
Pattern And Antibiotic Sensitivity in Neonates with Sepsis- A Retrospective Study

Ashfaq Ahmed¹, Arshad Karim², Adnan Khan³, Mohammand Hamayon⁴, Neelum Zahir⁵, Sara⁶

¹Associate Professor, Pediatric Medicine Department, Saidu Teaching Hospital, Swat

²Assistant Professor, Pediatric Medicine Department, Saidu Teaching Hospital, Swat

³Trainee Medical Officer, Pediatric Medicine Department Saidu Teaching Hospital Swat

⁴Technical Officer, Immunization, World Health Organization (WHO)

⁵Assistant Professor, Gynecology & Obstetrics Department, Saidu Teaching Hospital, Swat

⁶Trainee Medical Officer Gynecology department MTI LRH Peshawar

Corresponding Author: **Arshad Karim**

Assistant Professor, Pediatric Medicine Department, Saidu Teaching Hospital, Swat

Email: karimarshad01@gmail.com

ABSTRACT

Background: Sepsis is among the cause of morbidity and mortality among neonates, need an understanding of bacterial isolates and their antibiotic sensitivities.

Objective: To identify bacterial pathogens in neonates with sepsis and evaluate their antibiotic sensitivity profiles.

Study Design: A retrospective cross-sectional study.

Place and Duration of study. Pediatrics Department at Saidu Teaching Hospital, Swat, from 1st January 2022 to 10th September 2024.

Materials and Methods: This retrospective cross-sectional study analyzed records of 195 neonates with blood culture-proven sepsis, selected via non-probability sampling. Inclusion criteria was both males and females neonates under one month of age, while those with comorbid conditions and prior antibiotic therapy were excluded. Blood samples were cultured using standard microbiological procedures, and isolates were identified through Gram staining and biochemical tests. Antibiotic sensitivity was determined using the Kirby-Bauer disc diffusion method.

Results: The mean age of participants was 8.15 ± 6.20 days, with a gender distribution of 42.56% female and 49.23% male. The most frequently isolated pathogen was *Salmonella* spp. (36.41%), followed by *Burkholderia cepacia* (34.87%). Other notable isolates included *Acinetobacter* species (9.74%), *Klebsiella* species (9.74%), and *Pseudomonas aeruginosa* (3.59%). Ampicillin resistance was predominant (60.00%),

followed by Ceftriaxone (50.77%) and Septran (45.13%). Additionally, significant resistance was observed against Cefotaxime (44.62%), Chloramphenicol (40.51%), and Nalidixic acid (38.97%). Imipenem and Meropenem exhibited lower resistance rates at 33.85% and 22.56%, respectively. Chi-square analysis indicated no significant difference in most of resistance patterns based on gender ($p > 0.05$).

Conclusion: The study show the alarming resistance rates among bacterial pathogens in neonatal sepsis to commonly used antibiotics. Continuous surveillance of antibiotic susceptibility is essential to guide effective treatment strategies.

KEYWORDS

Neonates, sepsis, bacterial isolates, antibiotic sensitivity, *Salmonella* spp., resistance

INTRODUCTION

Neonatal sepsis is a life-threatening infection occurring in infants under one month of age.¹ It can manifest as a variety of infections, including meningitis, pneumonia, joint infections, bone infections, or urinary tract infections, requiring prompt diagnosis and treatment.² Due to their immature immune systems, neonates are especially prone to infections.³ Common bacterial causes include Group B *Streptococcus*, *Escherichia coli*, *Listeria monocytogenes*, and *Staphylococcus aureus*.⁴ In developed countries, the incidence of neonatal sepsis is between 1 and 10 per 1,000 live births, whereas in developing nations like Pakistan, it is about three times greater.⁵ Despite advances in neonatal care, neonatal sepsis remains a major challenge, requiring prompt recognition and immediate intervention to reduce the high risk of death and long-term complications such as neurodevelopmental disabilities. Blood cultures remain the gold standard for the definitive diagnosis of neonatal sepsis, allowing for the identification of the causative organisms and their antibiotic susceptibility.⁶ The increasing prevalence of antibiotic resistance has complicated treatment efforts, particularly in low-resource settings where neonatal sepsis is more prevalent.⁷ Many factors contribute to antibiotic resistance in low-income countries, but the most important is the indiscriminate use of antibiotics. In these countries, antibiotics are readily available over the counter without a prescription, leading to their misuse for diseases such as viral infections, where they are either unnecessary or ineffective.⁸ Other factors include frequent suboptimal dosing, which allows bacteria to survive and develop resistance, and insufficient sterilization, along with overcrowded hospitals, which contribute to the spread of resistant bacteria. Poor infrastructure and limited access to diagnostic facilities further exacerbate the problem.⁹ The pattern of bacterial isolates and their susceptibility to antibiotics can vary significantly across different regions and healthcare settings.¹⁰ Regular monitoring of these patterns is needed to make sure that empirical regimens of antibiotics are effective in treating neonatal sepsis.¹¹ Studies in Pakistan have shown alarmingly high resistance rates to commonly used antibiotics, such as ampicillin, cefotaxime, and gentamin.¹² This study aims to investigate the patterns of bacterial isolates and antibiotic sensitivity in neonates with sepsis at a tertiary care hospital. There is a lack of studies on this population. By understanding bacterial resistance profiles, this research can provide pertinent information for the most effective treatment protocols for neonatal sepsis, which may help reduce morbidity and mortality in neonates. Additionally, this study can contribute to preventing antibiotic resistance.

MATERIALS AND METHODS

This retrospective cross-sectional study was conducted in the Pediatrics Department at Saidu Teaching Hospital, Swat, using records of 195 neonates selected through a non-probability consecutive sampling technique from 1st January 2022 to 10th September 2024. Ethical approval was obtained from the hospital's ethical committee prior to the study's inception. Informed consent had already been obtained from the parents of each neonate as part of treatment, allowing their records to be used for research purposes. Additionally, all neonates' records were anonymized to ensure confidentiality. The sample size of 195 was calculated through openepi at 5% margin of errors and 95% confidence interval using 85.11% ampicillin resistance from previous study.¹³ Neonates were defined as infants aged less than 28 days, and sepsis diagnosis was confirmed using positive blood culture results. The inclusion criteria were male and female neonates, Pakistani nationals, those aged less than one month, and cases with blood culture-proven sepsis. The exclusion criteria included infants with comorbid conditions (e.g., congenital heart disease, major congenital anomalies), those who had received prior antibiotic therapy, and cases with incomplete medical records. Data on neonates' demographic details, clinical presentations, bacterial isolates, and antibiotic sensitivity patterns were extracted from hospital records. Blood samples were collected from neonates suspected of having sepsis before initiating antibiotic therapy. Blood samples were cultured using standard procedures. The samples were inoculated on Blood agar, MacConkey agar, and Chocolate agar. The incubation was carried out at 37°C under aerobic conditions for a period of 5-7 days. The identification of bacterial isolates was confirmed through Gram staining and biochemical tests such as catalase and oxidase tests. Antibiotic sensitivity was assessed using the Kirby-Bauer disc diffusion method on Mueller-Hinton agar plates, following Clinical Laboratory Standards Institute (CLSI) guideline.¹⁴ Sensitivity to commonly used antibiotics, including ampicillin, cefotaxime, and gentamicin, was evaluated. Data analysis was conducted in R software 4.3.2. Age was computed as mean with SD while gender and antibiotic resistance was computed as frequency with percentages. Antibiotic resistance was stratified with respect to gender of the neonate using chi-square test. $P < 0.05$ was the significant edge.

RESULTS

The mean age was 8.15 ± 6.20 days. Of the total participants, 83 (42.56%) were female, 96 (49.23%) were male, and gender information was unavailable for 16 (8.21%) neonates. The majority of neonates (173, 88.72%) were aged between 1 and 15 days, with the remaining 22 (11.28%) aged between 1 and 28 days. **(Table 1)** Among the bacterial isolates identified in neonates with sepsis, the most common pathogen was *Salmonella spp.*, accounting for 71 cases (36.41%), followed by *Burkholderia cepacia* with 68 cases (34.87%). Other notable pathogens included *Acinetobacter species* and *Klebsiella species*, both with 19 cases (9.74%). Less frequently isolated bacteria were *Pseudomonas aeruginosa* (7 cases, 3.59%), *Citrobacter spp.* and *E. coli* (each with 4 cases, 2.05%). Rare isolates included *Enterobacter species*, *Proteus species*, and *Staphylococcus*, each found in 1 case (0.51%). **(Fig 1)** **Table 2** reveals that the most common resistant drug in neonatal sepsis was Ampicillin, with a significant resistance rate of 117 isolates (60.00%). This was followed by Ceftriaxone, which exhibited resistance in 99 isolates (50.77%). The third most commonly resistant drug was Septran, showing resistance in 88 isolates (45.13%). Other notable antibiotics included Cefotaxime with 87 resistant isolates (44.62%), Chloramphenicol at 79 (40.51%), and Nalidixic acid with resistance in 76 isolates (38.97%). Additionally, Ciprofloxacin and Colistin presented resistance in 68 (34.87%) and 67 (34.36%) isolates, respectively. Imipenem and Meropenem had lower resistance rates at 66 (33.85%) and 44 (22.56%) resistant

isolates. **Table 3** indicate that Azithromycin demonstrated more resistance in females (2 cases, 0.37%) compared to males, who showed no resistance (0%). Similarly, Levofloxacin had resistance in females (10 cases, 1.86%) while males exhibited higher sensitivity, with 44 males (15.07%) sensitive, though the resistance rates were similar (1.61%) in males. Additionally, Nalidixic acid showed more resistance in females (28 cases, 5.20%) compared to males, who had 0% resistance.

Table 1. Demographics of the participants with neonatal sepsis

Characteristic	N = 195
Age(days), Mean \pm SD	8.15 \pm 6.20
Gender	
Female	83 (42.56)
Male	96 (49.23)
Gender information not available	16 (8.21)
Age group	
1-15 days	173 (88.72)
1-28 days	22 (11.28)

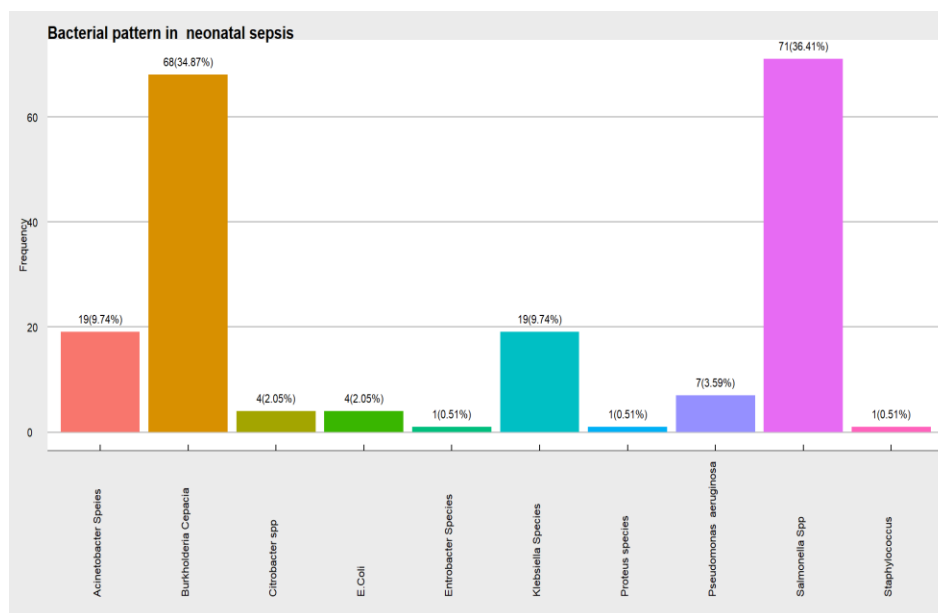


Fig 1: Bacterial pattern in neonate sepsis

Table 2. Resistance of individual antibiotics

Drug	Intermediate	resistance	sensitive	Not tested
Augmentin	0 (0.00)	35 (17.95)	4 (2.05)	156 (80.00)
Amikicin	0 (0.00)	48 (24.62)	35 (17.95)	112 (57.44)
Ampicillin	0 (0.00)	117 (60.00)	4 (2.05)	74 (37.95)
ATM	0 (0.00)	10 (5.13)	2 (1.03)	183 (93.85)
azithromycin	0 (0.00)	2 (1.03)	72 (36.92)	121 (62.05)
cefotaxime	0 (0.00)	87 (44.62)	17 (8.72)	91 (46.67)
cefoxitim	0 (0.00)	0 (0.00)	1 (0.51)	194 (99.49)
ceftrazidime	0 (0.00)	53 (27.18)	40 (20.51)	102 (52.31)
ceftriaxone	0 (0.00)	99 (50.77)	6 (3.08)	90 (46.15)
Cefuroxime	0 (0.00)	82 (42.05)	4 (2.05)	109 (55.90)
chloramphenicol	0 (0.00)	79 (40.51)	56 (28.72)	60 (30.77)
ciprofloxacin	5 (2.56)	68 (34.87)	13 (6.67)	109 (55.90)
Colistin	3 (1.54)	67 (34.36)	40 (20.51)	85 (43.59)
doxycillin	2 (1.03)	27 (13.85)	38 (19.49)	128 (65.64)
cefepime	0 (0.00)	28 (14.36)	9 (4.62)	158 (81.03)
fusidic acid	0 (0.00)	0 (0.00)	1 (0.51)	194 (99.49)
gentacin	0 (0.00)	41 (21.03)	26 (13.33)	128 (65.64)
Imipenem	2 (1.03)	66 (33.85)	44 (22.56)	83 (42.56)
levofloxacin	1 (0.51)	24 (12.31)	89 (45.64)	81 (41.54)
linzid	0 (0.00)	0 (0.00)	1 (0.51)	194 (99.49)
meropenem	1 (0.51)	44 (22.56)	72 (36.92)	78 (40.00)
Moxifloxacin	0 (0.00)	0 (0.00)	1 (0.51)	194 (99.49)
nalidixic acid	0 (0.00)	76 (38.97)	2 (1.03)	117 (60.00)
Norfloxacin	0 (0.00)	0 (0.00)	0 (0.00)	195 (100.00)
penicillin	0 (0.00)	1 (0.51)	0 (0.00)	194 (99.49)
Piperacillin/tazobactam	0 (0.00)	48 (24.62)	34 (17.44)	113 (57.95)
seprazone/sulbactam	0 (0.00)	27 (13.85)	6 (3.08)	162 (83.08)
septran	0 (0.00)	88 (45.13)	51 (26.15)	56 (28.72)
teicoplanin	0 (0.00)	0 (0.00)	1 (0.51)	194 (99.49)
tobramycin	0 (0.00)	16 (8.21)	2 (1.03)	177 (90.77)
vancomycin	0 (0.00)	0 (0.00)	1 (0.51)	194 (99.49)

Table 3. Comparison of resistance of individual antibiotics between genders

drug	Female		Male		p-value**
	resistance	sensitive	resistance	sensitive	
Augmentin	13 (2.42)	1 (0.34)	13 (2.09)	1 (0.31)	0.98
amikicin	26 (4.83)	13 (4.45)	16 (2.57)	16 (4.97)	0.55
Ampicillin	52 (9.67)	2 (0.68)	55 (8.84)	2 (0.62)	0.92
Azteronam	4 (0.74)	0 (0.00)	6 (0.96)	1 (0.31)	0.58
azithromycin	2 (0.37)	25 (8.56)	0 (0.00)	46 (14.29)	0.01
cefotaxime	37 (6.88)	6 (2.05)	50 (8.04)	11 (3.42)	0.19
ceftrazidime	25 (4.65)	21 (7.19)	24 (3.86)	14 (4.35)	0.65
ceftriaxone	41 (7.62)	3 (1.03)	54 (8.68)	3 (0.93)	0.88
Cefuroxime	32 (5.95)	1 (0.34)	49 (7.88)	3 (0.93)	0.68
chloramphenicol	30 (5.58)	30 (10.27)	48 (7.72)	22 (6.83)	0.12
ciprofloxacin	25 (4.65)	3 (1.03)	42 (6.75)	10 (3.11)	0.75
Colstin	36 (6.69)	17 (5.82)	26 (4.18)	15 (4.66)	0.44
doxycillin	13 (2.42)	19 (6.51)	10 (1.61)	15 (4.66)	0.23
Cefipime	11 (2.04)	3 (1.03)	14 (2.25)	4 (1.24)	0.88
gentacin	24 (4.46)	8 (2.74)	14 (2.25)	12 (3.73)	0.43
Imipenem	31 (5.76)	16 (5.48)	28 (4.50)	24 (7.45)	0.56
levofloxacin	10 (1.86)	44 (15.07)	10 (1.61)	35 (10.87)	0.01
meropenem	23 (4.28)	34 (11.64)	21 (3.38)	38 (11.80)	0.15
nalidixic acid	28 (5.20)	2 (0.68)	47 (7.56)	0 (0.00)	0.03
Piperacillin_tazobactam	25 (4.65)	15 (5.14)	21 (3.38)	16 (4.97)	0.79
seprazone_sulbactam	12 (2.23)	4 (1.37)	12 (1.93)	2 (0.62)	0.71
septran	31 (5.76)	24 (8.22)	55 (8.84)	25 (7.76)	0.81
tobramycin	7 (1.30)	1 (0.34)	6 (0.96)	1 (0.31)	0.92
cefoxitim			0 (0.00)	1 (0.31)	-
fusidic acid			0 (0.00)	1 (0.31)	-
linzid			0 (0.00)	1 (0.31)	-
Moxifloxacin			0 (0.00)	1 (0.31)	-
penicillin			1 (0.16)	0 (0.00)	-
teicoplanin			0 (0.00)	1 (0.31)	-
vancomycin			0 (0.00)	1 (0.31)	-

*Not tested drugs and not reported genders were omitted from calculation

** Chi-square/fisher exact test

DISCUSSION

The prevalence and antibiotic resistance patterns of bacterial pathogens in neonatal sepsis remain a significant concern in clinical practice, particularly in developing countries. Our findings indicate that *Salmonella* spp. was the most prevalent pathogen isolated from neonates with sepsis, followed closely by *Burkholderia cepacia*. This aligns with earlier research that highlights the significant role of *Klebsiella pneumoniae* and *Staphylococcus aureus* in neonatal infections. In the study conducted by Obaid Ullah et al.¹⁵, involving 2,685 neonates from Khyber Medical College Peshawar, *E. coli* was the dominant isolate (52.8%), followed by *Staphylococcus aureus* (19.5%) and *Klebsiella pneumoniae* (6.7%). They reported that *Klebsiella* and *Staphylococcus* were the most frequently identified pathogens, contrasting with our results that highlighted *Salmonella* spp. and *Burkholderia cepacia*. The differences in pathogen prevalence could be attributed to geographical variations, sample size, clinical setting, and specific risk factors within the populations studied, emphasizing the need for localized surveillance to inform treatment guidelines. In another study by Adnan et al.¹⁶ involving 84 neonates, *Staphylococcus aureus* was identified in 46.0% of the cases, making it the most common gram-positive isolate, while *Klebsiella pneumoniae* was the most common gram-negative isolate (38.2%). This study demonstrated a notable sensitivity to Linezolid and Amikacin, with high resistance rates against commonly used antibiotics like Ceftriaxone and Ampicillin. Our findings corroborate these resistance patterns, particularly regarding Ampicillin, which showed the highest resistance rate in our sample. The presence of *Staphylococcus aureus* may also suggest nosocomial infections, which can result from invasive procedures or prolonged hospital stays. Ehsan et al.¹⁷ focused on the burden of neonatal sepsis in Karachi, where *Acinetobacter* was reported as the most common isolate, followed by *Klebsiella* and *Burkholderia*. In this retrospective study involving 120 neonates, it was observed that all bacterial species were resistant to Ampicillin, highlighting a critical gap in effective first-line therapies. This is consistent with our findings, where Ampicillin also exhibited the highest resistance rate, underscoring the urgent need for reassessing empirical treatment regimens. The high resistance rates observed could be attributed to the overuse and misuse of antibiotics in the community and hospital settings, leading to the selection of resistant strains. The study by Mushtaq et al.¹⁸ indicated that *Pseudomonas* and *Enterobacter* were the predominant gram-negative organisms isolated from neonates, which further emphasizes the variability in prevalent pathogens across different regions and settings. The resistance patterns reported also align with our findings, particularly the noted high resistance rates against penicillins and cephalosporins. This variability could also be influenced by environmental factors, such as sanitation and infection control practices within hospitals. The current study indicates that Ampicillin, Ceftriaxone, and Septran have significant resistance rates among the bacterial isolates, resistance of Ciprofloxacin and Colistin is also quite common. In contrast, Imipenem and Meropenem showed lower resistance rates, suggesting they may still be effective options in treating severe infections in neonates. Similar results were found in other studies.^{19, 20} It is important to note that our study was retrospective in nature, which may have introduced limitations such as selection bias and incomplete data regarding antibiotic susceptibility testing. Some antibiotics were not tested in certain neonates due to clinical decisions or limitations in laboratory capabilities. Consequently, this could affect the overall resistance profiles reported. Therefore, our results should be interpreted with caution, as the lack of comprehensive testing may not provide a complete picture of the resistance landscape in our population.

CONCLUSION

We can conclude that *Salmonella spp.*, *Burkholderia Cepacia* and *Klebsiella spp* were the most prevalent pathogen in neonatal sepsis. Ampicillin, Ceftriaxone, Cefotaxime and Septran were resistant in nearly above half cases. About in one third cases the resistance was present for Chloramphenicol, Nalidixic acid, Ciprofloxacin and Colistin.

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Authors Contribution

Concept & Design of Study: Ashfaq Ahmed, Arshad Karim

Drafting: Neelum Zahir

Data Analysis: Mohammand Hamayon

Critically Review: Adnan khan, Sara

Final Approval of version: Ashfaq Ahmed, Arshad Karim

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