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Antimicrobial Susceptibility Pattern of Bacterial Isolates in Neonatal Sepsis at the Special Care Neonatal Unit of Chittagong Medical College Hospital

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Abstract

Background: Neonatal sepsis is one of the leading causes of neonatal mortality in Bangladesh. To effectively treat and prevent neonatal sepsis, continuous monitoring of microbial etiology and antimicrobial resistance profiles is essential in neonatal care units. This study aimed to identify the pathogens responsible for neonatal sepsis and understand their current antimicrobial resistance pattern.

Materials and methods: This retrospective study was conducted in the Neonatal Intensive Care Unit (NICU) of Chittagong Medical College Hospital, Chattogram from July, 2023 and March 2024. All neonates with a positive blood culture were identified. Patient demographics, clinical details and laboratory data including bacteriological profiles and antimicrobial susceptibilities were recorded and analyzed.

Results: The majority of the 108 culture-positive neonates were preterm (73.1%) and had low birth weight (78.7%). Most of them had late onset sepsis (66.7%). Most bacterial isolates were gram-negative, predominantly the Klebsiella (46.3%) which showed high resistance to commonly used antibiotics such as, Gentamicin (85.2%) Amikacin (78%) Cefepime (97.2%) and Meropenem (69.2%) and good susceptibility to Colistin (86.8%) and Tigecycline (95.1%). Among gram-positive isolates, Coagulase Negative Staphylococci (CONS) (13.8%) predominated. CONS showed high resistance to Meropenem (80%), Tazobactam-piperacillin (70%) and Cefepime (75%) but good susceptibility to Tigecycline, Vancomycin and Linezolid (100%). Nearly, two-third organisms were MDR (69.1%) and one-third were XDR (37.1%). Deaths were more common among preterm, late onset sepsis, nosocomial sepsis and sepsis with MDR organisms.

Conclusions: Klebsiella and CONS were the most common causes of neonatal sepsis in our study with an alarming prevalence of MDR strains. Implementation of effective preventive strategies to combat the emergence of antibiotic resistance is urgently needed.

Key words: Antibiotic susceptibility; Klebsiella; Multi-drug resistance; Neonatal sepsis; NICU.

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Introduction

In the year 2021, 5 million children died before reaching the age of five. Among them, 2.3 million children died in the first month.[1,2] According to the Global Burden of Disease study in 2019, neonatal sepsis and other neonatal infections rank as the third leading cause of neonatal death.[3]

Multi drug-resistant pathogens were responsible for a significant proportion of these deaths.[4] In Bangladesh, the first month of an infant's life carries the highest risk, with a mortality rate of 20 deaths per 1,000 live births during that period. Neonatal sepsis contributes to 20% of total neonatal mortality.[5]

The emergence of Antimicrobial Resistance (AMR) poses a global threat to the healthcare system. Multi Drug-Resistance (MDR) is becoming increasingly prevalent among pathogenic bacteria, both in healthcare and community settings. Scarcity in resources, inadequate surveillance and infection control management, indiscriminate use of antibiotics may contribute to this situation in Low-Income and Middle-Income Countries (LMICs).[6] Among all the WHO regions, the risk of emergence and spread of antimicrobial resistance is highest in South East Asia.[7] Targeted antibiotic therapy may play a significant role in reduction of antimicrobial resistance.[8]

Neonatal sepsis is defined as any sepsis diagnosed within the first 28 days of life and remains a significant contributor to mortality and long-term morbidity in neonates.[9] Neonatal sepsis is

categorized into Early Onset Sepsis (EOS) and Late Onset Sepsis (LOS). EOS, occurring within 72 hours after birth, often results from vertical transmission of maternal pathogens during prenatal or intrapartum infection. LOS, however, develops after 72 hours of life and involves a higher proportion of nosocomial and community-acquired infections.[6,10] The clinical signs and symptoms of neonatal sepsis are subtle and nonspecific, making early diagnosis difficult and leading to high rate of empiric antibiotic utilization which could contribute for the emergence and spread of antimicrobial resistant strains of bacteria. Knowing the causative agents of neonatal sepsis and their antimicrobial sensitivity patterns could enable to choose appropriate therapy for neonatal sepsis, hence improving the survival of neonate.

To effectively prevent and treat infections caused by MDR bacteria, continuous monitoring of microbial etiology and antimicrobial resistance profiles is essential in neonatal care units. This study aimed to comprehensively assess the spectrum of bacterial pathogens, analyze their antimicrobial susceptibility patterns, and identify the prevalence of multi drug-resistant pathogens in the Special Care Neonatal Unit (SCANU) of Chittagong Medical College Hospital.

Materials and methods

This retrospective study was conducted in the Special Care Neonatal Unit (SCANU) of Chittagong Medical College Hospital over a period from July 2023 to March 2024. All the neonates with culture proven sepsis were included in the study. Culture specimens were collected and processed following standard laboratory procedures. Clinical records of the neonates with positive blood cultures were retrieved from hospital medical records and collected in a clinical record form. All the data were collected anonymously.

Data regarding gestational age, birth weight, sex, place and mode of delivery, clinical presentation, type of sepsis, name of the organism isolated along with their sensitivity pattern and outcomes were recorded in a data collection sheet. Patients infected within 72 hours were classified into the early-onset group, while those infected later were assigned to the late-onset group. Hospital acquired infection was defined as infections acquired after hospitalization which manifested 48 hours after admission to the hospital.[11]

Extended Drug-Resistant organisms (XDR) and Multidrug-Resistant Organisms (MDR) were classified in accordance with the guidelines set forth by the Centers for Disease Control and Prevention (CDC) and the European Centre for Disease Prevention and Control (ECDC).[12] MDR was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial categories, XDR was 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). Thus, a bacterial isolate that was characterized as XDR was also categorized as MDR.

Outcome was measured as discharge with advice, discharge against medical advice and death.

Statistical analysis was performed using the SPSS software version 25.0 (SPSS Inc, Chicago, IL).

Descriptive analysis was performed to characterize the study population and pathogens. Categorical data were presented as percentages. p value less than 0.05 was considered statistically significant.

Necessary permission was taken before commence the study from proper authorities.

Results

Total 108 neonates with culture proven sepsis were admitted during the study period. Most of them were preterm (73.1%) and low birth weight (LBW) (78.7%). Male: female ratio was 1.3:1.

Majority of the patients were outborn (63%) and delivered by vaginal delivery (65.7%). Early and late onset sepsis were found in 33.3% (n=36) and 66.7% (n=72) of cases respectively. Nearly half of the cases were hospital acquired sepsis (45.4%) and 20.4% of them had history of previous NICU admission. Mortality was 34.6% (37/108) among culture positive cases (Table I).

Table I Characteristics and outcome of the culture positive cases (n=108)

Characteristics		Frequency (%)
Neonatal characteristics		
Gestational age	Term	29 (26.9)
Preterm	79 (73.1)	
Birth weight	<2500 gram	85 (78.7)
>2500 gram	23 (21.3)	
Growth at birth	AGA	89 (82.4)
SGA	19 (17.6)	
Sex	Male	62 (57.4)
Female	46(42.6)	
Mode of delivery	Per vaginal	71 (65.7)
LUCS	37 (34.3)	
Inborn/Outborn	Inborn	40 (37)
Outborn	68 (63)	
Place of delivery	Hospital	20 (18.5)
Home	88 (81.5)	
Multiple gestation		22 (20.4)
H/O previous hospitalization		22 (20.4)
Maternal variables		
PROM> 18 hours		27 (25)
Prolonged labor		12 (11.1)
Maternal fever within 2 weeks		6 (5.6)
Meconium stained liqour		14 (12.9)
Type of sepsis	EOS	36 (33.3)
LOS	72 (66.7)	
Hospital acquired sepsis		49 (45.4)
Outcome	Discharge	58 (53.3)
	Death	37(34.6)
	DAMA	13 (12.1)

AGA- Appropriate for Gestational Age, SGA- Small for Gestational Age, LUCS-Lower Uterine Cesarean Section, PROM- Prolonged Rupture of Membrane, EOS-Early Onset Sepsis, LOS-Late Onset Sepsis, DAMA-Discharge Against Medical Advice.

Gram-negative bacteria were isolated more frequently than gram-positive bacteria in this study, accounting for 70.3% (76/108) and 19.4% (21/108) of the total. Gram negative organisms were responsible for 83.8% of the deaths in culture positive cases. Klebsiella (46.3%) was the most common organism identified in both early and late-onset sepsis, followed by CONS (13.9%), Acinetobacter (9.3%), and Burkholderia (6/108, 5.6%). Klebsiella accounted for 64.9% of total mortality. Most common gram positive organism was Coagulase negative Staphylococci (15/21, 71.4%)). Among CONS, Staphylococcus hemolyticus was the most prevalent (7/15, 46.7%), followed by Staphylococcus epidermidis (2/15, 13.3%).

Fungus was isolated from 10.2% (11/108) cases. Among fungal sepsis 9 were Candida spp. and 2 were Cryptococcus (8.3% and 1.9% respectively) (Table II).

Table II Distribution of isolated organisms by type of sepsis and their relation to mortality (n=108)

Organism	EOS (n=36)	LOS (n=72)	Total (n=108) (%)	Death (n=37) (%)
Gram negative organism	26	50	76 (70.3)	31 (83.8)
Klebsiella	15	35	50 (46.3)	24 (64.9)
Acinetobacter	4	6	10 (9.3)	3 (8.1)
Burkholderia	2	4	6 (5.6)	1 (2.7)
Pseudomonas	1	1	2 (1.9)	1 (2.7)
E.coli	1	1	2 (1.9)	2 (5.4))
Other gram negative	3	3	6 (5.6)	0 (0)
Gram positive organism	8	13	21 (19.4)	4 (10.8)
Staphylococcus aureus	1	4	5 (4.6)	1 (2.7)
CONS	6	9	15 (13.9)	3 (8.1)
Enterococcus	1	0	1 (0.9)	0 (0)
Fungal isolates	2	9	11 (10.2)	2 (5.4)
Candida	2	7	9 (8.3)	2 (5.4)
Cryptococcus	0	2	2 (1.9)	0 (0)

EOS- Early Onset Sepsis, LOS- Late Onset Sepsis, E. coli- Escherechia coli, CONS- Coagulase Negative Staphylococci.

The most commonly isolated organism, Klebsiella demonstrated 100% resistance to Ampicillin and Ceftazidime. Overall resistance to Cefepime (97%), Gentamicin (85%), Amikacin (78%), Meropenem (70%), Tazobactam-piperacillin (78%), and Levofloxacin (73%) was notably high. However, Klebsiella displayed good sensitivity to Tigecycline (95%) and Colistin (87%). Second common gram negative organism was Acinetobacter, which showed 100% sensitivity to Colistin and Tigecycline, followed by Fluoroquinolones and Amikacin (50%). Acinetobacter were 100% resistant to Cefotaxime and Imipenem. Burkholderia showed 100% resistant to Imipenem and Tazobactam piperacillin, but good sensitivity to Tigecycline (100%).

Among gram positive isolates, both CONS and Staphylococcus aureus showed 100% resistance to Ampicillin. However, they showed 100% sensitivity to Tigecycline, Vancomycin, Teicoplanin and Linezolid (Table III).

Table III Susceptibility pattern of the major bacterial isolates to commonly used antibiotics

Antibiotics	Klebsiella (n=50) S/T (%)	Acinetobacter (n=10) S/T (%)	Burkholderia (n=6) S/T (%)	CONS (n=15) S/T (%)	S. aureus (n=4) S/T (%)
Ampicillin	0/11 (0)	-	-	0/10 (0)	0/3 (0)
Gentamicin	7/47 (14.9)	2/10 (20)	-	9/15 (60)	4/5 (80)
Amikacin	11/50 (22)	5/10 (50)	1/5 (20)	2/3 (66.7)	1/1 (100)
Ceftazidime	0/24 (0)	1/9 (11.1)	4/4 (100)	-	-
Cefotaxime	1/6 (16.7)	0/6 (0)	2/2 (100)	-	-
Cefepime	1/36 (2.8)	1/7 (14.3)	2/6 (33.3)	0/1 (0)	0/1 (0)
Meropenem	14/46 (30.4)	3/9 (33.3)	2/6 (33.3)	1/3 (33.3)	1/1 (100)
Imipenem	10/42 (23.8)	0/7 (0)	0/6 (0)	1/2 (50)	-
Tazo-pip	10/45 (22.2)	2/8 (25)	0/5 (0)	1/3 (33.3)	0/1 (0)
Amoxi-clav	5/35 (14.3)	-	0/1 (0)	0/1 (0)	0/1 (0)
Colistin	33/38 (86.8)	9/9 (100)	1/2 (50)	-	-
Levofloxacin	8/28 (28.6)	5/10 (50)	4/6 (66.7)	6/15 (40)	4/5 (80)
Ciprofloxacin	10/46 (21.7)	4/8 (50)	2/6 (33.3)	5/14 (35.7)	4/5 (80)
Tigecycline	39/41 (95.1)	3/3 (100)	3/3 (100)	12/12 (100)	4/4 (100)
Linezolid	-	-	-	12/12 (100)	5/5 (100)
Teicoplanin	-	-	-	12/12 (100)	5/5 (100)
Vancomycin	-	-	-	12/12 (100)	4/4 (100)

S/T- Sensitive/Total tested, (-) Indicating not tested, Tazo-pip: Tazobactam-piperacillin, Amoxiclav: Amoxicillin-clavulanic acid.

In this study, 69.1% (67/97) of bacterial isolates were multi-drug resistant. Among them 53.7% (36/67) were extended-drug resistant organisms, accounting for 37.1% (36/97) of all isolates (Fig. 1). Gram negative organisms exhibited higher prevalence of multidrug-resistance compared to gram positive organisms (80.3% and 28.5% respectively) and this difference was statistically significant (p<0.001). The majority of the isolates (79.5%) from hospital-acquired sepsis were MDR strains, compared to other sepsis. (35/44, p=0.04).

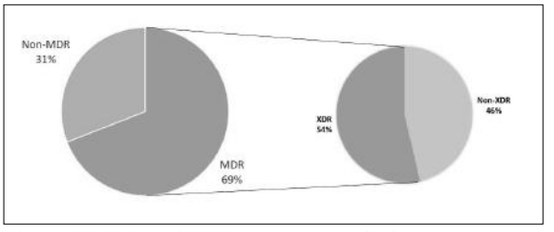

Figure 1 MDR and XDR cases among isolates

In this study, among the patients with culture proven sepsis, mortality was high in preterm infants (p=0.02) in case of LOS (p=0.03) and in those with hospital acquired sepsis (p=0.003). Though mortality was high among Gram negative (46.2%) sepsis compared to gram positive (22.2%) sepsis, but it was not statistically significant (p=0.06). High mortality was observed among multidrug resistant cases which was statistically significant (P=0.004).

Table IV Comparison of clinical parameters and drug resistance pattern of culture positive patients with mortality (n= 92)

		Discharge (n=55)	Death (n=37)	p value
Gestational age	Term	20	5	0.02
	Preterm	38	32	
Birth weight	>2500 grams	14	6	0.35
	<2500 grams	44	31	
Growth at birth	AGA	45	33	0.15
	SGA	13	4	
Place of birth	Inborn	19	15	0.44
	Outborn	39	22	
Sex	Male	37	21	0.49
	Female	21	16	
Mode of delivery	per vaginal	34	28	0.08
	LUCS	24	9	
PROM> 18 hours	No	45	19	0.01
	Yes	10	14	
Previous hospitalization	No	41	33	0.03
	Yes	17	4	
Type of sepsis	EOS	23	7	0.03
	LOS	35	30	
Organism type	Gram positive	14	4	0.06
	Gram negative	36	31	
Hospital acquired sepsis	Yes	35	12	0.003
	No	20	25	
Drug resistance pattern	Non-MDR	22	5	0.004
	MDR	28	30	

Statistical test:Chi square test.

Discussion

Neonatal sepsis is a life threatening condition and any delay in treatment can lead to significant morbidity and mortality. The rapid rise of Multi Drug-Resistant (MDR) organisms is a potential threat to the survival of newborns. Continuous monitoring of microbial etiology and the emergence of antimicrobial resistance is crucial in neonatal care units.

In this study, preterm (73.1%) and low birth weight (78.7%) neonates had the highest rates of culture-positive sepsis. These findings are consistent with studies by Dey et al. in Bangladesh and Pokhrel et al. in Nepal.[13,14] This population is particularly susceptible to infection because of their immature immune systems, lengthier hospital stays, and several invasive procedures, all of which increase their risk of developing sepsis.

In developing countries, nosocomial infections are a significant public health concern, especially in neonatal intensive care units. Nearly half of the pathogens identified in the current study (49/108, 45.4%) were accountable for hospital-acquired sepsis, which is significantly higher than reported by a multi-center study conducted in China.[6]

In the current study, 33.3% and 66.7% of newborns developed Early Onset Sepsis (EOS) and Late Onset Sepsis (LOS), respectively. We found that, LOS was more common than EOS, which is consistent with data from other research in Bangladesh and studies from neighboring countries, Nepal, Pakistan and India.[13,15-18] However, this contrasts with the findings of Alam et al. and Hussain et al. from Bangladesh, Chandra et al. from India and Getabelew A et al. from Ethiopia, where early onset sepsis was more prevalent.[19, 20, 21] The same bacterial isolates were prevalent in both the EOS and LOS, which is similar with the findings of Shrestha et al. in Nepal.[22]

The majority of the isolates were gram-negative (70.4%), similar to the findings of other studies from Bangladesh, Nepal, India and China.[13,19,16,22,23,6] In contrast, Hussain et al. and Mannan et al. from Bangladesh reported high prevalence of gram positive organism in their study.[24,25] Sorsa et al. from Ethiopia, Opare-Asamoah from Ghana showed preponderance of gram-positive organisms in their study.[8,26] Variations in local epidemiological factors, including regional differences in antibiotic usage, infection control practices, and microbial flora, could influence the distribution of gram-negative and gram-positive organisms in different settings.

Klebsiella was the primary causative agent of neonatal sepsis in our study, similar to the findings of the study conducted at the same institute by Mamtaz et al. and in other studies from Bangladesh, as well as studies from Nepal and India.[27,19,28,29,14,16,20] Conversely, earlier studies from Bangladesh by Dey et al. highlighted Acinetobacter as the predominant organism, while Ferdous et al. reported a prevalence of Coagulase-Negative Staphylococci (CONS) and Hussain et al. identified Staphylococcus aureus as prevalent.[13,15,24] This variation in major isolates could be due to variation in study setting and population.

Our study revealed that the majority of causative organisms have developed resistance to commonly used antibiotics from Beta-lactam group, such as Ampicillin, Cephalosporins, Carbapenems and Beta-lactamase inhibitors.[19] Additionally, high resistance to Aminoglycosides was observed. These findings are consistent with studies from other NICUs in Bangladesh as well as in Nepal, Pakistan and India.[15,19,24,28,14,16,20,30] It is alarming that organisms are developing resistance to most of the third-line antibiotics.

Both gram-positive and gram-negative organisms demonstrated high susceptibility to Tigecycline, consistent with findings of Pervez et al.[29] Similarly, gram-negative organisms showed considerable susceptibility to Colistin, aligning with the results of studies by Dey et al. and Pervez et al.[13,29] Our research revealed that 13.2% of the tested Klebsiella strains were resistant to Colistin, a higher proportion compared to a study conducted in China (7.9%).[30] Considering the fact that, Colistin has become a crucial component in clinical practice, either as monotherapy or in combination therapy, this poses a significant concern, particularly due to the rapid emergence of multi drug-resistant Gram-negative bacteria and the limited development of new anti-infective agents.

The second commonest organism in our study, CONS showed low susceptibility to Penicillin and Cephalosporins, but high susceptibility to Linezolid and Vancomycin (100%), similar to the findings of Pokhrel et al. and Fang et al.[14,30]

In our study, the overall mortality rate in culture positive sepsis was 34.6%, which is consistent with other studies from Bangladesh, such as Dey et al (24.7%), Ferdous et al (30.71%), but lower than reported by Chandra et al. from India (44.4%). The highest mortality was seen in the Klebsiella sepsis group.

The most concerning finding of this study is the high prevalence of MDR and XDR organisms. A majority of the organisms (69.1%) were identified as MDR, with approximately half of them (53.7%) classified as XDR. In our investigation, MDR rates among gram-negative and gram-positive organisms were 80.3% and 28.5%, respectively, a statistically significant finding ($p<0.001$) consistent with the results of studies by Dey et al. from Bangladesh, Pokhrel et al. from Nepal

and the DeNIS Collaboration from India.[13,14,4] Additionally, mortality was significantly higher among MDR cases (p=0.004) a finding similar to that of Dey et al.[13] Overall, this concerning prevalence of high antimicrobial resistance rates probably multifactorial and may include absence of standardized infection control policies, inadequate visitor control, increased use of broad-spectrum antibiotics and a low nurse-to-bed ratio within this NICU.

Limitations

The retrospective design of our study, together with its single centered, small study population and limited yield of some pathogens were all limitations in our study. Nonetheless, comprehensive clinical and demographic data of the patients aided in the analysis of correlation between clinical outcomes and resistant pattern of pathogens.

Conclusion

Klebsiella and CONS were the leading cause of neonatal sepsis in our study, with a concerning prevalence of MDR and XDR isolates. These bacterial strains were highly resistant to commonly used first- and second-line empiric antimicrobials in NICUs. Late onset sepsis, nosocomial sepsis and sepsis with MDR strains were associated with higher mortality.

Recommendations

To address the grave problem of antimicrobial resistance, it is essential to implement several measures. Regular monitoring of antimicrobial resistance patterns is necessary to promptly identify emerging trends. Strengthening infection prevention and control strategies, such as implementing hand hygiene protocols, controlling visitor access and ensuring thorough environmental cleaning, is crucial. Additionally, developing evidence-based antimicrobial prescribing guidelines is essential for neonatal care units.

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Contribution of authors

HA-Conception, design, acquisition of data, data analysis, manuscript drafting & final approval.
SHH- Conception, acquisition of data, critical revision & final approval.
MRK-Acquisition of data, critical revision & final approval.
MS- Data analysis, drafting & final approval.
MJBAC-Data analysis, drafting & final approval.
MMH-Design, critical revision & final approval.

Disclosure

The authors declared no conflict of interest.

References

1. UNICEF DATA [Internet]. Neonatal mortality. 2023. https://data.unicef.org/topic/child-survival/neonatal-mortality/.

2. United Nations Inter-agency Group for Child Mortality Estimation (UN IGME). Levels & Trends in child mortality: report. New York: Estimates Developed by the UN Inter-agency Group for Child Mortality Estimation', United Nations Children's Fund. 2022.

3. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: A systematic analysis for the Global Burden of Disease Study 2019. Lancet Lond Engl. 2020;396(10258):1204–1222.

4. Characterisation and antimicrobial resistance of sepsis pathogens in neonates born in tertiary care centres in Delhi, India: A cohort study. Lancet Glob Health. 2016;4(10):e752–760.

5. National Institute of Population Research and Training (NIPORT) and ICF. 2023. Bangladesh Demographic and Health Survey. Key Indicators Report. Dhaka, Bangladesh and Rockville, Maryland, USA: NIPORT and ICF. 2022.

6. Liu J, Fang Z, Yu Y, Ding Y, Liu Z, Zhang C, et al. Pathogens distribution and antimicrobial resistance in bloodstream infections in twenty-five neonatal intensive care units in China, 2017–2019. Antimicrob Resist Infect Control. 2021;10(1):121.

7. Chereau F, Opatowski L, Tourdjman M, Vong S. Risk assessment for antibiotic resistance in South East Asia. BMJ. 2017;358:j3393.

8. Sorsa A, Früh J, Stötter L, Abdissa S. Blood culture result profile and antimicrobial resistance pattern: a report from neonatal intensive care unit (NICU), Asella teaching and referral hospital, Asella, south East Ethiopia. Antimicrob Resist Infect Control. 2019;8(1):42.

9. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. The Lancet. 2017;390(10104):1770–1780.

10. Pace E, Yanowitz T. Infections in the NICU: Neonatal sepsis. Semin Pediatr Surg. 2022;31(4):151200.

11. Monegro AF, Muppidi V, Regunath H. Hospital-Acquired Infections. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. 2024. http://www.ncbi.nlm.nih.gov/books/NBK441857/.

12. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, et al. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: An international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect Off Publ Eur Soc Clin Microbiol Infect Dis. 2012;18(3):268–281.

13. Dey S, Shabuj MH, Jahan I, Akter H, Akhter M. Is Superbug imminent? Findings of a retrospective study in Bangladesh. J Clin Neonatol. 2020;9(1):38.

14. Pokhrel B, Koirala T, Shah G, Joshi S, Baral P. Bacteriological profile and antibiotic susceptibility of neonatal sepsis in neonatal intensive care unit of a tertiary hospital in Nepal. BMC Pediatr. 2018;18(1):208.

15. Ferdous N, Mannan MA, Yasmin S, Shahnewaz AA, Khan M, Anwar P. Outcome of Bacterial Sepsis in Neonate with Determination of Pathogens and Their Antimicrobial Susceptibility. Bangladesh Crit Care J. 2021;9(2):79–86.

16. Manandhar S, Amatya P, Ansari I, Joshi N, Maharjan N, Dongol S, et al. Risk factors for the development of neonatal sepsis in a neonatal intensive care unit of a tertiary care hospital of Nepal. BMC Infect Dis. 2021;21(1):546.

17. Madiha Naz, Maria Saleem, Asim Khurshid, Tooba Aleem, Muhammad Salman Zafar. Neonatal nosocomial sepsis in Level-III NICU: Causative pathogens and their antimicrobial sensitivity. Prof Med J. 2022;29(03):316–322.

18. Johnson J, Robinson ML, Rajput UC, Valvi C, Kinikar A, Parikh TB, et al. High Burden of Bloodstream Infections Associated With Antimicrobial Resistance and Mortality in the Neonatal Intensive Care Unit in Pune, India. Clin Infect Dis. 2021;73(2):271–280.

19. Alam D, Islam S, Roy TK, Rahman M, Shahid M, Sharmin S. Study of Bacteriological Profile and Antibiotic Sensitivity of Neonatal Sepsis in a Tertiary Care Hospital. J Chittagong Med Coll Teach Assoc. 2017;28(2):53–58.

20. Chandra P, Iqbal F, Unnikrisnan MK, Jayashree P, Shenoy PA, Anburaj SE et al. Neonatal outcomes associated with antimicrobial resistance: A retrospective cross-sectional study. J Appl Pharm Sci. 2023;13(5):081–94.

21. Getabelew A, Aman M, Fantaye E, Yeheyis T. Prevalence of Neonatal Sepsis and Associated Factors among Neonates in Neonatal Intensive Care Unit at Selected Governmental Hospitals in Shashemene Town, Oromia Regional State, Ethiopia 2017. Int J Pediatr. 2018;2018:7801272.

22. Shrestha S, Shrestha NC, Dongol Singh S, Shrestha RPB, Kayestha S, Shrestha M, et al. Bacterial isolates and its antibiotic susceptibility pattern in NICU. Kathmandu Univ Med J KUMJ. 2013;11(41):66–70.

23. Shah MH, McAleese S, Kadam S, Parikh T, Vaidya U, Sanghavi S, et al. Emerging Antibiotic Resistance Patterns in a Neonatal Intensive Care Unit in Pune, India: A 2-Year Retrospective Study. Front Pediatr. 2022;10:864115.

24. Hussain MA, Akram S, Khan MA, Nawaz S, Ali S, Amir M. Neonatal Sepsis; Incidence and Microbiological Profile along with Antibiotic Sensitivity of Causative Microorganisms. Life Sci. 2023;4(1):6.

25. Mannan MA, Iqbal S, Karim SR, Ahmed TU, Khan MHH, Ahmed AU, et al. Bacterial Isolates of Early Onset Neonatal Sepsis and Their Antibiotic Susceptibility Pattern. Chattagram Maa-O-Shishu Hosp Med Coll J. 2018;17(1):3–8.

26. Opare-Asamoah K, Vicar EK, Acquah SE, Quaye L, Alhassan AM, Majeed SF, et al. Bacteriological Profile and Antibiotic Susceptibility Patterns of Sepsis-Causing Bacteria at the Neonatal Intensive Care Unit of a Tertiary Health Care Facility in Ghana. Microbiol Insights. 2023;16:11786361231218169.

27. Mamtaz SSH, Chowdhury AHMSK. Comparison of Clinical, Hematological and

Bacteriological Profile of Neonatal Sepsis between Term and Preterm Babies. J Chittagong Med Coll Teach Assoc. 2021;32(1):21–25.

28. Islam QR, Shahidullah M, Islam MZ, Mridha MAA, Akter S. Bacterial Profile of Neonatal Septicemia and Antibiotic Susceptibility Pattern of the Isolates in Tertiary Care Hospital, Dhaka, Bangladesh. Bangladesh J Child Health. 2019;43(1):35–40.

29. Pervez AFM, Lee KH, Islam F, Hassan MK, Biswas R. Antimicrobial Resistance Situation in SCANU of Faridpur Medical College Hospital, a Tertiary Level Hospital in Bangladesh. Faridpur Med Coll J. 2020;15(1):28–33.

30. Fang P, Gao K, Yang J, Li T, Gong W, Sun Q, et al. Prevalence of Multidrug-Resistant Pathogens Causing Neonatal Early and Late Onset Sepsis, a Retrospective Study from the Tertiary Referral Children's Hospital. Infect Drug Resist. 2023;16:4213–4225.