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ORIGINAL ARTICLE

Pattern and trend of bacterial resistance in neonatal sepsis in infants admitted to the neonatal intensive care unit, from 2016 to 2021

Amir Naddaf[1], Mohammad Ansari Nasab[1], Mamak Shariat[1], Parvaneh Sadeghi-Moghaddam[2], Samaneh Salarvand[3], Zahra Omidi[2,4], Neda Sadat Kosari[1], Leyla Sahebi[1*]

[1]Maternal-Fetal and Neonatal Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[2]Breastfeeding Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran
[3]Department of Anatomical and Clinical Pathology, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
[4]Vali-E-Asr Reproductive Health Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran

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ABSTRACT

Background and Objectives: Neonatal septicemia is a significant cause of morbidity and mortality in neonatal intensive care units (NICUs). Understanding the patterns of antibiotic resistance and pathogen prevalence is crucial for effective treatment.
Materials and Methods: This cross-sectional study was conducted from 2016 to 2022 in the NICU of Vali-Asr Hospital in Tehran. All neonates diagnosed with septicemia were included. Data were collected using the hospital's registry system.
Results: A total of 477 infants were hospitalized with sepsis, with 71.7% classified as early-onset sepsis (EOS) and 28.3% as late-onset sepsis (LOS). The most common pathogens were coagulase-negative *Staphylococcus* (22.1%), *Klebsiella pneumoniae* (14.9%), and *Staphylococcus epidermidis* (14.3%). The highest antibiotic resistance was observed for erythromycin (89.8%), clindamycin (80.6%), gentamicin (66.1%), and ciprofloxacin (63.5%), while vancomycin showed the lowest resistance (11.2%). Significant associations were found between antibiotic resistance with low birth weight and chest tube intervention. Trends in antibiotic resistance varied over the study period, with a notable decrease in resistance in 2021.
Conclusion: The study highlights the high prevalence of antibiotic resistance in neonatal sepsis, emphasizing the need for continuous monitoring and tailored antibiotic stewardship programs. The findings underscore the importance of individualized treatment approaches to improve outcomes for neonates with sepsis.

Keywords: Sepsis; Neonatal; Drug resistance; Bacterial; Intensive care units; *Klebsiella pneumonia*; *Staphylococcus*; Coagulase-negative; Microbial sensitivity tests; Blood culture

INTRODUCTION

Neonatal sepsis is a life-threatening condition affecting infants ≤28 days old, characterized by systemic infection symptoms and complex biochemical disturbances (1, 2).

Despite advancements in neonatal care, sepsis remains a leading cause of morbidity and mortality,

*Corresponding author: Leyla Sahebi, Ph.D, Maternal-Fetal and Neonatal Research Center, Family Health Research Institute, Tehran University of Medical Sciences, Tehran, Iran. Tel: +98-21-66591316 Fax: +98-21-66591316 Email: sahebileila@yahoo.com

accounting for 203,000 deaths annually worldwide, ranking as the third major cause of neonatal mortality (3). The prevalence of neonatal sepsis is notably higher in preterm and low-birth-weight neonates, with a reported mortality rate of 17.6% (2). This burden is especially pronounced in low- and middle-income countries, where infectious disease prevalence is heightened due to limited healthcare infrastructure (2).

Early-onset sepsis (EOS), occurring within the first 72 hours of life, is 2.6 times more common than late-onset sepsis (LOS), with incidences of 2,496 vs. 946 cases per 100,000 live births, respectively (2, 4). EOS is predominantly caused by Group B *Streptococcus* (GBS), *Escherichia coli*, and other *streptococci*, while LOS is often attributed to hospital-acquired pathogens (5).

Empirical treatment commonly includes ampicillin with gentamicin or third-generation cephalosporins, ensuring both efficacy and resistance coverage. Notably, 30% of EOS cases involve gram-negative bacteria resistant to ampicillin, necessitating tailored antibiotic strategies (5).

A comprehensive understanding of local antimicrobial resistance patterns is imperative for optimizing neonatal sepsis management. Resistance trends vary geographically, underscoring the need for data-driven antibiotic protocols. Misuse of antibiotics, coupled with the neglect of region-specific resistance trends, reduces treatment effectiveness and accelerates antimicrobial resistance (6).

Within neonatal intensive care units (NICUs), neonates, particularly preterm infants, face an elevated risk of acquiring multi-drug-resistant (MDR) infections (6). Empirical antibiotic use in NICUs often exceeds necessity, leading to concerns regarding antimicrobial stewardship. Continuous epidemiological monitoring is essential to track evolving bacterial resistance patterns, ensuring effective therapeutic decisions and minimizing adverse treatment outcomes (6).

This study aims to analyze bacterial resistance trends in neonatal sepsis among infants admitted to Vali-Asr Hospital's NICU from 2016 to 2021, addressing critical gaps in resistance profiling and treatment optimization. By elucidating pathogen prevalence and resistance dynamics, findings will contribute to more informed antibiotic selection, reducing neonatal morbidity and mortality associated with sepsis.

MATERIALS AND METHODS

Study design and setting. This cross-sectional study was conducted in the NICU of Vali-Asr Hospital between 2016 and 2022, focusing on neonates diagnosed with septicemia confirmed via positive blood culture during the study period. Data were retrieved from the hospital's registry system.

Study population. The study included all neonates admitted to the NICU at Vali-Asr Hospital with a confirmed diagnosis of septicemia between 2016 and 2021.

Data collection. Data were extracted from the Vali-Asr Maternal and Neonatal Information registry system, maintained by the Maternal, Fetal and Neonatal Research Center. The dataset included demographic details, clinical characteristics, and laboratory findings.

Bacterial culture techniques. Blood samples were collected aseptically from neonates suspected of having septicemia. These samples were inoculated into blood culture bottles and incubated in automated blood culture systems (e.g., BACTEC, BacT/ALERT) for up to seven days. Positive cultures were sub-cultured onto solid media, including blood agar and MacConkey agar, and incubated at 37°C for 24 to 48 hours. Pathogen identification was conducted using standard microbiological techniques, such as gram staining, biochemical tests, and, when necessary, automated identification systems (e.g., VITEK 2, MALDI-TOF MS).

Antibiotic susceptibility testing. Antibiotic susceptibility testing was performed on all identified pathogens using the Kirby-Bauer disk diffusion method, following Clinical and Laboratory Standards Institute (CLSI) guidelines. Mueller-Hinton agar plates were inoculated with standardized bacterial suspensions, and antibiotic-impregnated disks were placed on the surface. After incubation at 37°C for 16 to 18 hours, zones of inhibition were measured and interpreted according to CLSI criteria. Additionally, minimum inhibitory concentrations were determined for selected antibiotics using broth microdilution or automated systems (e.g., VITEK 2).

Data analysis. We examined antibiotic resistance patterns in relation to clinical characteristics. Chi-square tests were used to assess associations between categorical variables, while monthly trends in pathogen prevalence were analyzed. Time series analysis was performed to detect resistance patterns over the study period. All statistical analyses were conducted using SPSS software.

This project received ethical approval from the Tehran University of Medical Sciences Ethics Committee under ethics code IR.TUMS.IKHC.REC.1400.412.

RESULTS

Patient demographics and clinical characteristics. Between 2016 and 2021, a total of 477 neonates were hospitalized in the NICU at Vali-Asr Hospital, Tehran, with a confirmed diagnosis of sepsis. Of these cases, 342 (71.7%) were classified as EOS, while 135 (28.3%) were categorized as LOS.

The mean (SD) gestational age was 32.18 (4.36) weeks, with a mean birth weight of 1,797.1 (768.71) grams. The average age at sepsis diagnosis was 11.79 (6.05) days, while Apgar scores at the first and fifth minutes were recorded as 5.66 (2.53) and 7.89 (1.63), respectively.

Cesarean section deliveries accounted for 85.1% of all births. Additionally, 79.0% (377 neonates) were preterm (≤37 weeks of gestation), and 54.3% (259 neonates) were male. The birthplace of 95.2% of the neonates was Vali-Asr Hospital, where they were subsequently admitted for neonatal sepsis treatment. Among these cases, 76.9% (367 neonates) had low birth weight (<2,500 grams). Sadly, 64 neonates (14.1%) succumbed to complications associated with sepsis. The most commonly observed clinical manifestations among neonates diagnosed with sepsis were jaundice (70.4%), respiratory distress (58.3%), positive C-reactive protein (54.7%), and bleeding (39.0%) (Table 1).

Microbiological findings. The study also revealed that the most common strains causing neonatal sepsis in hospitalized infants were *Staphylococcus epidermidis* (32.08%), and *Klebsiella pneumoniae* (16.6%). Additional findings on bacterial distribution and prevalence can be found in Table 2.

Antibiotic usage and resistance patterns. Regarding antibiotics, the most frequently used for neonatal sepsis were gentamicin (319 cases), ciprofloxacin (299 cases), cotrimoxazole (280 cases), vancomycin (223 cases), clindamycin (221 cases), and erythromycin (216 cases), respectively. Among these, the highest antibiotic resistance proportion was seen in erythromycin (89.8%), clindamycin (80.6%), gentamicin (66.1%), and ciprofloxacin (63.5%); conversely vancomycin exhibited the lowest resistance rate (11.2%) (Fig. 1).

Furthermore, the study indicated that the highest proportion of sepsis antibiotic resistance (among all of antibiotics) was associated with aztreonam (98.9%; 8/9 cases), erythromycin (89.8%; 194/216), ceftriaxone (84.4%; 103/122), cefoxitin (80.3%; 110/137), and ampicillin (77.8%; 137/176) (Fig. 1).

Clinical correlations with antibiotic sensitivity. The study explored associations between antibiotic resistance and various clinical characteristics and treatment interventions among neonates. Key findings (Table 3) indicate that significant correlations were observed between antibiotic resistance and absence of respiratory distress, presence of neonatal apnea, absence of bleeding, low birth weight (<2,500 grams), non-use of umbilical venous catheter, requirement for chest tube insertion, and presence of neonatal hypotonia.

Trends in antibiotic resistance over time. The study tracked monthly trends of drug resistance for five commonly administered antibiotics: erythromycin, vancomycin, ciprofloxacin, gentamicin, piperacillin, and clindamycin over a six-year period (2016–2021) (Tables 4-8).

Resistance rates fluctuated significantly across months: erythromycin resistance peaked in January 2018, February 2019–2020, March 2019, May 2018–2019, July 2016–2019, September 2020, and December 2020. Clindamycin resistance showed the highest relative frequency in February 2019, March 2019, May 2018, July 2016, August 2018, October 2017–2021, and September 2017–2020. Gentamicin resistance peaked in February 2021, May 2017–2021, July 2017, August 2018, October 2017–2021, and December 2018–2021. Ciprofloxacin resistance was highest in February 2021, May 2020–2021, July 2017, and November 2019. Vancomycin resistance peaked in January 2020 and July 2016.

Corresponding graphs visualizing these resistance

Table 1. Distribution of clinical findings in hospitalized infants with sepsis in the NICU at Vali-Asr Hospital

Clinical findings	n (%)	Clinical findings	n (%)
Jaundice	321 (70.4)	Pneumonia	65 (11.3)
Respiratory distress	266 (58.3)	Intolerance PO	36 (7.5)
Bleeding	186 (39.0)	Cyanosis	27 (7.5)
Premature Rupture of Membranes (PPROM)	80 (18.6)	Hypotonia	27 (5.7)
Tachypnea (TTN)	85 (17.8)	Fever	14 (2.9)
Apnea	58 (12.7)	Decreased infant reflexes	13 (2.7)
Seizure	56 (11.7)	Lethargy	3 (0.6)

Table 2. Frequency of the main strains causing neonatal sepsis in neonates admitted to Vali-Asr Hospital from 2016-2021

Pathogens	n (%)	Pathogens	n (%)
Staphylococcus epidermidis	153 (32.07)	*Escherichia coli*	11 (2.3)
Klebsiella pneumoniae	79 (16.6)	*Strep non-hemolytic*	9 (1.9)
Acinetobacter baumannii	43 (9.01)	*Staphylococcus aureus*	5 (1.0)
**Candida*	46 (9.64)	*Enterococcus faecalis*	3 (0.6)
Stenotrophomonas maltophilia	27 (5.7)	*Alcaligenes* sp.	4 (0.8)
Enterococcus faecium	24 (5.0)	*Streptococci viridans*	2 (0.4)
Staphylococcus haemolyticus	24 (5.03)	*Staphylococcus saprophyticus*	5 (1.05)
Enterobacter cloacae and *aerogenes*	10 (2.1)	*Staphylococcus lentus*	5 (1.05)
Streptococcus mitis	8 (1.7)		

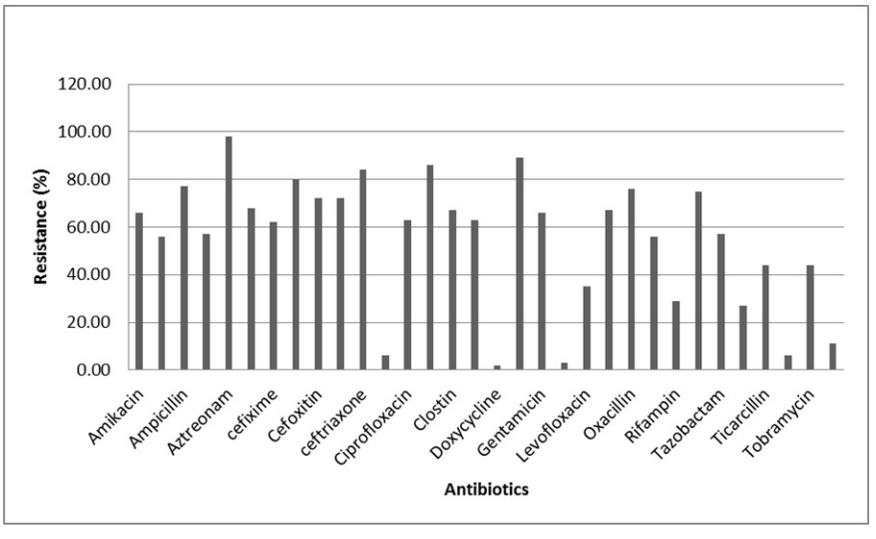

Fig. 1. The pattern of antibiotic resistance in neonatal sepsis from 2016 to 2021

trends are presented in Figs. 2-6. Notably, drug resistance rates showed a significant decline in 2021, with only 11 reported cases of erythromycin-resistant infections, suggesting an overall downward trend in antibiotic resistance in the final year of the study.

DISCUSSION

This study, conducted in the NICU of Vali-Asr Hospital (2016–2021), identified 192 coagulase-negative *Staphylococcus* isolates (40.25% of total cases), including *Staphylococcus epidermidis*, *Staphylococ-*

Table 3. Distribution of maternal and neonatal characteristics based on sensitivity to commonly used antibiotics

Variables	Co-Factors	Sensitive to antibiotics; N (%)	Resistance to antibiotics, N (%)	X^2(P-Value)
Gender	Female	27 (11.7)	203 (88.3)	0.178 (0.392)
	Male	24 (13.1)	159 (86.9)	
Type of Sepsis	Early	29 (13.4)	187 (86.6)	0.034 (0.854)
	Late	22 (12.8)	150 (87.2)	
Respiratory distress	No	9 (4.9)	176 (95.1)	20.53 (<0.001)
	Yes	42 (20.3)	165 (79.7)	
Neonatal apnea	No	49 (14.4)	291 (85.6)	4.60 (0.032)
	Yes	2 (3.8)	51 (96.2)	
Pneumonia	No	47 (14.0)	289 (86.0)	1.99 (0.159)
	Yes	4 (7.1)	52 (92.9)	
Jaundice	No	11 (10.2)	97 (89.8)	1.03 (0.311)
	Yes	40 (14.0)	245 (86.0)	
Bleeding	No	24 (9.2)	238 (90.8)	10.14 (0.002)
	Yes	27 (20.6)	104 (79.4)	
Gestational age, week	<38	15 (0.048)	298 (95.2)	1.46 (0.23)
	≥38	2 (2.0)	97 (98.0)	
Low birth weight	No	50 (16.8)	248 (83.2)	18.68 (<0.001)
	Yes	1 (0.9)	110 (99.1)	
Place of birth	The same hospital	49 (12.5)	342 (87.5)	0.166 (0.683)
	Another hospital	2 (9.5)	19 (90.5)	
Type of delivery	Cesarean section	42 (12.2)	303 (87.8)	0.059 (0.808)
	Vaginal	9 (13.2)	59 (86.8)	
Intubation	No	22 (10.0)	199 (90.0)	3.57 (0.059)
	Yes	28 (16.8)	143 (86.4)	
Umbilical vein catheter	No	35 (11.0)	284 (89.0)	4.89 (0.027)
	Yes	15 (20.5)	58 (79.5)	
Chest tube	No	50 (14.8)	287 (85.2)	9.18(0.007)
	Yes	0 (0)	54 (100.0)	
Neonatal hypotonia	No	51 (13.9)	315 (86.1)	4.32 (0.038)
	Yes	0 (0.0)	27 (100.0)	

Table 4. Frequency and percentage of antibiotic resistance to erythromycin in neonatal sepsis in Vali-Asr Hospital from 2016 to 2021.

Month	2016		2017		2018		2019		2020		2021		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
1	1	50.0	0	0.0	6	75.0	5	45.45	0	0.0	0	0.0	12
2	2	33.33	3	75.0	2	18.18	4	80.0	1	100.0	0	0.0	12
3	3	42.85	4	66.67	3	37.5	2	100.0	3	27.27	0	0.0	15
4	3	37.5	1	25.0	3	37.5	0	0.0	2	33.33	4	28.57	13
5	2	66.67	1	100.0	8	72.72	3	37.5	9	60.0	0	0.0	25
6	2	33.33	2	25.0	3	37.5	2	33.3	7	58.33	0	0.0	16
7	1	100.0	3	100.0	4	40.0	3	75.0	1	20.0	0	0.0	12
8	2	33.33	1	33.33	5	71.4	2	28.57	6	30.0	0	0.0	16
9	3	42.85	3	75.0	4	44.45	1	16.67	4	100.0	3	13.04	18
10	4	40.0	4	80.0	4	66.67	5	33.33	7	46.67	3	60.0	27
11	3	75.0	4	57.14	4	44.45	8	80.0	2	33.33	1	33.33	22
12	1	33.33	1	16.67	4	50.0	3	50.0	1	100.0	0	0.0	10
Total	29		27		50		38		43		11		198

Table 5. The frequency and percentage of antibiotic resistance to clindamycin in neonatal sepsis in Vali-Asr Hospital 2016-2021

Month	2016		2017		2018		2019		2020		2021		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
1	1	50.0	0	0.0	5	62.5	5	45.45	0	0.0	1	50.0	12
2	2	33.33	3	75.0	1	9.09	4	80.0	0	0.0	0	0.0	10
3	1	14.28	4	66.67	3	37.5	2	100.0	4	36.36	0	0.0	14
4	3	37.5	2	50.0	3	37.5	0	0.0	2	33.33	4	28.57	14
5	1	33.33	0	0.0	8	72.72	3	37.5	9	60.0	1	20.0	22
6	2	33.33	2	25.0	3	37.5	2	33.33	7	58.33	1	12.5	17
7	1	100.0	2	66.67	4	40.0	2	50.0	1	20.0	0	0.0	10
8	2	33.33	1	33.33	5	71.42	2	28.57	5	25.0	0	0.0	15
9	3	42.85	3	75.0	3	33.33	1	16.67	4	100.0	5	21.39	19
10	5	50.0	4	80.0	4	66.67	4	26.67	7	58.0	4	80.0	28
11	2	50.0	4	57.14	4	44.44	8	80.0	2	33.33	1	33.33	21
12	1	33.33	2	33.33	4	50.0	2	33.33	1	60.0	0	0.0	10
Total	24		27		47		35		42		17		192

Table 6. Frequency and percentage of antibiotic resistance to gentamicin in neonatal sepsis in Vali-Asr Hospital from 2016 to 2021

Month	2016		2017		2018		2019		2020		2021		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
1	1	50.0	0	0.0	5	62.5	7	63.6	0	0.0	0	0.0	13
2	4	66.7	2	50.0	3	27.3	2	40.0	0	0.0	2	100	13
3	3	42.9	1	16.7	2	25.0	1	50.0	2	18.2	4	50.0	13
4	4	50.0	2	50.0	5	62.5	3	50.0	2	33.3	8	57.1	24
5	2	66.7	1	100.0	6	54.5	3	37.5	4	16.7	4	80.0	20
6	4	66.7	4	50.0	3	37.5	2	33.3	4	33.3	5	62.5	22
7	0	0.0	3	100.0	4	40.0	3	75.0	3	60.0	0	0.0	13
8	3	50.0	1	33.3	4	57.1	5	71.5	5	25.0	0	0.0	18
9	5	71.4	2	50.0	6	66.7	0	0.0	0	0.0	14	60.9	27
10	5	50.0	3	60.0	4	66.7	4	26.7	3	20.0	2	40.0	21
11	2	50.0	4	57.1	5	55.6	3	30.0	2	33.3	2	66.7	18
12	0	0.0	1	16.7	6	75.0	1	16.7	0	0.0	7	100.0	15
Total	48		33		24		53		34		25		217

cus haemolyticus, Staphylococcus saprophyticus, Staphylococcus lentus, and *Staphylococcus hominis.* Among these, 153 isolates (32.08%) were confirmed as *S. epidermidis,* while 24 isolates (5.03%) were *S. haemolyticus.* Additionally, *K. pneumoniae* accounted for 16.6% of total isolates (79/477 cases).

These findings are consistent with previous studies in Iran, which identify coagulase-negative *Staphylococcus* and *K. pneumoniae* as common neonatal sepsis pathogens (7-10). In contrast, *E. coli,* which was the second most common organism in studies by Akbarian Rad and Moftian (7, 9), was responsible for only 2.3% of neonatal sepsis cases in our study.

Globally, variability in pathogen prevalence has been observed. Research in India (2019) reported coagulase-negative *Staphylococcus, Staphylococcus aureus, Acinetobacter,* and *Klebsiella* as leading neonatal sepsis agents (11, 12). Similarly, a study in Ethiopia (2023) identified *Klebsiella* species (44%), *E. coli* (21.6%), and coagulase-negative *Staphylococ-*

Table 7. Frequency and percentage of antibiotic resistance to ciprofloxacin in neonatal sepsis in Vali-Asr Hospital from 2016 to 2021

Month	2016		2017		2018		2019		2020		2021		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
1	1	50.0	0	0.0	5	62.5	7	63.6	0	0.0	0	0.0	13
2	4	66.7	2	50.0	3	27.3	2	40.0	0	0.0	2	100	13
3	3	42.9	1	16.7	2	25.0	1	50.0	2	18.2	4	50.0	13
4	4	50.0	2	50.0	5	62.5	3	50.0	2	33.3	8	57.1	24
5	2	66.7	1	100.0	6	54.5	3	37.5	4	16.7	4	80.0	20
6	4	66.7	4	50.0	3	37.5	2	33.3	4	33.3	5	62.5	22
7	0	0.0	3	100.0	4	40.0	3	75.0	3	60.0	0	0.0	13
8	3	50.0	1	33.3	4	57.1	5	71.5	5	25.0	0	0.0	18
9	5	71.4	2	50.0	6	66.7	0	0.0	0	0.0	14	60.9	27
10	5	50.0	3	60.0	4	66.7	4	26.7	3	20.0	2	40.0	21
11	2	50.0	4	57.1	5	55.6	3	30.0	2	33.3	2	66.7	18
12	0	0.0	1	16.7	6	75.0	1	16.7	0	0.0	7	100.0	15
Total	48		33		24		53		34		25		217

Table 8. Frequency and percentage of antibiotic resistance to vancomycin in neonatal sepsis in Vali-Asr Hospital from 2016 to 2021

Month	2016		2017		2018		2019		2020		2021		Total
	n	%	n	%	n	%	n	%	n	%	n	%	
1	1	50.0	0	0.0	0	0.0	0	0.0	1	100.0	0	0.0	2
2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0
3	1	14.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1
4	1	12.5	1	25.0	0	0.0	0	0.0	0	0.0	7.1	0.0	2
5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0
6	1	16.7	1	12.5	0	0.0	0	0.0	0	0.0	0	0.0	2
7	1	100.0	1	33.3	0	0.0	1	25.0	0	0.0	0	0.0	3
8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0
9	0	0.0	1	25.0	0	0.0	1	16.7	0	0.0	1	4.3	3
10	1	10.0	0	0.0	0	0.0	3	20.0	1	6.7	0	0.0	5
11	1	25.0	1	14.3	1	11.1	1	10.0	1	16.7	0	0.0	5
12	1	33.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1
Total	8		5		1		6		3		1		24

cus (15.47%) as primary culprits (13).

In this study, the most frequently administered antibiotics for neonatal sepsis were: gentamicin (66.1%), ciprofloxacin, cotrimoxazole, and vancomycin. In comparison, a 2019 study in India found that the most frequently used antibiotics were amikacin (86.7%), vancomycin (52.3%), and ampicillin (40.6%) (11).

In the present study, among the five commonly used antibiotics, the highest rates of antibiotic resistance were observed for erythromycin (89.8%), clindamycin (86.0%), gentamicin (66.1%), and ciprofloxacin (63.6%). In contrast, the lowest resistance rate was found for vancomycin (11.2%). It is noted that gentamicin was administered based on an empirical regimen, while vancomycin was prescribed after receiving the antibiogram results. The resistance rate for gentamicin was significantly higher than that for vancomycin (66.1% compared to 11.2%).

In the study by Moftian et al. (2023), the highest resistance observed in *K. pneumoniae* was 80.6% for cefixime (7) In contrast, research conducted by Saei-

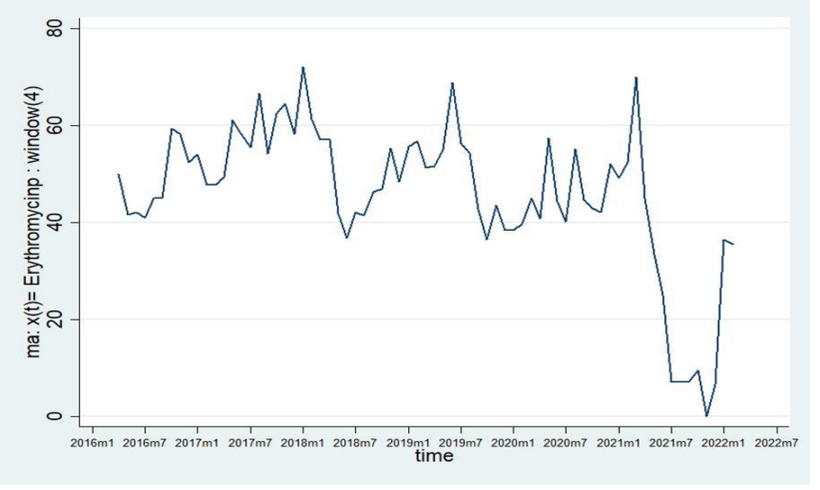

Fig. 2. The percentage of bacterial resistance to erythromycin in patients with neonatal sepsis admitted to Vali-Asr Hospital 2016-2021

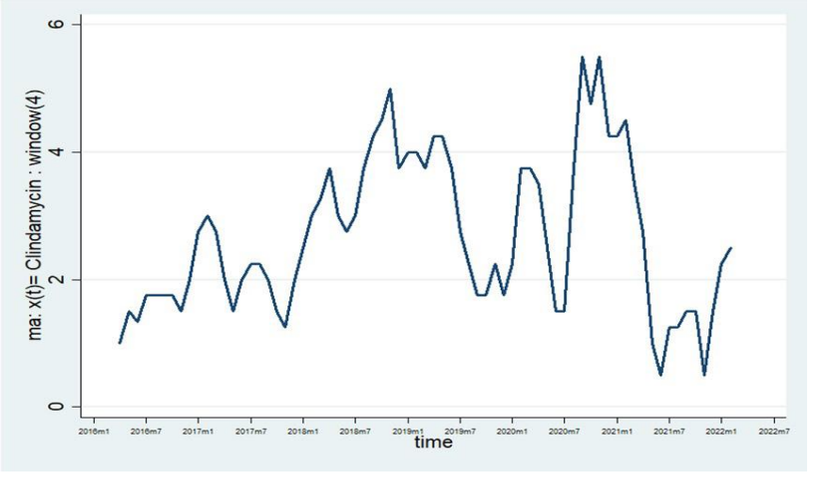

Fig. 3. The percentage of bacterial resistance to clindamycin in patients with neonatal sepsis admitted to Vali-Asr Hospital 2016-2021

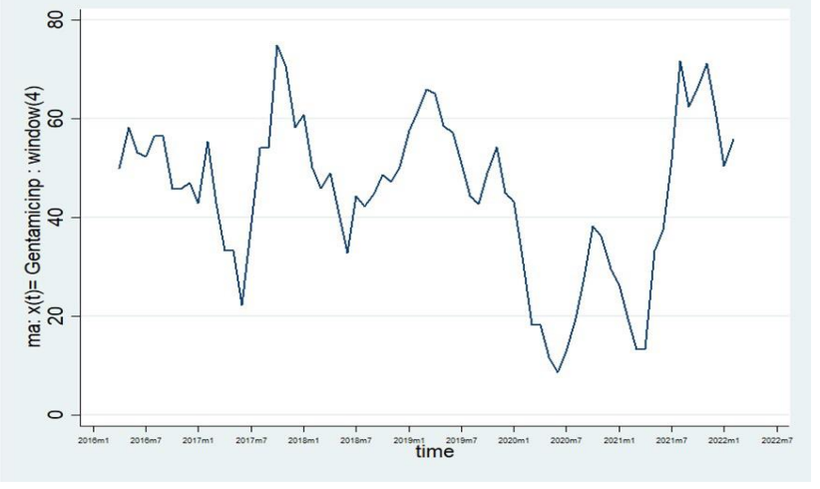

Fig. 4. The percentage of bacterial resistance to gentamicin in patients with neonatal sepsis admitted to Vali-Asr Hospital 2016-2021

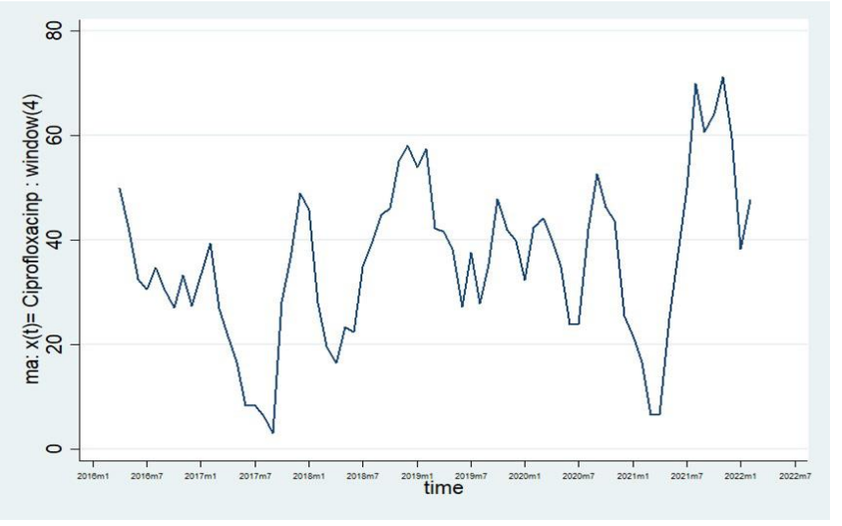

Fig. 5. The percentage of bacterial resistance to ciprofloxacin in patients with neonatal sepsis admitted to Vali-Asr Hospital 2016-2021

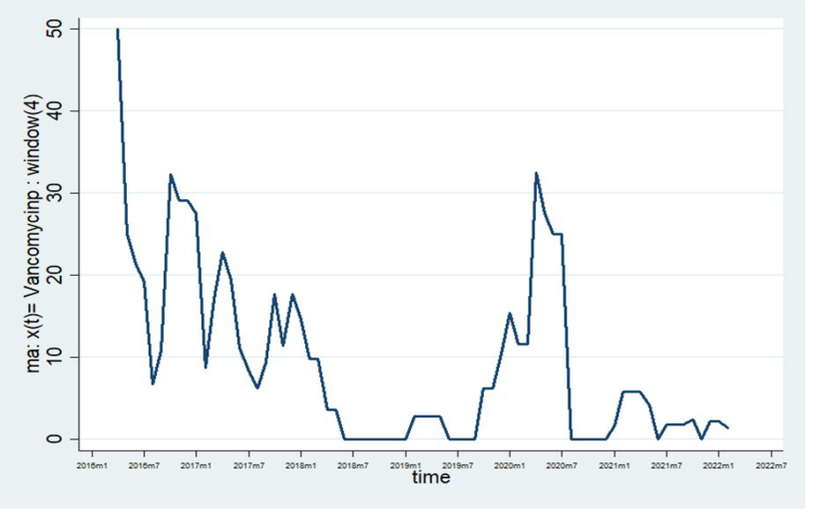

Fig. 6. The percentage of bacterial resistance to vancomycin in patients with neonatal sepsis admitted to Vali-Asr Hospital 2016-2021

di et al. (2023) in Tabriz revealed nearly 100% antibiotic resistance to ampicillin and gentamicin(10). Additionally, Rashmi's retrospective study indicated that gram-positive exhibited the least resistance to vancomycin and linezolid (11).

The findings suggest regional variations in antibiotic sensitivity among pathogens causing neonatal sepsis, likely due to differences in prescribing patterns and adherence to antimicrobial guidelines. These factors influence drug resistance development, reinforcing the need for localized antibiograms to guide treatment strategies.

In our study, 71.7% of cases presented with EOS, while 28.3% exhibited LOS. Similar trends have been reported in Iran, where Afshar Paiman et al. (2012) found the incidence of EOS to be nearly twice that of LOS(14). Rashmi et al. (2019) reported EOS in 58.1% of cases and LOS in 41.9%, suggesting that perinatal factors play a larger role in neonatal sepsis than post-delivery environmental exposure (11).

The mortality rate in this study was 14.1%, aligning closely with Rashmi et al. (13.5%) (14), but lower than Afshar Paiman et al.'s findings (27.4%) (11). A meta-analysis by Fleischmann et al. (2021) estimated a global neonatal sepsis mortality rate of 17.6% (2,824 deaths per 100,000 births) (2).

Neonatal sepsis symptoms. Neonatal sepsis often presents with non-specific symptoms, including fever, hypothermia, respiratory distress, feeding difficulties, hypotonia, seizures, and abdominal distension (15, 16). In the current study, the reported symptoms included: respiratory distress (58.3%), bleeding (39%), apnea (12.7%), pneumonia (11.3%), tachypnea (17.8%), and cyanosis (5.7%). Hypotonia was observed in 0.6% of cases, decreased reflexes in 5.7%, lethargy in 2.7%, and fever in 2.9%.

A study in China (2022) by You et al. found a significant association between respiratory distress and sepsis, highlighting the impact of hypoxia and acidosis during fetal life (17).

The study also identified notable trends in antibiotic resistance related to neonatal sepsis from 2016 to 2021. Vancomycin and rifampin showed a decreasing trend in resistance, while erythromycin, piperacillin, and cefoxitin exhibited an increasing trend. Other antibiotics did not show significant changes in resistance.

Afshar Paiman et al. (2012) observed a gradual decline in sensitivity to imipenem and gentamicin in Iran from 2003 to 2006, demonstrating evolving resistance patterns (14). Similarly, Karimi et al. (2019) documented changing antibiotic resistance trends in India (18).

Antibiotic resistance fluctuates based on prescribing frequency, particularly when empirical regimens are used indiscriminately. Increased antibiotic use correlates with higher resistance levels, whereas reduced consumption in a population may lead to lower resistance among microorganisms (18). In Iran, studies indicate rising antibiotic consumption rates, emphasizing the urgent need for stricter antibiotic control policies. Neonatal sepsis poses unique diagnostic challenges, often leading to excessive antibiotic use, which further drives antimicrobial resistance (18).

Study limitations. One notable limitation in this study was the lack of detailed resistance classification for certain bacterial isolates. Due to data constraints, we were unable to categorize resistance patterns into subtypes such as methicillin-resistant vs. methicillin-sensitive *Staphylococcus epidermidis* (MRSE/MSSE) or extended-spectrum β-lactamase (ESBL)-producing *Klebsiella pneumoniae*. This limitation may impact clinical applicability; as precise resistance profiling is crucial for targeted antimicrobial therapy. Future research should incorporate more detailed resistance characterizations to enhance the clinical relevance of resistance pattern analyses.

CONCLUSION

The findings of this study highlight the high prevalence of EOS and significant antibiotic resistance, particularly to erythromycin, clindamycin, gentamicin, and ciprofloxacin. However, the relatively low resistance to vancomycin suggests that it remains an effective treatment option for neonatal sepsis. This study emphasizes the critical need for continuous monitoring of antibiotic resistance patterns and the implementation of targeted antibiotic stewardship programs to address the growing challenge of drug-resistant infections in neonates. Furthermore, the observed significant associations between antibiotic resistance and specific clinical conditions highlight the importance of individualized treatment strategies to improve clinical outcomes.

The declining antibiotic resistance trend in 2021 may reflect changes in prescribing practices and infection control measures, reinforcing the need for adaptive healthcare strategies. These findings provide valuable insights for healthcare providers and policymakers, informing efforts to reduce the burden of neonatal sepsis and enhance care quality in NICUs.

REFERENCES

1. Vergnano S, Sharland M, Kazembe P, Mwansambo C, Heath PT. Neonatal sepsis: an international perspective. *Arch Dis Child Fetal Neonatal Ed* 2005; 90: F220-F224.
2. Fleischmann C, Reichert F, Cassini A, Horner R, Harder T, Markwart R, et al. Global incidence and mortality of neonatal sepsis: a systematic review and meta-analysis. *Arch Dis Child* 2021; 106: 745-752.
3. Attia Hussein Mahmoud H, Parekh R, Dhandibhotla S, Sai T, Pradhan A, Alugula S, et al. Insight into neonatal sepsis: an overview. *Cureus* 2023; 15(9): e45530.
4. Kuhl DA. Current strategies for managing the patient with sepsis. *Am J Health Syst Pharm* 2002; 59 Suppl 1: S9-S13.
5. Scheurer JM, Fanta ML, Colbenson GA, Arbefeville S, Ferrieri P. Early-onset neonatal sepsis caused by vertical transmission of Pasteurella multocida. *AJP Rep* 2022; 12(2): e123-e126.

6. Barcellini L, Bresesti I, Folgori L. Neglected populations not to be Forgotten: Tackling antimicrobial resistance in Neonatal infections. *Antibiotics (Basel)* 2023; 12: 1688.
7. Moftian N, Rezaei-Hachesu P, Arab-Zozani M, Samad-Soltani T, Esfandiari A, Tabib MS, et al. Prevalence of gram-negative bacteria and their antibiotic resistance in neonatal sepsis in Iran: a systematic review and meta-analysis. *BMC Infect Dis* 2023; 23: 534.
8. Shariat M, Youssefkhani AB, Dalili H, Hajinasab N, Farrokhzad N, Nozarian Z, et al. Associated factors and common Pathogens of positive cultures in infants with Definitive Septicemia Admitted to NICU. *Acta Med Iran* 2023; 61: 355-360.
9. Akbarian-Rad Z, Riahi SM, Abdollahi A, Sabbagh P, Ebrahimpour S, Javanian M, et al. Neonatal sepsis in Iran: A systematic review and meta-analysis on national prevalence and causative pathogens. *PLoS One* 2020; 15(1): e0227570.
10. Saeidi F, Kialashaki A, Sadighi A, Bahadori A, Valizadeh S, Hosseini M, et al. A Survey of the Prevalence Rate and Antibiotic resistance pattern of Microbial agents in Preterm Neonatal Sepsis. *Arch Pediatr Infect Dis* 2023; 12(1): e137546.
11. Rashmi P, Praveen B. Clinico-bacteriological profile of neonatal sepsis. *Int J Contemp Pediatr* 2019; 6: 796-802.
12. Ullah O, Khan A, Ambreen A, Ahmad I, Akhtar T, Gandapor AJ, et al. Antibiotic sensitivity pattern of bacterial isolates of neonatal septicemia in Peshawar, Pakistan. *Arch Iran Med* 2016; 19: 866-869.
13. Sherif M, Abera D, Desta K. Prevalence and antibiotic resistance pattern of bacteria from sepsis suspected neonates at St. Paul's Hospital Millennium Medical College, Addis Ababa, Ethiopia. *BMC Pediatr* 2023; 23: 575.
14. Afsharpaiman S, Torkaman M, Saburi A, Farzaampur A, Amirsalari S, Kavehmanesh Z. Trends in incidence of neonatal sepsis and antibiotic susceptibility of causative agents in two neonatal intensive care units in Tehran, IR Iran. *J Clin Neonatol* 2012; 1: 124-130.
15. Gerdes JS. Diagnosis and management of bacterial infections in the neonate. *Pediatr Clin North Am* 2004; 51: 939-959.
16. Kim F, Polin RA, Hooven TA. Neonatal sepsis. *BMJ* 2020; 371: m3672.
17. You T, Zhou Y-R, Liu X-C, Li L-Q. Risk factors and clinical characteristics of neonatal acute respiratory distress syndrome caused by early onset sepsis. *Front Pediatr* 2022; 10: 847827.
18. Karimi F, Lewis LE, Thunga G, Najmi A, Sahu P, Kunhikatta V. Relationship between antibiotic consumption pattern and antibiotic resistance in neonatal sepsis. *Med Pharm Rep* 2023; 96: 35-40.