

# BACTERIOLOGICAL PROFILE AND RESISTANCE PATTERN IN CULTURE-POSITIVE SEPTIC NEONATES PRESENTING TO TERTIARY CARE HOSPITAL, PESHAWAR

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## ABSTRACT

**Objective:** To determine the bacteriological profile and sensitivity pattern from blood cultures of neonates diagnosed with neonatal sepsis.

**Methods:** It was a cross-sectional study conducted in a tertiary care hospital, i.e., Lady Reading Hospital Peshawar Neonatology Department, for 6 months from 1st July 2023 to 31st December 2023. All the neonates admitted with clinical signs and symptoms of sepsis were included in the study on confirmation of sepsis by positive blood cultures. Their resistance patterns and antibiotic sensitivity patterns were determined. The outcome of sepsis in the form of discharge or death was reported.

**Results:** The blood culture showed that the highest frequency of organisms isolated was gram-negative Klebsiella in 38.2% of neonates, followed by E. coli in 35.4% of neonates. There is significant sensitivity of antibiotic meropenem, imipenem, ampicillin tazobactam, amikacin, and colistin to various organisms with a p-value <0.001. However, the resistance pattern was seen with antibiotics like ampicillin and cephalosporins.

**Conclusion:** Antibiotics like amikacin, ampicillin-tazobactam, and ampicillin-sulbactam have shown promising results in treating neonatal sepsis other than carbapenems and colistin. The hypervirulent-resistant strains of bacteria need to be further analyzed beyond antibiotic susceptibility testing alone. This will facilitate the roadway to the development of neonatal vaccines.

**Keywords:** Neonatal Sepsis, Resistance, Culture Resistance.

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## INTRODUCTION

Systemic infections occurring in neonates are defined as neonatal sepsis. It may be accompanied by septic shock and multiple organ failure as well. <sup>1</sup> About 3 million cases of sepsis occur in neonates globally. <sup>2</sup> The incidence varies from 1 to 4/1000 births in developed countries but 49 to 170/1000 births in developing countries, with a case fatality rate of 24%. Neonatal sepsis occurring within 72 hours of life is called Early onset sepsis, and the one after 72 hours is late-onset sepsis. <sup>3</sup> Prematurity, low birth weight, premature rupture of membranes for more than 18 hours, need for mechanical ventilation, home deliveries,

and male gender are the different risk factors for neonatal sepsis. Several studies have been done using risk factor assessment for early diagnosis and treatment of neonatal sepsis. <sup>4-6</sup>

Neonatal sepsis can be diagnosed with complete blood count assays, immature to mature granulocyte ratio, and markers of systemic inflammation and immune response. <sup>7</sup> Blood culture remains the gold standard for the diagnosis of neonatal sepsis. <sup>8</sup> Procalcitonin and C-C-reactive protein are other tests, and the most specific of them all is the Multiplex polymerase chain reaction, which can detect bacterial growth within hours. <sup>7,9</sup>

Over the last two decades, there has been increasing bacterial resistance being reported in neonatal sepsis cases due to improper antibiotic usage and lack of infection control services. Regular monitoring of antibiotic resistance and sensitivity patterns is important, and a strict antibiotic stewardship program is essential to curtail the rising challenges in neonatal sepsis management. <sup>10</sup> This study will help to know the current perspective of neonatal sepsis to detect the pattern of growths obtained and to

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overcome the challenge of introducing antibiotics to neonates in sepsis.

## MATERIALS AND METHODS

It was a cross-sectional study conducted in a tertiary care hospital, i.e., Lady Reading Hospital Peshawar Neonatology Department, for 6 months, from 1<sup>st</sup> July 2023 to 31<sup>st</sup> December 2023. Nonprobability consecutive sampling was used for enrolling the neonates. All the neonates admitted to the nursery with clinical signs and symptoms of sepsis were included in the study after confirmation of sepsis by positive blood cultures. The signs and symptoms of sepsis were fever, lethargy, reluctance to feed, hypothermia, convulsions, grunting, jaundice, and abdominal distention. Neonates with negative culture results and inborn errors of metabolism were excluded from the study. About 1 to 3 ml of blood was collected from neonates after cleaning the prick site with povidone-iodine solution and put in BactecPLus culture bottles. Culture bottles containing Tryptone Soya Broth were also used. It was transported to the laboratory on 2-24°C. The cultures were incubated, and sensitivity to various antibiotics was tested by standard disc diffusion technique.

Data was collected prospectively using a pre-designed proforma after obtaining informed consent from the parents of the neonate. Data regarding blood culture results was obtained from HMIS and documented. The outcome of sepsis in the form of discharge or death was reported. Data was analyzed using SPSS version 27. Categorical variables and scale variables were analyzed by descriptive statistics. Scale variables were reported as mean and SD and categorical variables were reported as frequency and percentages.

## RESULTS

A total of 212 neonates with symptoms of sepsis were included in the study after positive blood cultures. The demographic detail shows the mean weight of these neonates was 2.9 kg  $\pm$ 0.68SD, the mean age was 8.7 days  $\pm$ 7.9SD, and the mean gestation age at the time of delivery was 36.6 weeks  $\pm$ 2.7SD. About 69.8% were male gender, and 28.3% were female. In these septic neonates, about n=167 (78.8%) survived and recovered completely and were discharged, while n=41 (19.3%) expired even after initiation of antibiotics. The blood culture reports (Table 1) showed the highest frequency of organisms was Klebsiella at 38.2%, followed by gram-negative E. coli, present in 35.4% of cases. There is significant sensitivity of antibiotic meropenem, imipenem, ampicillin tazobactam, amikacin, and colistin to various organisms with a p-value <0.001. However, the resistance pattern was seen with antibiotics like ampicillin and cephalosporins.

## DISCUSSION

Klebsiella 15.35% were the predominant pathogens.<sup>11</sup>

**Table No 1: Organisms Involved in Neonatal Sepsis, Obtained After Blood Culture**

Organisms	Frequency	Percentage
klebsiella	81	38.2%
E coli	75	35.4%
Citrobacter	32	15.1%
Acinobacter	10	4.7%
pseudomonas aureginosa	8	3.8%
streptococcus	1	0.5%
staph aureus (MRSA)	1	0.5%

**Table No 2: Sensitivity Pattern Of Antibiotics To Various Organisms**

Medications	Sensitivity (%)	Resistance (%)	Intermediate (%)	p-value
Ampicillin	12.5	87	0.5	0.85
Cefotaxime	25.5	71.2	3.4	0.31
Ceftriaxone	24.5	69.3	4.2	0.175
Ceftazidime	20.8	73.6	3.8	0.36
Amikacin	74.1	15.9	8.7	<0.001
Ciprofloxacin	61.1	21.2	17.8	0.006
Ampicillin-Sulbactam	89.4	5.8	4.8	<0.001
Ampicillin-Tazobactam	87.5	9.1	3.4	<0.001
Meropenem	93.3	6.7	0	<0.001
Imipenem	95.3	2.8	0	0.005

Multidrug-resistant pathogens are an emerging problem and are responsible for morbidity and mortality in cases of neonatal sepsis.<sup>11,12</sup> Timely and adequate treatment of neonatal sepsis is essential, but injudicious and indiscriminate use of antibiotics in neonates who are not septic is causing the emergence of resistant strains.<sup>13</sup> Antibiotic stewardship is important to prevent the misuse of antibiotics.<sup>14</sup>

In our study, 90% of the microorganisms isolated were gram-negative, and 10 were gram-positive. Among gram-negative, 38.2% were Klebsiella, followed by E. coli, which were 35.4%. Acinobacter was present in 4.7 % of cases, while pseudomonas in 8%. Another study done in Pakistan in 2020 by Hashmi et al. reported klebsiella in 15.2%, E. coli in 6.3%, pseudomonas in 2.5% Acinobacter in 17.7% with overall gram-negative involvement of 53.2%.<sup>15</sup>

A study done in India by Dudeja et al. in 2020 reported that gram negatives such as Acinetobacter, Klebsiella, and E. coli were most commonly isolated.<sup>12</sup> A study done in China by Zou H et al. showed that E. coli 34% and

Another study done by Sands et al., which was conducted across seven different low to middle-income countries of Africa and South Asia, including Pakistan, revealed that *Klebsiella*, *E. coli*, and *Acinetobacter* are the main causative organisms causing neonatal sepsis. Among *Klebsiella*, six different species were identified.<sup>16</sup>

There has been an increasing incidence of sepsis caused by *Klebsiella* over the last two decades. It's a hypervirulent organism acquiring resistance to antibiotics. It's one of the ESKAPE pathogens, and it belongs to the WHO global priority pathogen list due to its ability to acquire antibiotic resistance. *Klebsiella* has around 400 antibiotic-resistance genes, which is double that of other pathogens.<sup>17</sup> Carbapenem-resistant *Klebsiella* is emerging due to increasing antibiotic resistance.<sup>11, 12, 17</sup>

In a study done by Zou H et al. in China in 2021, there was high resistance to cephalosporins, and 13.5% of *klebsiella* were carbapenem-resistant.<sup>13</sup> *Acinetobacter* in our study were mostly sensitive to colistin, similar to Dudeja et al. and Hashmi et al.<sup>12, 15</sup>

WHO guidelines still follow first-line antibiotics Ampicillin and Gentamicin for the treatment of neonatal sepsis and cephalosporins as second-line antibiotics, but it needs to be modified.<sup>16, 17</sup>

Results from our study also showed high resistance to ampicillin and cephalosporins, similar to Sands et al., which also reported the presence of resistant genes for cephalosporins and carbapenems and virulent factors.<sup>16</sup>

With escalating rates of cephalosporin use in health-care settings, the increasing dependency on carbapenems has led to the emergence of carbapenem-resistant *K. pneumoniae*. It is difficult to change things overnight, and the economic implications of these changes may also be a constraint on health systems in developing countries.<sup>17</sup>

## CONCLUSION

Antibiotics like amikacin, ampicillin-tazobactam, and ampicillin-sulbactam have shown promising results in treating neonatal sepsis other than carbapenems and colistin. The hypervirulent-resistant strains of bacteria need to be further analyzed beyond antibiotic susceptibility testing alone. This will facilitate the roadway to the development of neonatal vaccines.

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**Authors Contribution:**

Following authors have made substantial contributions to the manuscript as under

Authors	Conceived & designed the analysis	Collected the data	Contributed data or analysis tools	Performed the analysis	Wrote the paper	Other contribution
Zahoor F	✓	✗	✓	✗	✓	✗
Parvaiz H	✓	✓	✗	✓	✓	✗
Kalsum UE	✗	✓	✗	✗	✓	✗
Shah G	✓	✓	✓	✗	✓	✓

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

**Ethical Approval:**

This Manuscript was approved by the Ethical Review Board of Lady Reading Hospital, Peshawar. Vide No.793/LRH/MTI.

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