KJMS / OPEN ACCESS Print ISSN: 2790-0207 Online ISSN: 2790-0215

Original article

Bacterial neonatal sepsis and outcome in kirkuk city 2021

Hussein Ibrahim Mahdi[1], Jameel Ibrahim Azeez [1,*], and Ali Qais Abdulkafi[2]

[1] Pediatrics Department, Azadi Teaching Hospital, Kirkuk, Iraq.

[2] Pediatric Department, Nasr Hospital, Kirkuk, Iraq.

Corresponding author Email address: jameel.azeez@yahoo.com

DOI: https://doi.org/10.32894/kjms.2021.169937

Abstract:

- ***Background*:** Neonatal sepsis remains a leading cause of neonatal mortality, accounting for 30–50% of neonatal deaths annually in developing countries. It is defined as bacteremia with clinical signs of infection during the first month of life. This study aimed to identify the prevalent pathogens causing neonatal sepsis in neonates admitted to the Special Care Baby Unit (SCBU), assess the differences in microbial patterns between early-onset (EOS) and late-onset sepsis (LOS), determine associated risk factors, and evaluate pathogen-specific case fatality rates.
- ***Methods:*** A prospective study was conducted in SCBUs of pediatric hospitals in Kirkuk, Iraq, over six months (January 1 to June 1, 2021). Neonates with clinical suspicion of sepsis underwent blood cultures and were assessed for risk factors and outcomes.
- ***Result:*** Out of 200 neonates, 87.5% had culture-proven sepsis. Common risk factors included prematurity, prolonged rupture of membranes, and maternal fever. Gram-negative bacteria predominated, with *E. coli* and *Klebsiella* common in early and late-onset sepsis, respectively. Mortality reached 41%, highest with *Candida albicans* and *Pseudomonas aeruginosa*.
- ***Conclusions:*** Neonatal sepsis remains a major health burden in developing countries. Prematurity, prolonged membrane rupture, and maternal fever are significant risk factors. Gram-negative organisms are the predominant pathogens, with notable differences between EOS and LOS.

- **Keywords:** Neonate, Bacterial, Sepsis, Kirkuk

INTRODUCTION

Sepsis remains a major contributor to global morbidity and mortality and has been designated a health priority by the World Health Organization (1). Among all age groups, neonates are particularly vulnerable, with an estimated 3 million affected annually worldwide—approximately 22 per 1,000 live births—resulting in a mortality rate of 11–19% and a range of unquantified long-term neurological complications (2). However, the lack of standardized criteria for diagnosing neonatal sepsis complicates efforts to harmonize international data. In adults, the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) defines sepsis as a life-threatening organ dysfunction resulting from a dysregulated host response to infection (3). The Sequential Organ Failure Assessment (SOFA) score, developed for adults, has been adapted to pediatric populations and shown to be a reliable predictor of in-hospital mortality (4). More recently, a neonatal version of SOFA (nSOFA) has been introduced and found effective in predicting mortality in very low birth weight infants with late-onset sepsis (5).

Neonates differ significantly from older children and adults due to their immature immune systems and potential intrauterine exposure to infections (6). Neonatal immunology remains poorly characterized and is often inferred from umbilical cord blood studies, which tend to be more immunotolerant and may not fully reflect postnatal immune responses (7). A recent meta-analysis showed that the use of the neonatal early-onset sepsis (EOS) calculator led to

a significant reduction in the use of empirical antibiotics for suspected EOS (8). Additionally, biomarkers such as procalcitonin and C-reactive protein (CRP) have shown promise in guiding shorter antibiotic therapy in neonates who recover quickly and have negative blood cultures (9). While histological confirmation of chorioamnionitis may support the diagnosis of neonatal sepsis, it is not always conclusive (10). The lack of a globally accepted consensus definition for neonatal sepsis and the absence of long-term outcome measures continue to hinder collaborative research and benchmarking efforts. Establishing standardized core outcomes and involving families in prioritizing research goals are essential steps forward (11, 12).

This study was conducted to identify the prevalent pathogenic agents in neonatal sepsis among neonates admitted to the Special Care Baby Unit (SCBU), examine differences in microbial patterns between early-onset and late-onset sepsis, determine the risk factors associated with an increased incidence of sepsis, and assess the case fatality rates of various pathogens.

PATIENT and METHOD

This prospective study was conducted to identify the patterns of pathogenic organisms responsible for neonatal sepsis in neonates admitted to the Special Care Baby Units (SCBUs) of pediatric hospitals. Between January 1 and June 1, 2021, a total of 200

neonates presenting with clinical signs suggestive of sepsis were enrolled. These signs included reluctance to feed, apnea, cyanosis, dyspnea, or a history of infection during the perinatal period.

Neonates were eligible for inclusion if they exhibited clinical features consistent with sepsis. Data collected included age, sex, date and reason for admission, age at symptom onset, prior hospitalization history, and blood culture results. Each neonate was monitored throughout their hospital stay to assess the course of illness and final outcome. Neonates who had received antibiotic therapy before admission were excluded from the study.

Participants were categorized into two groups based on age at symptom onset: early-onset sepsis (EOS), occurring within the first 0–7 days of life, and late-onset sepsis (LOS), presenting between 8–30 days of life.

To identify causative organisms, 2 mL of blood was drawn aseptically from two separate peripheral venipuncture sites prior to antibiotic administration. Each sample was inoculated into brain-heart infusion broth and incubated aerobically at 37°C for seven days. For neonates at risk of anaerobic infections—such as those with EOS, omphalitis, or necrotizing enterocolitis—a third blood sample was collected and inoculated into thioglycolate broth for anaerobic culture.

Subcultures from conventional bottles were performed after 6–12 hours on blood and MacConkey agar. A second subculture followed at 48 hours. Culture bottles were

inspected macroscopically every day for seven days. Upon visual evidence of bacterial growth, the bottles were opened aseptically, and a small amount of broth was transferred using a sterile loop for a third subculture.

Bacterial isolates were identified using conventional methods as outlined in *Bailey & Scott's Diagnostic Microbiology*. Gram-positive streptococci were recognized on blood agar by their complete hemolysis zones and were further tested using bacitracin to rule out Group A streptococci. *Listeria monocytogenes* was identified as Gram-positive rods with characteristic motility and catalase positivity. *Candida albicans* was identified by its colony morphology and confirmed by the germ tube test.

Data were analyzed using percentage distributions, means, chi-square test, z-test, and P-values. A P-value > 0.05 was considered not significant, < 0.05 was considered significant, and < 0.001 was considered highly significant.

RESULTS

Over the six-month study period, 200 neonates presenting with clinical features of septicemia were enrolled. Neonates who had received prior antibiotic therapy were excluded. Blood cultures confirmed the presence of causative organisms in 175 cases, representing 87.5% of the total.

As shown in **Table 1**, 118 (59%) of the neonates were preterm, while 82 (41%) were full-term. **Table 2** illustrates that 120 neonates (60%) were male and 80 (40%) were female.

Table 1: Classification of 200 cases of neonatal sepsis according to gestational age.

Variable	No.	Percentage
Full term	82	41
Preterm	118	59
Total	200	

P value > 0.06 (not significant)

Table 2: Sex distribution of neonatal sepsis

Variable	No.	Percentage
Male	120	60
Female	80	40
Total	200	

P value > 0.08 (not significant)

Table 3 shows that prolonged rupture of membranes (defined as >18 hours) was documented in 123 out of 200 cases (61.5%). Maternal fever at the time of delivery was reported in 130 neonates (65%), while 70 (35%) had no maternal fever history **(Table 4).**

Table 3: Effect of prolonged rupture of amniotic membranes on neonatal sepsis

Variable	No.	Percentage
More than 18 hours	123	61.5
Less than 18 hours	77	38.5

P value < 0.04 (significant)

Table 4: Association between maternal fever and neonatal sepsis

Maternal fever	No.	Percentage
Yes	130	65
No	70	35
Total	200	

P value < 0.001 (highly significant)

Early-onset sepsis (EOS), defined as occurring within the first 0–7 days of life, was observed in 69 neonates (34.5%), while 131 (65.5%) had late-onset sepsis (LOS), occurring from 8–30 days **(Table 5)**. Among the culture-positive cases, 63 (36%) were associated with EOS and 112 (64%) with LOS.

Table 5: Classification of 200 patients with neonatal sepsis according to early and late onset of disease

Patient group	Early onset (0–7 days)		Late onset (8–28 days)	
	No.	%	No.	%
Culture +ve	63	36%	112	64%
Culture -ve	6	24%	19	76%
Total	69	34.5%	131	65.5%

P value > 0.07 (not significant)

Gram-negative bacteria were the predominant pathogens, isolated in 138 out of 175 culture-positive cases (78.8%), followed by Gram-positive organisms in 34 cases (19.42%) and *Candida albicans* in 3 cases (1.71%) **(Table 6)**.

Table 6: Distribution of pathogenic agents of 175 culture-positive neonatal sepsis cases

Pathogenic agent	No.	Percentage
Gram -ve	138	78.85
Klebsiella	58	33.14
E. coli	47	26.8
E. aerogenes	24	13.7
Pseudomonas	3	1.7
Proteus	6	3.42
Gram +ve	34	19.42
Strept. faecalis	13	7.42
GBS	7	4
Listeria	1	0.57
Pneumococci	5	2.85
Staph.	8	4.57
Candida albicans	3	1.73
Total	175	

P value < 0.05 (significant)

Table 7 details pathogen distribution: in EOS, *E. coli* was the leading organism (31 cases, 49.2%), followed by *Klebsiella* (8 cases, 12.69%). In LOS, *Klebsiella* was most common (50 cases, 44.64%), followed by *E. coli* (16 cases, 14.28%). Other organisms showed no statistically significant variation between early and late-onset cases.

Table 7: Classification of 175 cases of culture-positive sepsis according to age of onset of disease

Patient group	Early onset		Late onset	
	No.	%	No.	%
Klebsiella	8	12.69	50	44.64
Escherichia coli	31	49.20	16	14.28
E. aerogenes	6	9.52	18	16.07
Proteus	2	3.17	4	3.57
Pseudomonas	1	1.58	2	1.78
GBS	5	7.93	2	1.78
Listeria	1	1.58	0	0
Strept. faecalis	8	12.69	5	4.46
Staph.	1	1.58	7	6.25
Pneumococci	0	0	5	4.46
Candida	0	0	3	2.67
Total	63	36%	112	64%

P value < 0.001 (highly significant)

Prior hospitalization was associated with a substantial proportion of LOS caused by *Klebsiella* (32 cases, 53.3%), *Enterobacter aerogenes* (12 cases, 20%), and *E. coli* (6 cases, 10%) **(Table 8)**.

Table 8: History of prior hospitalization among different bacterial isolates in late onset disease

Patient group	Late onset disease	History of hospitalization	
		No	%
Klebsiella	50	32	53.3
E. aerogenes	18	12	20
E. coli	16	6	10
Proteus bacteria	4	2	3.33
Strept. faecalis	5	1	1.66
Staph.	7	3	5
Pseudomonas	2	2	3.33
GBS	2	0	0
Pneumococci	5	1	1.66
Candida	3	1	1.66
Total	112	60	53.57%

P value > 0.08 (not significant)

The overall mortality among the studied neonates was 82 out of 200 (41%) **(Table 9)**. Among culture-positive cases, the mortality rate was 24/63 (42.8%) in EOS and 52/112 (46.42%) in LOS. In the culture-negative group, 2/6 (33.33%) in EOS and 4/19 (21.05%) in LOS died.

Table 9: Case fatality rate in early and late neonatal sepsis among 200 patients

Patient group	Early	Late	Total death
Culture +ve	24/63 (42.8%)	52/112 (46.42%)	76/175 (43.42%)
Culture -ve	2/6 (33.33%)	4/19 (21.05%)	6/25 (24%)
Total	26/69 (42.02%)	56/131 (42.7%)	82/200 (41%)

P value > 0.06 (not significant)

As illustrated in Table 10, the case fatality rates varied widely by pathogen. Both *Pseudomonas aeruginosa* and *Candida albicans* infections were associated with 100% mortality. In EOS, the leading fatal organisms were *Staphylococcus* (1/1, 100%), Group B Streptococcus (GBS) (3/5, 60%), and *Klebsiella* (4/8, 50%). In LOS, *Staphylococcus* (4/7, 57.14%), *Klebsiella* (28/50, 56%), and *Proteus* (3/6, 50%) were associated with the highest mortality.

Table 10: Comparison of pathogenic isolates and case fatality in early and late onset sepsis among 175 culture-positive patients

Pathogenic agent	No.	Death	
		Early (%)	Late (%)
Klebsiella	58	4/8 (50)	28/50 (56)
E. coli	47	9/31 (29.03)	4/16 (25)
E. aerogenes	24	1/6 (16.66)	8/18 (44.4)
Strept. faecalis	13	3/8 (37.5)	1/5 (20)
Staph.	8	1/1 (100)	4/7 (57.14)
Proteus	6	0	3/6 (50)
GBS	7	3/5 (60)	0
Pseudomonas	3	1/1 (100)	2/2 (100)
Listeria	1	1/1 (100)	0
Pneumococci	5	0	0
Candida	3	1/1 (100)	2/2 (100)
Total	175	24	52

P value < 0.05 (significant)

DISCUSSION

Neonatal sepsis continues to be a leading cause of mortality in neonates despite advances in hygiene practices, the availability of more effective antimicrobial agents, and improved diagnostic and therapeutic techniques. This highlights the persistent challenge posed by sepsis in this vulnerable age group.

In this study, sepsis was more frequently observed among preterm neonates (59%), a finding consistent with the data reported by Asindi A. (13). Male neonates were affected more often than females, with a male-to-female ratio of approximately 3:2 (60% vs. 40%). This gender-based disparity aligns with the results of Bennet R. (61%) and Samanci (58%) (14,15).

Risk factors such as premature rupture of membranes and maternal fever were frequently reported, in 61.5% and 65% of cases respectively, supporting earlier findings by Gladstone I.M. (16). These maternal factors appear to play a significant role in both early-onset and late-onset neonatal sepsis.

Early-onset sepsis (EOS) was observed in 34.5% of neonates, which is similar to the incidence reported by Al-Harthi A. in Saudi Arabia (36%) (17). However, this figure is lower than that recorded by Sanghavi in the USA (49%) and higher than David J.'s report from London (29.25%) (18). Such variation may reflect differences in patient populations; notably, many of the neonates in this study were referred from district hospitals or had

prior hospitalization, contributing to the predominance of late-onset nosocomial infections.

Gram-negative bacteria were the predominant isolates in both early and late-onset sepsis, accounting for 78.8% of cases. This observation is consistent with reports from Koutouby A. in Saudi Arabia (80%), Stockholm (77%), and the United Arab Emirates (77.8%) (19). Gram-negative organisms are commonly encountered in neonatal care settings, including SCBUs and nurseries.

Among Gram-negative pathogens, *Pseudomonas aeruginosa* was identified in only three cases (1.78%), with two of these being late-onset infections in low-birth-weight neonates who had prolonged hospital stays. This incidence is markedly lower than that reported by Al-Harthi A. in Saudi Arabia (11.47%) and Gladstone in London (7.0%) (19). The variation in *Pseudomonas* incidence likely reflects differences in nosocomial pathogens across intensive care units. Despite its low frequency, *Pseudomonas* infection requires close monitoring due to its association with high mortality, highlighting the need for targeted infection control measures in our unit.

Staphylococcal infections were detected in eight cases (4.57%), with *Staphylococcus aureus* in two cases and *Staphylococcus epidermidis* in six. Prolonged hospitalization was the primary risk factor. This incidence aligns with findings from Mohammed S. in Kuwait (4.02%) but is significantly lower than the 25% reported by Mitchison R. in Stockholm

(20). The relatively low incidence in our study may be attributed to the exclusion of neonates who had received prior antibiotic therapy and the absence of central venous catheters for total parenteral nutrition in our unit.

The overall mortality rate in this study was 41%, which is considerably higher than that reported by Battistio O. in the USA (18.8%) and Schat A. in Stockholm (22%) (20,21). Several factors may contribute to this elevated mortality, including the predominance of preterm neonates, delayed diagnosis due to patient transfers from district hospitals, and the presence of severe complications such as apnea, disseminated intravascular coagulation (DIC), and intraventricular hemorrhage. Many affected neonates succumbed shortly after admission, despite receiving available antimicrobial and supportive therapies.

CONCLUSION

Neonatal septicemia remains more prevalent in developing countries compared to developed nations, with a distinct predominance of Gram-negative bacterial pathogens and an unacceptably high mortality rate. Key risk factors identified include prematurity, prolonged rupture of membranes, and maternal fever during pregnancy. These findings underscore the need for improved preventive strategies, early diagnosis, and targeted interventions to reduce the burden of neonatal sepsis.

RECOMMENDATIONS

Strengthening antenatal care and ensuring timely obstetric management are essential for the early identification and treatment of mothers at risk of neonatal sepsis. Efforts should also focus on preventing prematurity and low birth weight, both of which significantly contribute to the incidence of neonatal infections. Additionally, implementing effective infection control measures within neonatal care units is crucial to reducing the spread of nosocomial infections, which are associated with high frequency and poor outcomes. Ensuring the consistent availability of appropriate antibiotics and enhancing the quality of neonatal intensive care services are also vital components in improving sepsis-related outcomes.

Ethical Clearance:

In accordance with the 2013 WMA Helsinki Declaration, all ethical aspects of this study were approved. Before enrolling the participants, an informed oral consent was obtained from their families as an ethical agreement. Additionally, approval from the hospital administrator was obtained.

Financial support and sponsorship:

Nil.

Conflicts of interest:

There are no conflicts of interest.

References

1. Reinhart K. Recognizing sepsis as a global health priority—a WHO resolution. N Engl J Med. 2017;377:414–417.
2. Fleischmann-Struzek C, et al. The global burden of paediatric and neonatal sepsis: a systematic review. Lancet Respir Med. 2018;6:223–230.
3. Singer M, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). JAMA. 2016;315:801–810.
4. Matics TJ, Sanchez-Pinto LN. Adaptation and validation of a pediatric sequential organ failure assessment score and evaluation of the sepsis-3 definitions in critically ill children. JAMA Pediatr. 2017;171:e172352.
5. Wynn JL, Polin RA. A neonatal sequential organ failure assessment score predicts mortality to late-onset sepsis in preterm very low birth weight infants. Pediatr Res. 2019. https://doi.org/10.1038/s41390-019-0517-2
6. Zhang X, Zhivaki D, Lo-Man R. Unique aspects of the perinatal immune system. Nat Rev Immunol. 2017;17:495–507.
7. Olin A, et al. Stereotypic immune system development in newborn children. Cell. 2018;174:1277–1292.

8. Achten NB, et al. Association of use of the neonatal early-onset sepsis calculator with reduction in antibiotic therapy and safety: a systematic review and meta-analysis. JAMA Pediatr. 2019. https://doi.org/10.1001/jamapediatrics.2019.2825
9. Agyeman PKA, et al. Epidemiology of blood culture-proven bacterial sepsis in children in Switzerland: a population-based cohort study. Lancet Child Adolesc Health. 2017;1:124–133.
10. Higgins RD, et al. Evaluation and management of women and newborns with a maternal diagnosis of chorioamnionitis: summary of a workshop. Obstet Gynecol. 2016;127:426–436.
11. Molloy EJ, et al. Developing core outcome set for women's, newborn, and child health: the CROWN Initiative. Pediatr Res. 2018;84:316–317.
12. Molloy EJ, Mader S, Modi N, Gale C. Parent, child and public involvement in child health research: core value not just an optional extra. Pediatr Res. 2019;85:2–3.
13. Asindi AA, Bilal NE, et al. Neonatal septicemia. Saudi Med J. 2004;25(14):822–825.
14. Bennet R, Eriksson M. Increasing incidence of neonatal sepsis. Chin J, Charles MD. In: Rudolf Textbook of Pediatrics. 18th ed. Churchill Livingstone; 2003. p. 128–132.

15. Samanci N, Ovali F, Akdogan Z. Neonatal septicemia in a neonatal ICU: results of four years. Am Public Health Assoc. 2005. Available from: www.emedicine.com

16. Gladstone IM, Ehreenkranz RA, Edberg S. A ten-year review of neonatal sepsis and comparison with the previous fifty years' experience. J Child Health. 2000:91–94.

17. Al-Harthi A, Dagriri KA. Neonatal sepsis. Saudi Med J. 2000;30(4):331–335.

18. Sanghavi KP, Tudehope D. Neonatal bacterial sepsis in intensive care unit. Pediatr Child Health. 2004;58:93–96.

19. Koutouby A, Habibulla J. Neonatal sepsis in Dubai, United Arab Emirates. J Trop Pediatr. 2007;21(28):251–253.

20. Battisti O, Mitchison R, Davies P. Changing blood culture isolate in referral neonatal ICU. Arch Dis Child. 2000;42:610–613.

21. Schat A, Zywicki S, Smoor M. Risk factors and prevention of early neonatal sepsis. J Trop Pediatr. 2005;26(12):27–31.