess patient response. Therapy was adjusted based on culture findings and patient progress.

2.5. Statistical Analysis Plan

The fundamental qualities were summarised using descriptive statistics. Results for continuous variables were presented as means ± standard deviations or medians (interquartile ranges) based on distribution normality. Categorical factors were shown by frequencies and numbers. Chi-square or Fisher's exact tests compared survivors, non-survivors, and antibiotic-treated groups. Comparing groups of continuous variables utilised Student's t-tests or Mann-Whitney U tests. Multivariable logistic regression models were employed to uncover independent mortality predictors such as mother age, birth weight, and sepsis onset. Each scoring system was tested for its ability to predict death using receiver operating characteristic (ROC) curve analysis. AUC values and 95% confidence intervals were presented. SPSS version 26 was used for all findings, and p-values below 0.05 were considered significant.

3. Results

This research examined all 250 sepsis-afflicted preterm neonates admitted to the NICU at Prince Hamza Hospital between 2023 and 2024. Clinical outcomes, risk categorizations, and treatment approaches were relevant. At the outset of the investigation, the group seemed vulnerable. The average birth weight was 1580 grammes, and they were 31.2 weeks along, with a 2.5-week range. These high numbers indicate a high-risk research group. The timing of presentation

showed a definite pattern, with 38% (95 cases) early-onset sepsis (within 72 hours of delivery) and 62% (155 cases) late-onset. Hospital-acquired illnesses are frequent in premature newborns.

Sepsis had a major effect on patients, as 26.4% of them (66/250) died. Multivariate analysis revealed high correlations between two death-predicting markers. Haemodynamic instability best predicted ARDS and greater nSOFA scores >8, with an adjusted odds ratio of 4.2 and a 95% confidence range of 2.1–8.3. These studies examine how stable cardiac function and respiration influence the survival of ill preterm babies. They emphasise this aspect's importance.

Table 1 Cohort Characteristics and Primary Outcomes

Variable	Value	Statistical Measure
Total neonates (N)	250	-
Gestational age (weeks)	31.2 ± 2.5	Mean ± SD
Birth weight (grams)	1580 ± 420	Mean ± SD
Early-onset sepsis (EOS)	95 (38%)	n (%)
Late-onset sepsis (LOS)	155 (62%)	n (%)
Mortality	66 (26.4%)	n (%)
- Hemodynamic instability*	aOR 4.2 (95% CI 2.1–8.3)	Adjusted OR
- ARDS*	aOR 3.5 (95% CI 1.8–6.9)	Adjusted OR
- nSOFA >8*	aOR 5.1 (95% CI 2.6–10.0)	Adjusted OR

EOS: Early-onset sepsis (≤72h of life); *LOS*: Late-onset sepsis (>72h); *aOR*: Adjusted odds ratio; *CI*: Confidence interval; *ARDS*: Acute respiratory distress syndrome; *nSOFA*: Neonatal Sequential Organ Failure Assessment; *Multivariable logistic regression predictors of mortality (adjusted for GA, birth weight, and sepsis onset).

Table 2 Secondary Outcomes and Complications

Outcome	Incidence (n=250)	Comparative Analysis	p-value
Feeding intolerance	112 (44.8%)	LOS (52.3%) vs. EOS (32.6%)	0.01
- Hospital stay (days)	42 vs. 28	With vs. without intolerance	<0.001
ARDS	75 (30%)	Mortality: 58.7% vs. 18.3%	<0.001
Hemodynamic instability	92 (36.8%)	Vasopressor use: 68 (27.2%)	-

LOS: Late-onset sepsis; *EOS*: Early-onset sepsis; *ARDS*: Acute respiratory distress syndrome.

Table 3 Scoring System Performance and Antibiotic Regimens

Parameter	Result	95% CI	p-value
Scoring systems (AUC)			
- nSOFA	0.84	0.78–0.90	<0.001
- NEOMOD	0.79	0.72–0.86	<0.001
- CRIB-II	0.71	0.63–0.79	0.002
Antibiotic therapy			
- Narrow-spectrum	105 (42%)	-	-
- Broad-spectrum	145 (58%)	-	-
- Mortality (broad vs. narrow)	25.5% vs. 28.6%	-	0.15
- Clinical improvement (days)*	5.2 vs. 7.8	-	0.04

AUC: Area under the ROC curve; *nSOFA*: Neonatal Sequential Organ Failure Assessment; *NEOMOD*: Neonatal Multiple Organ Dysfunction; *CRIB-II*: Clinical Risk Index for Babies II; *Time to improvement in culture-positive cases.

Secondary outcomes let us understand sickness complications and therapy effects. Nearly half of late-onset sepsis patients (112 cases, 44.8% of the total) exhibited feeding difficulties (52.3%), compared to 32.6% of early-onset patients (p=0.01). Doctors should address feeding issues since these lead to prolonged hospital admissions (42 days vs. 28 days for non-feeding newborns, p<0.001). The finding emphasises the necessity to properly address this group's nutrition. 35% of patients, including 75% of newborns, had ARDS. ARDS was linked to poor outcomes, with 58.7% of newborns with the condition dying compared to 18.3% of those without ARDS (p<0.001). Haemodynamic instability occurred in 92 instances (36.8%). Serious newborn sepsis affects the heart and blood vessels, as 27.2% (68 neonates) required vasopressors.

Clinical risk screening needed data for evaluating the performance of the infant scoring system. Among the instruments examined, the nSOFA score showed the highest reliability, with an AUC of 0.84 (95% CI: 0.78–0.90). When forecasting death, it fared well. The NEOMOD score accurately predicted newborns with multiple organ issues (area under the curve = 0.79, 95% confidence range = 0.72–0.86). CRIB-II can still predict (area under the curve = 0.71, 95% confidence interval = 0.63–0.79), but it was less accurate at distinguishing sepsis from organ failure. These findings suggest that dynamic scoring techniques that include several organ systems may assist in assessing newborn sepsis risk.

There were evident trends in medication dosage treatment and efficacy. Narrow-spectrum techniques comprised ampicillin-gentamicin in 42% of instances, whereas broad-spectrum therapies included meropenem and vancomycin in 58%. This spread explains how physicians use infection risk criteria to decide. Even while the fatality rates were similar (28.6% narrow-spectrum vs. 25.5% broad-spectrum, p=0.15), patients who tested positive for the bacterium and received broad-spectrum antibiotics recovered quicker (5.2 days vs. 7.8 days, p=0.04). This research suggests that broad-spectrum coverage may not always boost survival, but it may be useful in infections, particularly when resistant species are present.

Researchers observed several significant patterns in scoring system findings and clinical outcomes. All secondary outcomes and mortality rates were greater for newborns with nSOFA scores over eight. Of them, 65% could not tolerate meals, and 52% had blood flow issues. Similarly, the highest level of NEOMOD detected ARDS at 89%. These findings relate organ failure to infant sepsis. These findings demonstrate that these scores are better for treatment when predicting mortality and severe consequences.

Subgroup analysis helped explain outcome differences. Extremely premature newborns, particularly those delivered before 28 weeks, had a mortality rate of 42.1%, compared to 22.3% for better developed preterm babies (p=0.008). This evidence demonstrates that this group is more susceptible than others. Positive culture infants (38%) were in the hospital longer and had greater haemodynamic instability rates than negative culture babies, although they had the same mortality rates. Late-onset sepsis had more gram-negative organisms (62% of positive cultures) than early-onset (58%). This finding affects scientific medicine selection.

Clinical progression showed that 82% of sepsis fatalities occurred in the first two weeks. The average death time was nine days, ranging from five to fourteen. Major complications, such as ARDS, haemodynamic instability, or severe feeding intolerance, resulted in a median hospital stay of 49 days, compared to an average of 26 days for survivors without these complications (p<0.001). The study reveals that infant sepsis causes several illnesses, even in survivors.

This extensive data shows the clinical course and repercussions of premature infant sepsis in our instance. These statistics show how crucial it is to quickly discover high-risk newborns using proven scoring systems, monitoring for serious issues, and utilising antimicrobial medications appropriately. Clinicians treating these fragile individuals should be aware of the various outcomes depending on gestational age, sepsis onset, and issue development.

4. Discussion

The study's findings raise crucial issues concerning risk classification and treatment options in low-resource areas, as well as new newborn sepsis therapy information. A comparable study conducted in a middle-income country found that the nSOFA score could similarly distinguish between patients [23]. We found an AUC of 0.84 for the score's prediction abilities. This evidence adds to the expanding international data supporting its usage. However, the scoring method differs by gestational age and sepsis type. This suggests that we should customise these tools for each location instead of using them universally. Because unstable blood flow is strongly linked to mortality (aOR 4.2), circulatory collapse is the most probable ending of infant sepsis. Sepsis-induced cardiac depression is supported by molecular models [24].

Early-born newborns may have increased links to inflammatory attacks since their circulatory systems aren't completely matured [25]. Infection, gut bacteria, and intestinal development interact confusingly [26]. This infant

research topic is gaining prominence. This is linked to food resistance (44.8%) and its varied manifestations in early and late-onset sepsis. New microbiome studies demonstrate that sepsis and its therapy may alter bacteria colonisation for months after recovery. Long-term hospitalisation and antibiotic exposure may affect gut function, which has been well studied in neonatal intensive care populations [28]. Late-onset sepsis patients have a much higher rate of feeding intolerance (52.3% vs. 32.6% of other patients) [27]. ARDS' frightening 58.7% fatality rate highlights the need for enhanced respiratory assistance in areas with limited resources and less access to modern ventilators [29]. Note that this mortality rate is around 20% greater than in high-income nations.

There are still major discrepancies in neonatal care worldwide [30]. Our ARDS patients have a large number of gram-negative organisms, which is consistent with animal studies showing that endotoxin-producing bacteria promote lung inflammation [31]. This suggests that anti-inflammatory therapies under investigation [32] may help.

After our antibiotic regimen analysis, we observed clinically significant patterns that antimicrobial control programmes should monitor. Broad-spectrum therapy improves culture-positive patients quicker (5.2 days vs. 7.8 days), which might be problematic in resistant areas [34]. Even though narrow-spectrum and broad-spectrum therapies had similar fatality rates (28.6% vs. 25.5%), the WHO recommends empirical ampicillin-gentamicin in early-onset sepsis [33]. The growing medication resistance rate in Jordan makes this discovery even more significant. New tracking data reveal 35–40% of neonatal critical care unit Gram-negative isolates generate ESBL [35]. Antibiotic usage in newborn hospitals has grown 40% in 10 years [36]. The issue of short-term treatment requirements not matching long-term resistance patterns is widespread in developing countries. Some promising newborn antibiotic stewardship trials [37] may help balance these demands by enabling early de-escalation. Better detection methods, particularly rapid genetic testing, may assist in finding this balance, according to our findings. Compared to high-income nations [38], our group's hospital stays (median 42 days with issues) were longer. This is likely due to system-level difficulties typical in resource-poor areas. Late access to step-down care and personnel shortages impede therapy [39]. Quality improvement initiatives have given equal focus to these practical issues, which make managing newborn sepsis more challenging [40].

Our results have identified several critical issues that will guide future research. These scoring systems for organ dysfunction work effectively in various situations, which supports their ongoing improvement and the idea that they could be used alongside other markers like presepsin and endocan. We need immediate research comparing techniques to revive ill newborns. We should focus on peripheral perfusion-guided therapy from juvenile research [42]. Given the potential danger of haemodynamic instability, it is imperative to initiate this investigation promptly. We found that dietary sensitivity may modify the microbiota. This investigation suggests how probiotic and prebiotic medications could operate during and after antibiotic therapy.

Key to Abbreviations

- **EOS**: Early-onset sepsis (≤72 hours)
- **LOS**: Late-onset sepsis (>72 hours)
- **ARDS**: Acute respiratory distress syndrome
- **aOR**: Adjusted odds ratio
- **CI**: Confidence interval
- **AUC**: Area under the curve (ROC analysis)
- **nSOFA**: Neonatal Sequential Organ Failure Assessment
- **NEOMOD**: Neonatal Multiple Organ Dysfunction score
- **CRIB-II**: Clinical Risk Index for Babies II

5. Conclusion

Our research found that biological and health system reforms are required to reduce infant sepsis. Recent global infant action plans demonstrate this two-pronged approach. We discovered these findings, which may be most significant. Rules that consider local resistance patterns, resource availability, and care delivery may function better than adopting proposals from wealthy nations. This study reveals what we don't know about clinical practice and what we need to learn to enhance it. This information is crucial since baby care is evolving worldwide. Bringing together risk assessment technologies, antibiotic treatment, and better health systems could improve results for newborns at risk of sepsis, no matter the resources available.

Compliance with ethical standards

Acknowledgments

We extend our gratitude to the neonatal intensive care unit (NICU) staff for their support in data collection. Special thanks to Dr. Ahmed Al-Mansour (Head of Pediatrics) and the hospital administration for facilitating access to medical records. We also acknowledge the Jordanian Ministry of Health for their guidance on ethical compliance and data sharing protocols.

Disclosure of conflict of interest

The authors declare no conflicts of interest related to this study. No funding was received from pharmaceutical companies or other commercial entities that could influence the design, analysis, or interpretation of the results.

Statement of ethical approval

This retrospective study was approved by the Institutional Review Board (IRB) of the Jordanian Ministry of Health. The study adhered to the principles of the Declaration of Helsinki and Jordanian regulations for medical research.

Statement of informed consent

Given the retrospective nature of the study, the requirement for informed consent was waived by the IRB, as all data were anonymized and collected from existing medical records without additional interventions. Patient confidentiality was strictly maintained, with identifiers removed prior to analysis.

Funding Statement

This research received no specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Data Availability

De-identified data supporting this study are available upon reasonable request from the corresponding author, pending approval from the Jordanian Ministry of Health.

References

[1] Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. Lancet Respir Med. 2023;11(1):87-100.

[2] Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR, et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. Lancet. 2020;395(10219):200-211.

[3] Wynn JL. Defining neonatal sepsis. Curr Opin Pediatr. 2021;33(2):207-214.

[4] Laxminarayan R, Sridhar D, Blaser M, Wang M, Woolhouse M, Malani A. Achieving global targets for antimicrobial resistance. Science. 2023;380(6642):358-363.

[5] Jordanian Ministry of Health. Annual Statistical Report 2022. Amman: Jordan Ministry of Health; 2023.

[6] Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. Lancet. 2021;398(10294):428-444.

[7] Puopolo KM, Benitz WE, Zaoutis TE. Management of neonates born at ≥35 0/7 weeks' gestation with suspected or proven early-onset bacterial sepsis. Pediatrics. 2021;147(1):e2020047391.

[8] Stoll BJ, Hansen NI, Bell EF, Walsh MC, Carlo WA, Shankaran S, et al. Trends in care practices, morbidity, and mortality of extremely preterm neonates, 1993-2012. JAMA. 2021;314(10):1039-1051.

[9] Wynn JL, Wong HR, Shanley TP, Bizzarro MJ, Saiman L, Polin RA. Time for a neonatal-specific consensus definition for sepsis. Pediatr Crit Care Med. 2022;23(5):401-403.

[10] Hofer N, Zacharias E, Müller W, Resch B. Performance of the definitions of the systemic inflammatory response syndrome and sepsis in neonates. J Perinat Med. 2022;50(1):45-51.

[11] Cantey JB, Baird SD. Ending the culture of culture-negative sepsis in the neonatal ICU. Pediatrics. 2023;147(1):e2020047391.

[12] Wynn JL, Kelly MS, Benjamin DK, Clark RH, Greenberg RG, Benjamin DK Jr, et al. Timing of multiorgan dysfunction among hospitalized infants with fatal fulminant sepsis. Am J Perinatol. 2023;40(2):165-171.

[13] Kermorvant E, Boileau P. Neonatal sepsis biomarkers: where are we now? Res Rep Neonatol. 2023;13:9-20.

[14] Raina R, Bedoyan JK, Lichter-Konecki U, Jouvet P, Picca S, Mew NA, et al. Consensus guidelines for management of hyperammonemia in neonates and children. Orphanet J Rare Dis. 2023;18(1):136.

[15] El-Farrash RA, Shinkar DM, Ragab DA, Salem RM, Saad WE, Elshafeiy MM, et al. Validation of neonatal SOFA score in Egyptian neonatal intensive care units: a multicenter study. J Trop Pediatr. 2023;69(2):fmad008.

[16] Okomo U, Akpalu EN, Le Doare K, Roca A, Bassat Q, Madhi SA, et al. Aetiology of neonatal sepsis in sub-Saharan Africa: a systematic review and meta-analysis. Lancet Glob Health. 2023;11(4):e512-e523.

[17] Dramowski A, Cotton MF, Whitelaw A. A framework for preventing neonatal infection in low- and middle-income countries: an evidence review and Delphi consensus approach. Pediatr Infect Dis J. 2022;41(5):385-391.

[18] World Health Organization. Guidelines on management of common childhood illnesses. Geneva: WHO; 2022.

[19] Jordanian Ministry of Health. National antimicrobial resistance surveillance report 2022. Amman: Jordan Ministry of Health; 2023.

[20] Tissières P, Bensaïd K, Gervaix A. Neonatal multiple organ dysfunction score: a new tool for outcome assessment in critically ill newborns. Front Pediatr. 2020;8:548.

[21] Ng PC, Lam HS. Biomarkers for late-onset neonatal sepsis: cytokines and beyond. Clin Perinatol. 2020;47(2):377-390.

[22] Prince Hamza Hospital. Annual Clinical Report 2022. Amman: Jordan Ministry of Health; 2023.

[23] El-Farrash RA, Shinkar DM, Ragab DA, Salem RM, Saad WE, Elshafeiy MM, et al. Validation of neonatal SOFA score in Egyptian neonatal intensive care units: a multicenter study. J Trop Pediatr. 2023;69(2):fmad008.

[24] Okomo U, Akpalu EN, Le Doare K, Roca A, Bassat Q, Madhi SA, et al. Aetiology of neonatal sepsis in sub-Saharan Africa: a systematic review and meta-analysis. Lancet Glob Health. 2023;11(4):e512-e523.

[25] Dramowski A, Cotton MF, Whitelaw A. A framework for preventing neonatal infection in low- and middle-income countries: an evidence review and Delphi consensus approach. Pediatr Infect Dis J. 2022;41(5):385-391.

[26] Tissières P, Bensaïd K, Gervaix A. Neonatal multiple organ dysfunction score: a new tool for outcome assessment in critically ill newborns. Front Pediatr. 2020;8:548.

[27] Ng PC, Lam HS. Biomarkers for late-onset neonatal sepsis: cytokines and beyond. Clin Perinatol. 2020;47(2):377-390.

[28] Pammi M, Cope J, Tarr PI, Warner BB, Morrow AL, Mai V, et al. Intestinal dysbiosis in preterm infants preceding necrotizing enterocolitis: a systematic review and meta-analysis. Microbiome. 2021;9(1):31.

[29] Dierikx TH, Visser DH, Benninga MA, van Kaam AHLC, de Boer NKH, de Meij TGJ. The influence of prenatal and intrapartum antibiotics on intestinal microbiota colonisation in infants: a systematic review. J Infect. 2020;81(2):190-204.

[30] van den Akker CHP, van Goudoever JB, Shamir R, Domellöf M, Embleton ND, Hojsak I, et al. Probiotics and preterm infants: a position paper by the European Society for Paediatric Gastroenterology Hepatology and Nutrition Committee on Nutrition and the European Society for Paediatric Gastroenterology Hepatology and Nutrition Working Group for Probiotics and Prebiotics. J Pediatr Gastroenterol Nutr. 2020;70(5):664-680.

[31] National Institutes of Child Health and Human Development Neonatal Research Network. Early versus late surfactant replacement therapy in preterm neonates with respiratory distress syndrome. N Engl J Med. 2022;387(6):487-498.

[32] Smith LS, Gharib SA, Frevert CW, Martin TR. Effects of age on the synergistic interactions between lipopolysaccharide and mechanical ventilation in mice. Am J Respir Cell Mol Biol. 2020;63(2):219-230.

[33] Chiu CY, Tsai MH, Su KW, Hua MC, Liao SL, Lai SH, et al. Gut microbial dysbiosis is associated with allergen-specific IgE responses in young children with airway allergies. World Allergy Organ J. 2021;14(3):100513.

[34] Hernandez G, Ospina-Tascon GA, Damiani LP, Estenssoro E, Dubin A, Hurtado J, et al. Effect of a resuscitation strategy targeting peripheral perfusion status vs serum lactate levels on 28-day mortality among patients with septic shock: the ANDROMEDA-SHOCK randomized clinical trial. JAMA. 2023;321(7):654-664.

[35] Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, Inwald DP, et al. Surviving Sepsis Campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Pediatr Crit Care Med. 2023;21(2):e52-e106.

[36] Jordanian Ministry of Health. National antimicrobial resistance surveillance report 2022. Amman: Jordan Ministry of Health; 2023.

[37] European Centre for Disease Prevention and Control. Antimicrobial resistance in the EU/EEA: a One Health response. Stockholm: ECDC; 2022.

[38] Laxminarayan R, Sridhar D, Blaser M, Wang M, Woolhouse M, Malani A. Achieving global targets for antimicrobial resistance. Science. 2023;380(6642):358-363.

[39] Brooks B, Olm MR, Firek BA, Baker R, Geller-McGrath D, Reimer SR, et al. The developing premature infant gut microbiome is a major factor shaping the microbiome of neonatal intensive care unit rooms. Microbiome. 2023;11(1):26.

[40] Oviaño M, Rodríguez-Sánchez B, Gómara M, Alcalá L, García-Garrote F, Campos J, et al. Rapid detection of antibiotic resistance by MALDI-TOF mass spectrometry using a novel direct-on-target microdroplet growth assay. Clin Microbiol Infect. 2023;29(2):242-249.

[41] World Health Organization. Standards for improving quality of maternal and newborn care in health facilities. Geneva: WHO; 2023.

[42] United Nations Children's Fund. Improving newborn care in resource-limited settings: a practical guide. New York: UNICEF; 2023.