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Bacteraemia and Antibiotic Sensitivity in Baghdad Teaching Hospital NICU

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Abstract: Neonatal sepsis is often lethal and results in considerable long-term morbidity among survivors if not treated adequately and expeditiously. It can be categorized into two somewhat separate syndromes based on the age of onset: early-onset and late-onset sepsis. Infants acquire harmful microorganisms that are prevalent in their surroundings, including the microbiota of their caretakers. The combination of invasive procedures frequently performed in the NICU significantly elevates the risk of sepsis in neonates.

This study sought to ascertain the incidence of positive blood cultures and delineate the discovered organisms along with their corresponding antibiotic susceptibility patterns in the NICU of a tertiary hospital. This was a prospective descriptive research encompassing all newborns with positive sepsis cultures admitted to the NICU at Baghdad Teaching Hospital, Iraq, from January 1, 2024, to November 30, 2024.

Throughout the trial duration, a total of 980 newborns were admitted to the facility. Ninety infants with positive blood cultures were documented, yielding an incidence rate of 9.2%. Among these, 75.6% experienced early-onset sepsis, whereas 24.4% experienced late-onset sepsis. Gram-positive bacteria constituted 32.2%, but gram-negative bacteria were more prevalent at 67.8%, with Acinetobacter being the predominant species. In the 90 sepsis cases, gram-negative bacterial isolates were more prevalent in both early-onset (63.2%) and late-onset (81.8%) instances. The frequency distribution of bacterial growth types and their antibiotic resistance indicated that Acinetobacter exhibited the lowest sensitivity to antibiotics at 36.4%. The case-fatality rates were 36.4% for Acinetobacter, 17.2% for Staphylococcus spp., 66.7% for E. coli, 50.0% for Serratia marcescens, and 0.0% for Klebsiella. Acinetobacter isolates were substantially correlated with both early and late onset of sepsis, an elevated incidence of comorbidities, and increased fatality rates (P-value < 0.05).

This study concludes that early-onset sepsis is more prevalent, with nosocomial infections, particularly gram-negative bacteria, being the predominant kind of sepsis. The majority of clinically significant organisms exhibited resistance to the primary antibiotic regimen.

Key words: Neonatal sepsis, Bacteraemia, Antibiotic sensitivity, NICU, Baghdad Teaching Hospital, Acinetobacter, Gram-negative bacteria, Early-onset sepsis, Late-onset sepsis, Case-fatality rate.

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Introduction

Neonatal sepsis is often lethal and results in considerable long-term morbidity among survivors if not treated effectively and immediately (1,2). Neonatal sepsis is a systemic inflammatory response syndrome (SIRS) resulting from infection. Systemic inflammatory response syndrome is characterized by the presence of two or more of the following criteria: fever or hypothermia, tachycardia, tachypnea or hyperventilation, feeding difficulties, seizures, and an abnormal white blood cell count (either elevated or diminished) (3,5,6). It can be categorized into two relatively distinct syndromes based on the age of onset: early-onset and late-onset sepsis (7,8). Early-onset sepsis (EOS) is characterized by the Centers for Disease Control and Prevention (CDC) as a blood and/or cerebrospinal fluid (CSF) culture-confirmed infection in a baby occurring within the first 7 days of life. In the case of a newborn that is constantly hospitalized, early-onset sepsis (EOS) is characterized as a culture-confirmed infection developing within 72 hours of birth (7,9). According to the CDC, neonatal late-onset sepsis (LOS) is characterized as a blood and/or cerebrospinal fluid (CSF) culture-confirmed infection in newborns developing after 7 days of age, resulting from postnatal acquisition from either nosocomial or community sources. In the case of a newborn who remains hospitalized, length of stay (LOS) is characterized as a culture-confirmed infection manifesting after 72 hours of age (7,9). Risk factors for infection in EOS can be categorized into intrapartum factors and those associated with the infant post-delivery (3). Maternal intrapartum factors that elevate the risk of infection encompass maternal GBS colonization, maternal fever, chorioamnionitis, prolonged rupture of membranes (exceeding 18 hours), and insufficient intrapartum antibiotic prophylaxis before to birth (3,10). Newborn factors that elevate the risk of infection encompass the extent of preterm and reduced birth weight (3). In late-onset sepsis, infection is primarily acquired via the infant's environment (3,6). The infant becomes colonized by pathogenic bacteria that are prevalent in their surroundings, including the flora of its caretakers. The gut microbiome frequently plays a role in the etiology of late-onset sepsis (3). Neonates, especially preterm infants, exhibit an elevated susceptibility to sepsis (11). Implicated variables include poor cytokine production, diminished expression of adhesion molecules in neutrophils, and decreased cytotoxic T-cell activity (11,12). The combination of invasive procedures frequently performed in the NICU significantly elevates the risk of sepsis in newborns (4,11). Sepsis is up to 1000 times more prevalent in preterm infants than in term infants and is linked to increased mortality rates and enduring neurological disabilities. Timely identification and efficient treatment are essential to avert fatalities and consequences associated with septicemia (13). Various interleukins, tumor necrosis factor (TNF), procalcitonin (PCT), C-reactive protein (CRP), immunoglobulins, and other indicators have been employed in the diagnosis of sepsis (13). Blood culture is the definitive laboratory method for diagnosing infections; however, findings may need 48–72 hours. Treatment for suspected sepsis should commence prior to obtaining culture findings due to its elevated mortality rate (14). The NICU at the tertiary hospital administers ampicillin and gentamicin as the primary empirical treatment for newborns with suspected infection or sepsis (15,16). The rising resistance to penicillin and gentamicin need critical knowledge regarding local antibiotic susceptibility patterns (17). The majority of infection-related fatalities during the neonatal era transpire in low- and middle-income nations, attributable to inadequate hygiene and insufficient infection control procedures (18). A substantial percentage of these fatalities is attributed to multidrug-resistant organisms (19). Multidrug-resistant (MDR) is characterized by acquired non-susceptibility to at least one agent across three or more antimicrobial categories; extensively drug-resistant (XDR) is defined as non-susceptibility to at least one agent in all but two or fewer antimicrobial categories (i.e., bacterial isolates remain susceptible to only one or two categories); and pandrug-resistant (PDR) is defined as non-susceptibility to all agents in all antimicrobial categories. Infections caused by multi-drug-resistant (MDR) organisms are rapidly escalating among infants globally (21). Recent reports indicate a disproportionate incidence of newborn sepsis attributed to multidrug-resistant Gram-negative bacteria in poor and middle-income nations. Newborns infected with multidrug-resistant pathogens that have restricted treatment alternatives may gain advantages from innovative

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antimicrobials (21,22). The AAP guidance advises that broader-spectrum empiric therapy may be necessary for severely unwell children at elevated risk for EOS (15,16). Recent studies from low-income and middle-income countries (LMICs) indicated a greater incidence of early-onset sepsis (EOS) compared to high-income countries (HICs), comprising 70–80% of all neonatal sepsis cases, alongside a significant prevalence of Gram-negative strains, including multidrug-resistant (MDR) bacteria, in both EOS and late-onset sepsis (LOS). Gram-negative bacteria accounted for 39–64% of all cases of neonatal sepsis, with the most often identified species being Klebsiella spp., S. marcescens, E. coli, Enterobacter, and A. baumannii (25,26). Recent investigations indicate that Gram-negative bacteria responsible for newborn sepsis in low- and middle-income countries (LMICs) in Africa and Asia exhibited resistance to aminoglycosides in roughly 70% of instances, to cephalosporins in up to 84% of instances, and to carbapenems in 16–81% of instances (25,26). In China, E. coli and Klebsiella spp. responsible for neonatal sepsis were identified as multidrug-resistant organisms in 42% and 61% of cases, respectively, while carbapenem resistance was observed in up to 31% of late-onset sepsis cases. Multiple clinical research have identified the risk factors for infections caused by resistant strains of Acinetobacter species. Nevertheless, limited research has concentrated on the risk variables associated with MDRAB infection in neonates (27). Patients with MDRAB infections experience a markedly prolonged duration of intensive care unit (ICU) stay and hospitalization, as well as an elevated death rate in comparison to infections caused by the susceptible strain of A. baumannii (27).

Patients and method

This was a prospective descriptive study that included all neonates with positive cultures for sepsis admitted to the NICU at Baghdad Teaching Hospital in Iraq, from January 1, 2024, to November 30, 2024.

Data regarding patient demographics, dates of blood culture collection, detected pathogens, and antibiotic susceptibilities was gathered. Data were inputted into an Excel spreadsheet. Patients were evaluated for sepsis, and aseptic techniques were employed to collect blood cultures at admission when risk factors were present or after 48 hours, as well as during episodes of clinical deterioration. Blood volumes ranging from 1 mL to 2 mL were collected from a single location in each subject and subsequently inoculated into one blood culture vial. Samples were sent to the Microbiology Laboratory for incubation and then underwent susceptibility testing. The blood culture bottle apparatus incubates and monitors the bottle for microbial growth by detecting pH changes in the indicator located at the bottom of the bottle. Alterations in pH indicate growth, and the bottle is marked as positive. The positive blood culture bottle is subsequently extracted from the instrument, a Gram stain is prepared, and the contents of the bottle are subcultured onto agar plates. The bottles are retained in the apparatus for 5 days, following which they are extracted if no growth is observed. The VITEK system, utilizing the broth microdilution method, was employed for organism identification and determining the antibiotic susceptibility of isolated microbes. The antibiotic protocol for infants with suspected infection or sepsis in the unit is as follows: First-line empirical therapy consists of amoxicillin and amikacin; second-line antibiotics include ciprofloxacin and amikacin, which provide broader spectrum coverage against most Gram-positive and Gram-negative bacteria. This regimen was utilized during the initial six months of the study before transitioning to meropenem, which offers the widest coverage against Gram-positive and Gram-negative bacteria. Third-line antibiotics comprise either colistin or tigecycline and amikacin due to multidrug resistance (MDR). Fluconazole antifungal medication was administered to preterm infants with persistent deterioration.

Setting: Baghdad Teaching Hospital, the largest tertiary hospital in Baghdad, features a level three NICU with a capacity of 20 beds, only admitting inborn neonates and handling approximately 1000 deliveries annually, with no referrals accepted.

Inclusion criteria

All neonates with positive blood cultures regardless gestational age or postnatal age were included.

Exclusion criteria

Neonates with positive cultures results for sources other than blood were excluded.

Quantitative analysis

The Statistical Package for the Social Sciences (SPSS) version 28 is utilized for statistical analysis. Scale variables were assessed for normal distribution. The Kruskal-Wallis Test was utilized to compare birth weight and gestational age at birth. The chi-square test is employed to compare frequencies. Fisher's exact tests were employed when the chi-square test was unsuitable. The significance level was two-tailed with $P \leq 0.05$.

Results

During the study period, a total of 980 neonates admitted to the unit. Ninety with positive blood cultures neonate patients were reported providing an incidence rate of 9.2%, of them 68 (75.6%) early onset and 22(24.4%) were late onset sepsis. In total, gram positive bacteria contributed for 32.2% while gram negative bacteria were more frequent, contributed for 67.8%, (Table 1).

Table 1. Baseline characteristics of the studied group

Variable	
Total admission	980
Total mortalities	172
Overall mortality rate	17.55%
Number of Sepsis cases	90
Incidence of culture positive sepsis	9.2%
Early onset sepsis	68 (75.60%)
Late onset sepsis	22 (24.40%)
Gram positive bacteria	29 (32.2)
Gram negative bacteria	61 (67.80%)

The median birth weight of neonates was 1600 (IQR: 1175-2500) gram. The median gestational age at birth was 33 (IQR: 29-35) weeks. Cesarean section was the more frequent mode of delivery where 72 out of 90 neonates, (80%), delivered by cesarean section, (Table 2).

Table 2. Demographic characteristics

Mean Birth weight (IQR) gram	1600 (1175 – 2500)
Mean gestational age at birth (IQR) week	33 (29 – 35)
Cesarean section	72 (80.0)
IQR: Interquartile range	

Among the 90 sepsis cases, early onset and late onset were more frequent in cases with gram negative bacterial isolates (63.2% and 81.8%). (Table 3).

Table 3. Distribution of onset of sepsis according to the type of bacteria

Onset of sepsis	**Type of bacteria**		**Total**
	Gram positive	**Gram negative**	
	No. (%)	No. (%)	
Early	25 (36.80%)	43 (63.20%)	68 (75.60%)
Late	4 (18.20%)	18 (81.80%)	22 (24.40%)
Total	29 (32.20%)	61 (67.80%)	90 (100.00%)
Chi-Square test, P. value = 0.2 not significant			

Table 4 summarizes the frequency distribution of the types of bacterial growths and their resistance to antibiotics, most Staphylococcus bacteria were sensitive to antibiotics, where the sensitivity rate was

93.1%, 36.4% of Acinetobacter, 66.7% of E.Coli, 100% of Serratia marcescens and 100% of Klebsiella were sensitive to antibiotics.

Table 4. Types of bacterial growths and their resistance to antibiotics (N=90)

Type of bacteria	Resistant to AB		Total
	Sensitive	Resistant	
	No (%)	No (%)	
Acinobacter	**20** (36.40%)	**35** (63.60%)	**55** (61.10%)
Staphylococcus spps	**27** (93.10%)	**2** (6.90%)	**29** (32.30%)
E-Coli	**2** (66.70%)	**1** (33.30%)	**3** (3.30%)
Serratia marcescens	**2** (100.00%)	**0** (0.00%)	**2** (2.20%)
Klebsiella	**1** (100.00%)	**0** (0.00%)	**1** (1.10%)
Total	**52** (57.80%)	**38** (42.20%)	90 (100.00%)
Fisher's exact test, P. value <0.001 significant			

The case-fatality rate ranged between 36.4% of acinetobacter, 17.2% of staphylococcus spps, E-Coli, Serratia marcescens, and Klebsiella the case fatality rate was 66.7%, 50.0%, and 0.0% respectively, (Table 5).

Total resistant cases that died were 14 cases of 38 cases, about 34.2% were acinetobacter, and 50.0% for staphylococcus spp, and 100.0% for E.coli. (Table 6)

Table 5. Number of Isolates and Case-fatality rates

Type of bacteria	Total Isolates	Number of death	Case-Fatality rate
Acinetobacter	55	20	36.4%
Staphylococcus spps	29	5	17.2%
E-Coli	3	2	66.7%
Serratia marcescens	2	1	50.0%
Klebsiella	1	0	0.0%

Table 6. Number of Isolates resistance cases and Case-fatality rates

Type of bacteria	Total Isolates resistance	Number of death	Case-Fatality rate
Acinetobacter	35	12	34.2%
Staphylococcus spps	2	1	50.0%
E-Coli	1	1	100.0%
Serratia marcescens	0	0	0.0%
Klebsiella	0	0	0.0%

Table 7 compares gestational age at birth (in weeks) and birthweight (in grams) across bacterial isolate groups. In the gestational age analysis, the Acinetobacter group (n =55) had a mean gestational age of 31.2 weeks (SD = 3.4; mean rank = 36.86), whereas the Staphylococcaceae group (n = 28) had a significantly higher mean of 34.4 weeks (SD = 3.5; mean rank = 59.48; p = 0.001). The "Others" group (n = 7) had a mean gestational age of 34.1 weeks (SD = 2.8; mean rank = 57.43).

For birthweight, the Acinetobacter group had a mean of 1,666.2 grams (SD = 864.4;mean rank = 38.73), while the Staphylococcaceae group showed a significantly higher mean birthweight of 2,278.6 grams (SD = 1,001.2; mean rank = 57.25; p = 0.007). The "Others" group had a mean birthweight of 1,942.9 grams (SD = 650.3; mean rank =51.71), (Table 7).

Table 7. Comparison of gestational age at birth and birthweight across types of bacterial isolates

Bacteria-Species		N	Mean	SD	Mean Rank	P. value
Gestational age (week)	Acinetobacter	55	31.2	3.4	36.86	0.001 sig
	Staphylococcaceae	28	34.4	3.5	59.48	
	Others	7	34.1	2.8	57.43	
Birth weight (gram)	Acinetobacter	55	1666.2	864.4	38.73	0.007 sig
	Staphylococcaceae	28	2278.6	1001.2	57.25	
	Others	7	1942.9	650.3	51.71	
sig: significant						

The cross-tabulation between types of bacteria from one side against each of sex, mode of delivery, onset of sepsis, complications and final outcomes revealed that neither sex nor mode of delivery was significantly associated with the type of bacterial isolates, (P. value >0.05). Acinetobacter isolates were significantly associated with early and late onset of sepsis, high rate of complications and higher mortality rates, (P. value <0.05), (Table 8). Complications includes, meningitis; BPD; and pulmonary hemorrhage.

Table 8. Cross-tabulation between types of bacteria against sex, mode of delivery, onset of sepsis, complications and final outcomes

		Bacteria-Species						
		Acinetobacter		Staphylococcaceae		Others		
		No.	%	No.	%	No.	%	
Sex	Male	30	56.6	21	39.6	2	3.8	0.057 ns
	Female	25	67.6	7	18.9	5	13.5	
Mode of delivery	Cesarean section	44	61.1	23	31.9	5	6.9	0.818 ns
	NVD	11	61.1	5	27.8	2	11.1	
Onset of sepsis	Early	41	60.3	24	35.3	3	4.4	0.048 sig
	Late	14	63.6	4	18.2	4	18.2	
Complications	Yes	39	75.0	9	17.3	4	7.7	0.003 sig
	No	16	42.1	19	50.0	3	7.9	
Final outcomes	Died	20	71.4	4	14.3	4	14.3	0.023 sig
	Survived	35	56.5	24	38.7	3	4.8	
Sig: significant, ns: not significant								

Dialogue

During this 11-month study period, the rate of clinically significant blood culture positivity was 9.2%, while the rates of clinically relevant culture positivity were 6.2% (1934 neonates), 16.8% (118/702), and 20.5% (69/336). Studies by the Indian Council of Medical Research, Staaden et al., and Pokhrel B et al. (28,29,30) reported higher rates than our study in Staaden et al. and Pokhrel B et al., but lower than that of the Indian Council of Medical Research. Disparities in the culture positivity rate of newborn sepsis across various studies appear to stem from variations in culture methodologies and research strategies (30). Our study revealed that early onset sepsis constituted the majority of culture-positive sepsis cases (75.6%), particularly significant within the first 72 hours, predominantly caused by nosocomial pathogens rather than those acquired from the mother. This was especially prevalent among preterm and low birth weight neonates, in contrast to late onset sepsis (24.4%). These findings align with those of the Indian Council of Medical Research and Pokhrel B et al., but contradict Staaden et al. and most studies conducted in Asian countries, which indicate that late onset sepsis (after 72 hours) is more common. The elevated incidence of early-onset sepsis and the prevalence of nosocomial-type pathogens may be attributable to ultra-early horizontal transmission from delivery rooms and NICUs, or vertical transmission from the maternal genital tract colonized by

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these pathogens due to unsanitary personal and obstetric practices. Gram-negative bacteria were more prevalent than gram-positive bacteria, with Acinetobacter spp. identified as the primary causal organisms, consistent with findings from the Indian Council of Medical Research, although Pokhrel B et al. largely identified Klebsiella species. This discrepancy may be attributed to disparities in adherence to infection prevention and control methods, as well as differences in research settings, populations, and hand hygiene practices. 30. A significant number of infections exhibited a concerning level of antibiotic resistance. Acinetobacter spp. is developing as the predominant pathogen, exhibiting a concerning level of antimicrobial resistance to even last-resort treatments, akin to findings from the Indian Council of Medical Research. In contrast, the study by Pokhrel B et al. revealed that Klebsiella shown significant resistance to frequently utilized antibiotics. Approximately 31.1% of newborns with culture-positive sepsis in our study succumbed, despite early detection and adequate supportive care, which is lower than reported by the Indian Council of Medical Research and Pokhrel B et al. This discovery likely does not stem from elevated antimicrobial resistance, considering the nearly equal case fatality rates between multidrug-resistant and non-multidrug-resistant infections. The exceptionally high pathogenicity of infections may be a potential explanation (28). The disparity in fatality rates may be attributed to the early alteration of antibiotics upon the observed decline of the neonate in our NICU. The prevalent microorganisms associated with early-onset sepsis comprise E. coli, group B streptococci, Listeria monocytogenes, and Enterococcus species. Our study's findings, however, contradict this concept and studies from high-income countries, like to those of the Indian Council of Medical Research and Pokhrel B et al. Our investigation revealed no prevalence of GBS. Potential explanations for this may include excessive antibiotic use during the prenatal period or inadequate culture techniques and microbiological methodologies. The recent emergence of colistin resistance in Acinetobacter has rendered antibiotic selection exceedingly challenging. We utilized higher-spectrum antibiotic classes (carbapenems, piperacillin–tazobactam) to delineate multidrug resistance instead of the WHO-recommended first-line alternatives such as ampicillin, gentamicin, and cefotaxime (28). Acinetobacter spp. and staphylococci, typically identified as nosocomial infections, were the predominant pathogens even in infants with early-onset sepsis. The significant prevalence of antibiotic resistance, particularly to carbapenems, suggests that the rising incidence of Acinetobacter sepsis may present a substantial concern in the forthcoming years.

Limitations of the study

1. The cases were small in number due to limited time for the study.
2. Not all the admitted cases were done for them blood culture.
3. The incidence of sepsis (particularly late-onset sepsis) might have been underestimated because not all the neonates were followed up after discharge from the hospital, and some cases were referred to other hospitals.

Recommendations

Based on the study done in the ward, we advocate enhancing infection control through consistent hand hygiene and sterilization, employing sterile techniques while interacting with neonates, boosting nursing staff, and providing ongoing training on infection control practices. Subsequent measures to enhance infection control have been instituted, including regular ward rounds with an infection control team, the establishment of refined antibiotic protocols, improved bed spacing in a new unit, and research initiatives to elucidate the pathogenesis of early-onset sepsis and develop strategies to mitigate associated morbidity and mortality. The findings additionally constitute as another urgent call for worldwide action to mitigate the rising threat of antibiotic resistance.

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