Original Research Article

# To Study the Microbiological Profile and Antibiotic Sensitivity Patterns in Neonatal Sepsis in a Tertiary Care Hospital

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**Abstract:**

**Background:** Neonatologists face a perpetual challenge in managing neonatal septicaemia due to changing patterns of the microbial flora and their antibiotic sensitivity. Neonatal sepsis is a major cause of neonatal mortality, the clinical outcome of which depends on early diagnosis and initiation of appropriate antibiotics. The emergence of multi-drug resistant strains has limited the choice of available antibiotics. Thus, antibiotic resistance pattern of pathogens is critical for both therapy and infection control. The present study was designed to evaluate the microbiological profile and antibiotic sensitivity patterns in neonatal sepsis patients.

**Methods:** We analyzed records of a total of 160 neonates with clinical sepsis who were admitted in our NICU during the study period and had blood culture sent for isolation of microbial agent. Out of 160 neonates (99 male and 61 female) grew pathogens on blood culture.

**Results:** In our study, 44 (27.5%) had positive blood cultures. However, 92 (57.5%) sepsis-suspected newborns showed negative blood cultures. 27.5 % of neonates with culture-positive sepsis had gram-positive infections, while 57.5 % had gram-negative infections. In Gram-positive sepsis patients, Acinetobactor 7 (4.38%), CONS 6 (3.75%), Escherichia Coli 8 (5%), Klebsiella Pneumoniae 13 (8.13%), MRSA 4 (2.50%), and Pseudomonas 6 (3.75% Further analysis showed that 27.5% of Gram-positive patients were susceptible to Piperacillin, Tazobactum, Imipenem, Amikacin, and Vancomycin. 72.5% of Gram-negative patients responded to Piperacillin + Tazobactum and Imipenem. In our 160 newborn sepsis cases, 44% (27.5) were culture positive. Most culture-positive cases were gram negative (72.5%, 116 cases), followed by positive. Preterm and low-birth-weight babies were more prone to sepsis. Many Gram-negative microbes were isolated. We found that most Gram-negative organisms were sensitive to Imipenem, followed by Piperacillin + Tazobactum, Cefoperazone + Sulbactum, Ceftazidime, Ceftriaxone, and Amikacin. Most Gram-positive organisms were responsive to Vancomycin, then Amikacin, Imipenem, Piperacillin + Tazobactum, Ceftriaxone, and Cefoperazone + Sulbactum.

**Conclusion:** Most Enterobactericeae isolates from neonatal sepsis produced ESBL. Gram-negative bacilli were resistant to ampicillin, gentamicin, and ceftriaxone. Vancomycin, teicoplanin, and linezolid were sensitive to gram-positive isolates in vitro, while Cefepime-tazobactam and imipenem were sensitive to gram-negative isolates. In our institution, CONS and Candida spices were the most common neonatal sepsis isolates. Preterm and low-birth-weight babies were more prone to sepsis. Many Gram-negative microbes were isolated. Despite their low virulence and commensality, they can cause neonatal sepsis, requiring strict observation and infection control. Our data suggests that Piperacillin + Tazobactum and Amikacin as first antibiotics would be most effective.

**Keywords:** Septicaemia; Antibiotic; Neonatal Sepsis; Pathogens; Positive Sepsis.

## Introduction

Sepsis is a dangerous condition caused by microorganisms entering the bloodstream. In newborns, sepsis can be classified into two types: early-onset sepsis (EOS) and late-onset sepsis (LOS). EOS happens within the first three days after birth, while LOS develops after the third day. [1]EOS is typically caused by organisms acquired from the mother during delivery or shortly after birth, whereas LOS is generally caused by organisms obtained from the environment, either in hospitals or the community.[1-3]. Neonatal sepsis (NS) continues to be a leading cause of illness and death in newborns, causing 225,000 deaths worldwide each year despite advancements in

newborn care. [2,4]. When clinical symptoms suggest a potential severe bacterial infection (PSBI), initiating antibiotic treatment is essential.[5]. Therefore, early screening for pathogens causing neonatal septicemia, prompt diagnosis, and judicious use of antibiotics are vital for creating effective treatment plans.

The rise of ESBLs, MRSA, and MDR strains is a major concern in NICUs worldwide. Sepsis in newborns is classified as early-onset (EOS) and late-onset (LOS). [6] The microorganisms most commonly associated with EOS are Group B Streptococcus (GBS), Escherichia coli, coagulase-negative Staphylococcus species (CONS), Haemophilus influenzae, and Listeria monocytogenes.[7] Late-onset sepsis (LOS) is caused by various pathogens, including CONS, Staphylococcus aureus, E. coli, Klebsiella, Pseudomonas, Enterobacter, Candida, GBS, Serratia, Acinetobacter, and anaerobes. CONS infections are increasingly common. [7]

The World Health Organization (WHO) recommends two empiric antibiotic regimens for suspected neonatal sepsis (NS): ampicillin-gentamicin and ampicillin-cefotaxime. Ampicillin targets infections caused by Listeria and other gram-positive bacteria such as Group B Streptococcus (GBS), while gentamicin and cefotaxime are effective against gram-negative bacteria.[8]

The effectiveness of the WHO empiric antibiotic regimen relies on several factors, including the prevalent bacterial pathogens in the region, their resistance profiles, and the clinical presentation and risk factors of the individual patient. The WHO advises that empiric antibiotic therapy should be guided by local epidemiological data and antibiotic susceptibility patterns to enhance the chances of choosing an effective regimen. They also recommend regular surveillance of antimicrobial resistance patterns to ensure timely updates of treatment guidelines.

In recent years, the rise of antimicrobial resistance has become a worldwide issue. [9] Having a comprehensive understanding of prevalent bacterial pathogens and their antibiotic susceptibility is crucial when selecting empirical therapy, as it can significantly decrease morbidity and mortality.[10] The escalating antimicrobial resistance presents a substantial challenge in the management of neonatal sepsis, given the finite supply of antibiotics available.[10]

In Palestine, the neonatal mortality rate was 9.3 deaths per 1000 live births in 2021. However, accurate data on neonatal deaths specifically attributed to sepsis is not available [11].

The research was conducted in three prominent tertiary governmental hospitals in the West Bank, Palestine, spanning from January 2019 to December 2021. The study additionally sought to assess how well WHO-recommended empiric antibiotic regimens matched the pathogens causing neonatal sepsis (NS) and to identify risk factors linked to multidrug-resistant organisms (MDRO) in the studied population. Enhancing neonatal care, which encompasses prevention, early detection, and treatment of sepsis, is crucial for lowering neonatal mortality rates in Palestine and other nations facing high rates of neonatal deaths.

## Aims and Objectives

**Aim:** To study microbiological profile and antibiotic sensitivity patterns in neonatal sepsis patients.

## Objectives

**Primary objective:** 1.To identify the organisms causing neonatal sepsis. 2. To review antibiotic sensitivity patterns of organisms causing neonatal sepsis.

**Secondary objective:** To study outcome of culture positive sepsis patients.

## Material and Methods

**Study site:** Department of Pediatrics,

**Inclusion Criteria:**

1. Neonates admitted to NICU.
2. Neonates with diagnosis of clinical/definitive/probable or culture positive sepsis.
3. Age group: birth to 28 days of life.

## Exclusion criteria

1. Babies with congenital anomaly rendering them easily susceptible to infections such as; Cystic fibrosis, Down's syndrome, etc.

**Sample size:** 160 consecutive neonates

**Study design:** Prospective observational study.

**Sepsis screen: A series of sepsis screening tests were performed on the blood samples of all neonates, which include:**

- C-reactive protein (CRP >1 mg/dl)
- Total leukocyte count (TLC) to identify leuko-cytosis (>15,000/cumm) or leukopenia
- (<5000/cumm)
- Absolute neutrophil count for neutropenia (<1800/cumm)
- Immature to total neutrophils ratio (I/TN >0.2)
- ESR

**The presence of two or more abnormal sepsis screen parameters suggests neonatal sepsis.**

- Clinical or probable sepsis: In a neonate with symptoms indicative of sepsis and one of the following:
- Factors such as maternal fever and foul-smelling amniotic fluid.
- X-ray indicative of pneumonia.
- Positive sepsis screen.
- Culture positive sepsis: Isolation of a micro-organism from normally sterile sites like blood, cerebrospinal fluid (CSF), or urine in a neonate with clinical signs of sepsis.
- Contaminant blood culture: Defined as the absence of clinical, perinatal, or laboratory evidence of sepsis with the growth of organisms such as CONS, Corynebacterium species, Bacillus species (excluding Bacillus anthracis), Propionibacterium acnes, Micrococcus species, viridans group streptococci, enterococci, and Clostridium perfringens.
- EONS and LONS: Early-onset neonatal sepsis (EONS) occurs within the first 72 hours of life, while late-onset neonatal sepsis (LONS) occurs after 72 hours of life.
- Shock: Defined by impaired perfusion requiring crystalloid bolus or vasoactive drug support.
- Acute kidney injury (AKI): Defined according to the Kidney Disease Improving Global Outcomes (KDIGO) guidelines.
- Disseminated intravascular coagulation (DIC): Characterized by thrombocytopenia (<150,000/cu mm) and coagulopathy (INR >1.5 or aPTT >35 seconds).

- Necrotizing Enterocolitis: Any episode meeting Bell stage 2 or 3 criteria.

**Antibiotic sensitivity**

We tested how well antibiotics work against bacteria following the Clinical and Laboratory Standards Institute (CLSI) 2018 guidelines.

We used the Kirby-Bauer disk diffusion method to do this. Antibiotic resistance was classified as either susceptible (meaning the antibiotics would likely work) or resistant (meaning the antibiotics might not work).

For Gram-negative bacteria, we looked at their resistance to different types of antibiotics:

- Extended-spectrum cephalosporins (like ceftazidime, ceftriaxone, or cefotaxime)

- Carbapenems (like imipenem or meropenem)
- Aminoglycosides (like gentamicin, amikacin, or netilmicin)
- Fluoroquinolones (like ciprofloxacin)
- Piperacillin–tazobactam

**Statistical analysis:**

The information we gathered was first coded with numbers and inputted into Microsoft Excel 2007. From there, it was moved into the Statistical Package for Social Sciences (SPSS) software, version 26.0, on a Windows platform.

**Results**

**Table 1: Age distribution of subjects**

| Age (in days) | CRP +ve | Culture +ve | P value |
|---|---|---|---|
| 1 days | 10 | 3 | 0.017 |
| 2 days | 15 | 4 | |
| 3 days | 10 | 5 | |
| 4 days | 35 | 21 | |
| 5 days | 22 | 11 | |

**Table 2: Sex distribution of subjects**

| Sex | Num. | % | P value |
|---|---|---|---|
| Male | 99 | 61.88% | 0.148 |
| Female | 61 | 38.12% | |

**Table 3: Isolate**

| | Num. | % | P value |
|---|---|---|---|
| Acinetobacter | 7 | 4.38% | 0.002 |
| Cons | 6 | 3.75% | |
| Escherichia Coli | 8 | 5% | |
| Klebsiella Pneumoniae | 13 | 8.13% | |
| Mrsa | 4 | 2.50% | |
| Pseudomonas | 6 | 3.75% | |
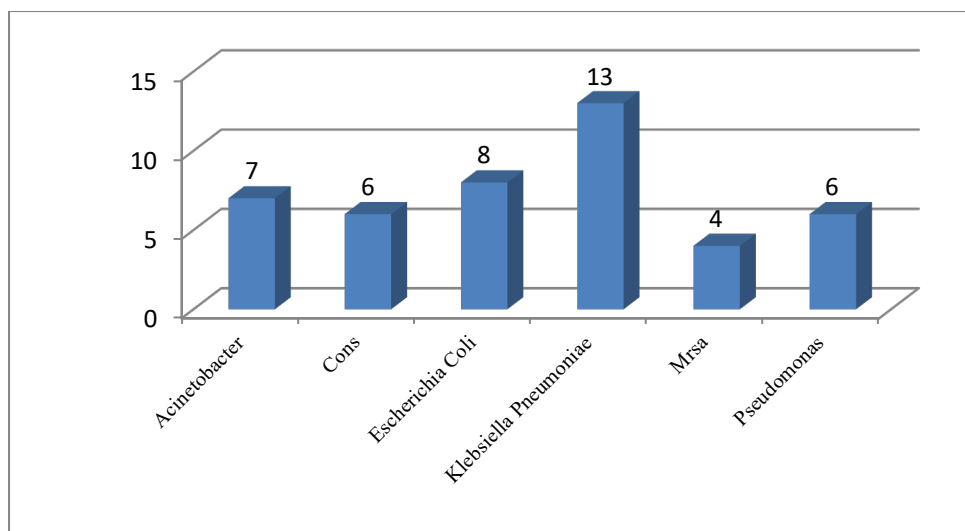
**Figure 1:**

**Table 4:  Birth weight**

| Birth weight (in kg) | CRP +ve | Culture +ve | P value |
|---|---|---|---|
| 1.9-2.3 | 43 | 68 | 0.048 |
| 2.4-2.9 | 30 | 4 | |
| 3.0-3.5 | 19 | 2 | |
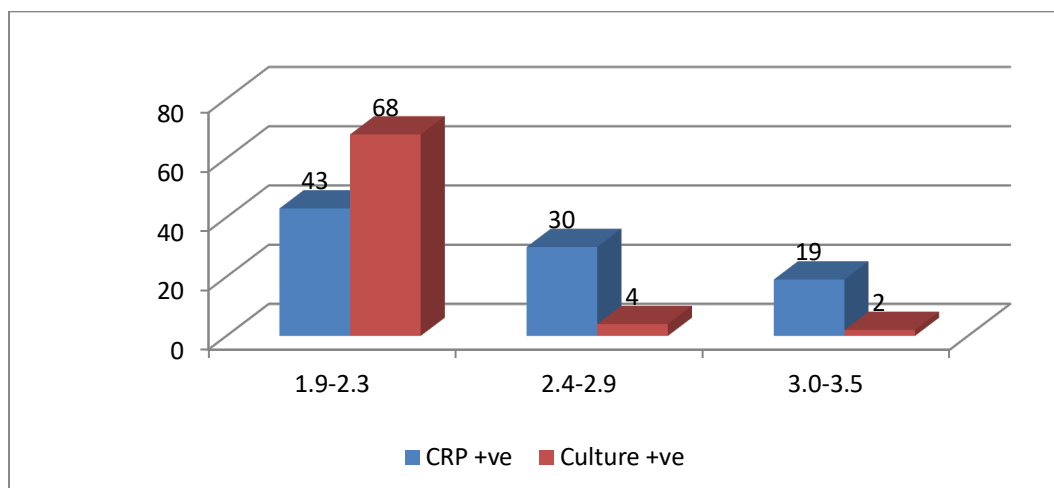


**Figure 2:**

**Table 5: Place of Delivery**

| Place of Delivery | Num. | % | P value |
|---|---|---|---|
| Inborn | 115 | 71.88% | 0.263 |
| Outborn | 45 | 28.12% | |
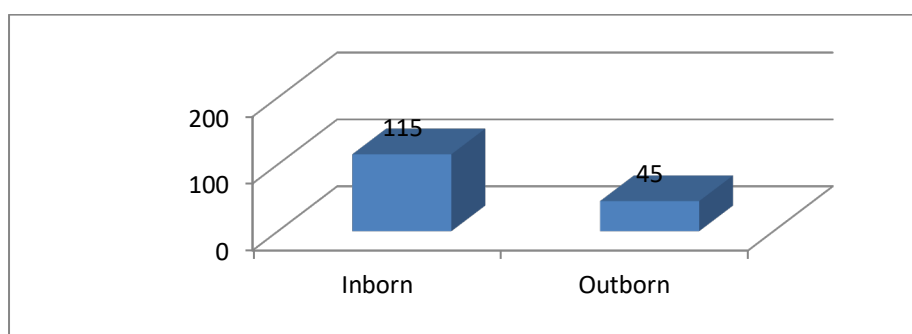


**Figure 3:**

**Table 6: Mode of Delivery**

| Mode of Delivery | CRP +ve | Culture +ve | P value |
|---|---|---|---|
| LSCS | 39 | 16 | 0.047 |
| NVD | 36 | 21 | |
| Delivery by untrained birth attainder | 17 | 7 | |
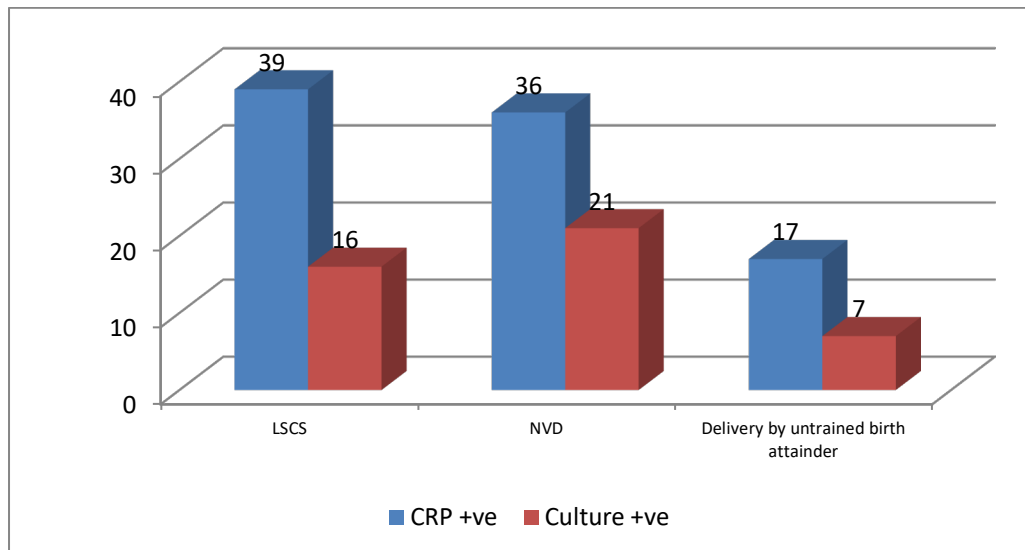


**Figure 4:**

**Table 7: Culture +ve/-ve in presenting complaints**

| Presenting complaints | Culture +ve | | Culture -ve | |
|---|---|---|---|---|
| | Yes | No | Yes | No |
| | Num. | Num. | Num. | Num. |
| Tachypnea | 32 (20%) | 12(7.50%) | 25 (15.63%) | 91 (56.88%) |
| Apnea | 3 (1.88%) | 41 (25.63%) | 3 (1.88%) | 113 (70.63%) |
| Vomiting | 16 (10%) | 28 (17.50%) | 16 (10%) | 100 (62.50%) |
| Retraction | 32 (20%) | 12(7.50%) | 37 (23.13%) | 79 (49.38%) |
| Hypotension | 12(7.50%) | 32 (20%) | 11 (6.88%) | 105 (65.63%) |
| Lethargy | 12(7.50%) | 32(20%) | 11 (6.88%) | 105 (65.63%) |
| Abdominal distension | 16 (10%) | 28 (17.50%) | 0 (%) | 116 (72.50%) |
| Bleeding | 0 (0%) | 44 (27.50%) | 0 (%) | 116 (72.50%) |
| Poor feeding | 12(7.50%) | 32 (20%) | 13(8.13%) | 103 (64.38%) |
| Poor perfusion | 13 (8.13%) | 31 (19.38%) | 1 (0.63%) | 115 (71.88%) |
| Seizures | 12(7.50%) | 32 (20%) | 11 (6.88%) | 105 (65.63%) |
| Tachycardia | 25 (15.63) | 19 (11.88%) | 30 (18.75%) | 86 (53.75%) |

**Table 8: Culture +ve/-ve in Sepsis**

| Sepsis | CRP +ve (Mean±SD) | Culture +ve (Mean±SD) | P value |
|---|---|---|---|
| CRP | 43.50±33.79 | 60.12±37.63 | 0.048 |
| TLC | 15428.95±3801.64 | 17260.43±4750.93 | 0.043 |
| ANC | 2515.22±394.58 | 2507.38±326.94 | 0.582 |

## Discussion

We observed that records of 160 neonates with clinical sepsis admitted to our NICU, including 115 inborns and 45 outborns referred from other facilities. All underwent sepsis screening and blood culture for pathogen identification and sensitivity. Pathogens were isolated in 44 cases.

In our study we found that positive blood culture was seen in 44 (27.5%) cases. However, 92 (57.5%) neonates clinically suspected of having sepsis had a negative blood culture. Of all babies having culture positive sepsis, 27.5 % cases had a gram-positive organism while 57.5 % had a gram-negative organism. Lumbar puncture was performed on 23 neonates presenting with seizure-like activity during admission, with CSF analyzed for microscopy and culture. Only 2 cultures were positive, both identifying gram-negative CONS. Among patients with sepsis, the pathogens identi-

fied included Acinetobacter (4.38%), CONS (3.75%), E. coli (5%), Klebsiella pneumoniae (8.13%), MRSA (2.5%), and Pseudomonas (3.75%). Sensitivity analysis revealed that 27.5% of gram-positive cases responded to piperacillin-tazobactam, cefotaxime, imipenem, amikacin, and vancomycin. In gram-negative cases, 72.5% were sensitive to cefotaxime, piperacillin-tazobactam, and imipenem.

In our study, 44 out of 160 neonatal sepsis cases (27.5%) were culture-positive, with 72.5% caused by Gram-negative organisms. Similar findings were reported by Jonnala RNR et al., where Gram-negative bacteria predominated (77.08%), followed by Gram-positive organisms and fungi. Preterm and low birth weight neonates were particularly vulnerable to sepsis.[12] In our study, Gram-negative and Gram-positive septicemia accounted for 72.5% and 27.5% of the culture-positive cases, respectively, which aligns with findings from Agnihotri et al.[13], who reported Gram-negative organisms responsible for 59% and Gram-positive organisms for 41% of septicemia cases. The bacterial isolation rates in our study are also consistent with those reported by A S M Nawshad et al. [14] (Gram-negative 73%, Gram-positive 27%).

The pathogens commonly observed in neonatal sepsis in developing countries differ from those in developed countries. The National Neonatal Perinatal Database reported Klebsiella as the predominant pathogen (8.13%). Similar findings have been documented in studies by Zakariya et al. [15] (66%) and Afroza et al. [16] (64%). In our study, Gram-negative organisms showed highest sensitivity to imipenem, followed by piperacillin-tazobactam and cefotaxime, while Gram-positive organisms were most sensitive to vancomycin, followed by amikacin and imipenem. Other effective antibiotics included linezolid, ceftriaxone, and teicoplanin. According to a study from Sydney Neonatal Infection Surveillance, all Gram-negative bacteria were reported to be susceptible to gentamicin and third-generation cephalosporins. Waheed et al. [17] identified cefotaxime as highly effective, with 80% sensitivity against Klebsiella, 70% against Staphylococcus aureus, and 65% against Escherichia coli. Imipenem showed high sensitivity (53%) specifically against Klebsiella but lower sensitivity against other organisms. Mokuolu et al. [18] found high sensitivity rates of 94% to azithromycin, 77.8% to streptomycin, 73.3% to gentamicin, and 69.2% to ampicillin-sulbactam. Common pathogens included Staphylococcus aureus, coagulase-negative staphylococci, Klebsiella species, and unclassified coliforms. Gram-positive organisms demonstrated good sensitivity to vancomycin, teicoplanin and imipenem but high resistance to penicillins. Similar

findings were reported in studies by Pooja et al. [19].

## Conclusion

In neonatal sepsis, most Enterobacteriaceae isolates produced ESBL enzymes, showing resistance to common antibiotics.

Cefotaxime and amikacin are recommended as first-line empirical treatments, with piperacillin-tazobactam, meropenem, and vancomycin as second-line options. Third-line treatments included linezolid, teicoplanin, and colistin for escalation.

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