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Original Research Article

Blood culture and drug sensitivity in neonatal sepsis and its outcome

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ABSTRACT

Background: Nearly one-third of neonatal mortality in India is due to neonatal sepsis and death occurs in 30% of culture-positive neonates. Pathogens such as *Klebsiella pneumoniae* and *Escherichia coli* are the most common bacteria responsible for neonatal sepsis in India and South Asia.
Methods: It was a retrospective study conducted in newborn intensive care units (NICUs) of J. K. Lon Hospital, Government Medical College, Kota, Rajasthan from January 2024 to May 2024. All neonates (<28 days of life) with – symptoms of sepsis or presence of maternal risk factors of sepsis were included in this study. Blood was collected in a BACT/ALERT® culture bottle. Blood culture was done by an automated method in BD BACTEC FX40.
Results: Blood cultures were sent for 733 neonates out of which 209 were culture positive. Most common organism isolated was *Klebsiella*, second most common organism isolated was *E. coli*, third most common organism isolated was *Staphylococcus aureus*. Fourth most common organism was *Pseudomonas* and the rest were Acinetobacter, coagulase-negative Staphylococci (CoNS), Enterococcus and yeast. Mortality due to sepsis is 22%.
Conclusions: *Klebsiella* followed by *E. coli* was found to be the most common cause of sepsis in present study NICU. A high degree of resistance of organisms to Aminoglycosides and penicillin group particularly Amoxyclav calls for a re-evaluation of antibiotic policy and protocols for empirical treatment in neonatal sepsis.

Keywords: Multidrug resistant, Culture positive, NICU, Neonate, Sepsis

INTRODUCTION

Nearly one-third of neonatal mortality in India is due to neonatal sepsis and death occurs in 30% of culture-positive neonates.[1,2] Neonatal sepsis is classified as early onset sepsis (EOS) (<72 hours) and late onset sepsis (LOS) (>72 hours) based on the onset of illness. EOS occurs usually due to pathogens present in the genital tract of the mother whereas LOS occurs due to pathogens acquired either from the hospital or from the community. There is a gradually increasing trend of multi-drug resistant (MDR) pathogens in tertiary care neonatal intensive care units (NICU) and special newborn care units (SNCUs) all over India. Multi-drug resistance was defined as the acquired resistance to at least one agent in three or more antimicrobial categories as per the Centers for Disease Control and Prevention (CDC) guidelines.[3] Strict antibiotics stewardship programs will enable us to counteract multi-drug resistance patterns of emerging pathogens. The major hallmark of antibiotic stewardship is to identify the isolated culture-positive organisms and their antibiotic sensitivity pattern. The prevalence of organisms in SNCUs also differs from tertiary care NICUs in our country and it is also different from that of the Western world. Strict monitoring of bacterial flora and the resistance pattern of a unit are always required as both change very frequently.

Pathogens such as *Klebsiella pneumoniae* and *Escherichia coli* are the most common cause of neonatal sepsis in India and South Asia.[4,5] The majority of studies were done in tertiary care units with SNCU hardly contributing to it. Gradually increasing trends of MDR strains in our SNCU prompted us to do this study to evaluate the isolated organism and their antibiogram pattern in neonatal sepsis.

METHODS

This is a hospital-based observational study conducted in J. K. Lon Hospital, Government Medical College, Kota from January 2024 to May 2024 after obtaining institutional ethics committee approval GMC/KOTA/JK LON/IEC/87/2023. Neonates with congenital malformations were excluded from the study. Blood cultures were sent from all the babies of SNCU with signs and symptoms of sepsis-like lethargy, refusal feeding, breathing difficulty, poor perfusion, seizures, and temperature instability or in any baby admitted with maternal risk factors like foul-smelling liquor, chorioamnionitis, and prolonged rupture of membrane for >24 hours. Two milliliters of blood were collected from peripheral blood with all aseptic measures in BACT/ALERT culture bottle. Blood culture was done by an automated method in BD BACTEC FX40. Diagnosis of culture-positive sepsis was confirmed after isolation of microorganisms in suspected cases of clinical sepsis. Identification and antibiotic sensitivity of isolated bacteria were done and interpretation was done as per the guidelines of the Clinical and Laboratory Standards Institute guidelines.

Statistical analysis

Demographic profiles such as gestation, sex, birth weight, day of onset of illness, inborn/outborn cases, isolated organisms, and their antibiogram pattern were recorded for analysis using Microsoft excel. Multi-drug resistance pattern among each Gram-negative and Gram-positive species was described.

For data collection, Microsoft excel 2021 (Microsoft, Redmond, WA, USA) was used whereas descriptive statistics like percentages and means±standard deviations were used to describe variables. The statistical package for the social sciences (SPSS) statistics for Windows, version 23.0 (IBM Corporation, Armonk, NY, USA) was used for statistical analyses.

RESULTS

Blood cultures were sent for 733 neonates out of which 209 were culture positive. Most common organism isolated was *Klebsiella* which was positive amongst 71 blood culture reports. Second most common organism isolated was *E. coli* which was positive in 38 blood cultures. Third most common organism isolated was *Staphylococcus aureus* positive in 37 blood cultures.

Fourth most common organism was *Pseudomonas* positive in 19 blood cultures. Fifth most common organism was *Acinetobacter* positive in 17 blood cultures. Sixth most common organism were CoNS positive in 12 blood culture isolates. Rest were *Enterococcus* and yeast like growth.

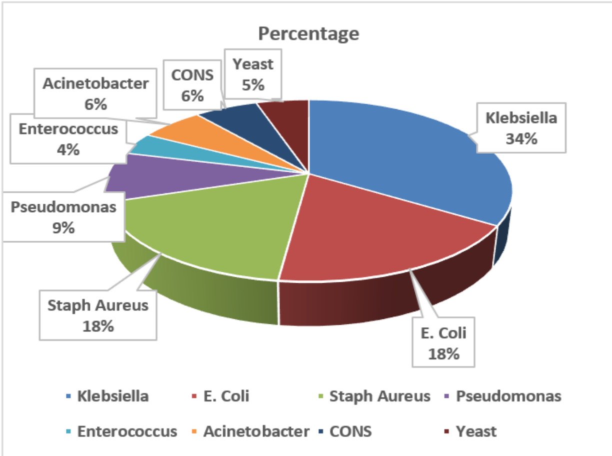

Figure 1: Distribution of isolated organisms in neonatal sepsis.

Table 1: Demographic characteristics of neonates with suspected sepsis.

Variables	Culture positive sepsis (n=209) (%)	Culture negative sepsis (n=524) (%)	Total (n=733) (%)
Gestation (weeks)			
<28	25 (11.9)	38 (7.2)	63 (8.5)
28-32	46 (22)	97 (18.5)	143 (19.5)
32-36	60 (28.7)	189 (36.06)	249 (33.9)
>37	78 (37.3)	200 (38.1)	278 (37.9)
Birth weight (kg)			
<1	19 (9)	28 (5.3)	47 (6.4)
1-1.5	42 (20)	98 (18.7)	140 (18.1)
1.5-2.5	70 (33.4)	143 (27.2)	213 (27.5)
>2.5	78 (37.3)	255 (48.6)	333 (43.07)
Sex			
Male	115 (55)	285 (54.3)	400 (51.7)
Female	94 (45)	239 (45.6)	333 (43.07)
Inborn	123 (58.8)	292 (55.7)	415 (56.6)
Outborn	86 (41.1)	232 (44.2)	318 (43.3)
Early onset sepsis	61 (29.1)	326 (62.2)	387 (52.7)
Late onset sepsis	148 (70.9)	198 (37.7)	346 (47.2)

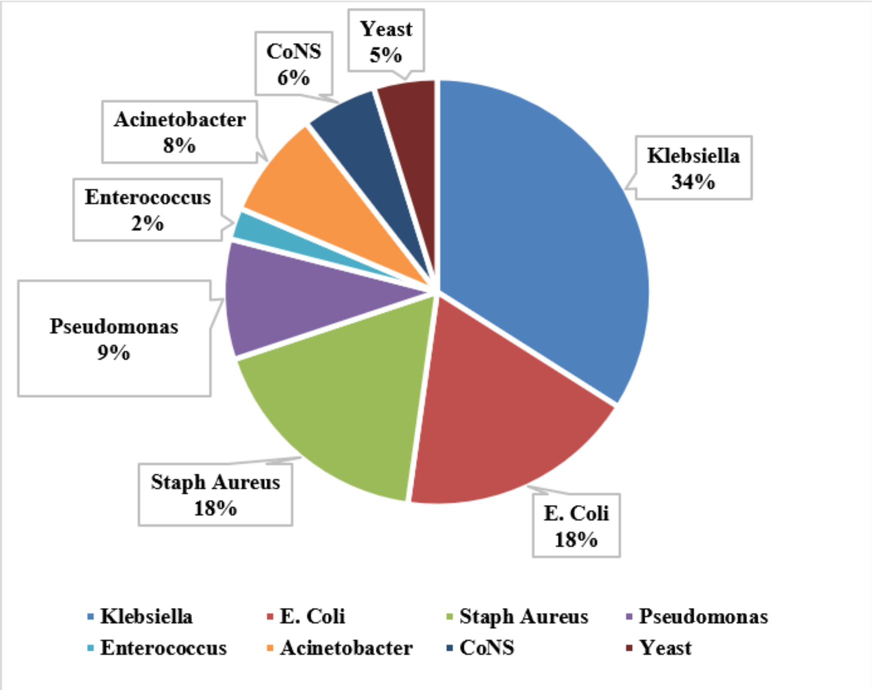

Figure 2: Prevalence of organisms in blood culture.

Pattern of sensitivity and resistance

Klebsiella species demonstrated a specific antimicrobial susceptibility profile, showing sensitivity to several key antibiotics. Specifically, the bacteria were susceptible to Cefepime+tazobactam, Colistin, Piperacillin+ Tazobactam, Cefoperazone+Sulbactam, Imipenem, and Amikacin. However, they exhibited resistance to Moxifloxacin, Gentamycin, Cefuroxime, Ceftriaxone, and Amoxyclav, highlighting the importance of tailored treatment strategies to combat antibiotic resistance (Table 2).

Table 2: Antibiotic sensitivity and resistance pattern of *Klebsiella*.

Klebsiella sensitivity	*Klebsiella* resistance
Cefepime+tazobactam, Colistin, Piperacillin+ Tazobactam, Cefoperazone +Sulbactam, Imipenem	Moxifloxacin, Gentamycin, Cefuroxime, Ceftriaxone, Amikacin, Amoxyclav

Escherichia coli (*E. coli*) exhibited a complex antimicrobial susceptibility profile. On one hand, it was susceptible to several antibiotics, including the combination therapies Cefoperazone+Sulbactam and Cefepime+tazobactam, as well as Colistin, Tigecycline, and Amikacin. Conversely, the bacterium demonstrated resistance to multiple agents, including Moxifloxacin, Gentamycin, Cefuroxime, Amoxyclav, and Ofloxacin. This pattern highlights the importance of antimicrobial stewardship and tailored treatment strategies to address the evolving resistance landscape of *E. coli* (Table 3).

Table 3: Antibiotic sensitivity and resistance pattern of *E. coli*.

E. coli sensitivity	*E. coli* resistance
Cefoperazone+Sulbactam Colistin, Tigecycline Moxifloxacin Cefepime +tazobactam	Gentamycin, Amikacin, Cefuroxime, Amoxyclav, Ofloxacin

Staphylococcus aureus susceptibility testing revealed sensitivity to several key antibiotics. Notably, the bacterium was susceptible to Nitrofurantoin, Linezolid, Vancomycin, and Moxifloxacin, indicating that these antibiotics may be effective treatment options. Conversely, Staphylococcus aureus demonstrated resistance to Ciprofloxacin, Gentamycin, Imipenem, Piperacillin+ tazobactam, Tetracycline, Amoxyclav, Ceftriaxone, and Amikacin, highlighting the importance of antibiotic stewardship and tailored treatment strategies to combat antibiotic resistance (Table 4).

Pseudomonas species demonstrated a distinct antimicrobial susceptibility pattern. The bacteria were found to be susceptible to Amikacin, Cefepime+ Tazobactam, Colistin, Imipenem+Cilastin, and Piperacillin+Tazobactam. However, they exhibited resistance to several antibiotics, including Tigecycline, Amoxyclav, Ofloxacin, Moxifloxacin, and Ciprofloxacin. This pattern highlights the importance of targeted antimicrobial therapy and the need for ongoing surveillance of antibiotic resistance in Pseudomonas species.

Table 4: Antibiotic sensitivity and resistance pattern of *Staphylococcus aureus*.

***Staphylococcus aureus* sensitivity**	***Staphylococcus aureus* resistance**
Nitrofurantoin, Linezolid, Vancomycin, Ciprofloxacin, Gentamycin, Imipenem, Piperecillin+tazobactam	Tetracycline, Amoxyclav, Moxifloxacin, Ceftriaxone, Amikacin

Table 5: Antibiotic sensitivity and resistance pattern of *Pseudomonas*.

***Pseudomonas* sensitivity**	***Pseudomonas* resistance**
Amikacin, Cefepime+ Tazobactam, Colistin, Imipenem+Cilastin, Piperacillin+Tazobactam, Tigecycline	Amoxyclav, Ofloxacin, Moxifloxacin, Ciprofloxacin

Acinetobacter species exhibited a specific antimicrobial susceptibility profile. The bacteria were found to be susceptible to Tigecycline, Colistin, and Piptaz (Piperacillin+Tazobactam), indicating potential treatment options. Conversely, Acinetobacter species demonstrated resistance to Aztreonam, Amoxyclav, Ciprofloxacin, Gentamycin, and Cefoperazone+Sulbactam, highlighting the importance of tailored antimicrobial therapy and ongoing surveillance of antibiotic resistance in this species (Table 6).

Table 6: Antibiotic sensitivity and resistance pattern of *Acinetobacter*.

***Acinetobacter* sensitivity**	***Acinetobacter* resistance**
Tigecycline, Colistin, Piptaz, Aztreonam	Amoxyclav, Ciprofloxacin, Gentamycin, Cefoperazone +Sulbactam

Prognosis correlation with culture reports

The culture report outcomes revealed notable differences in patient discharge success rates based on culture results. Specifically, among patients with culture-positive results, 72.2% were discharged successfully. In contrast, a significantly higher proportion of patients with culture-negative results, 83.8%, were discharged successfully. These findings suggest that patients with negative culture results may have had a better clinical outcome, potentially due to targeted treatment or underlying differences in disease severity.

The culture report outcomes revealed a striking disparity in mortality rates between culture- positive and culture-negative patients. A substantial 27.8% of patients with positive culture results succumbed to their infections, whereas a significantly lower proportion, 16.2%, of culture-negative patients were declared dead. This notable difference in mortality rates underscores the potential severity of culture-positive infections and highlights the importance of prompt and effective treatment.

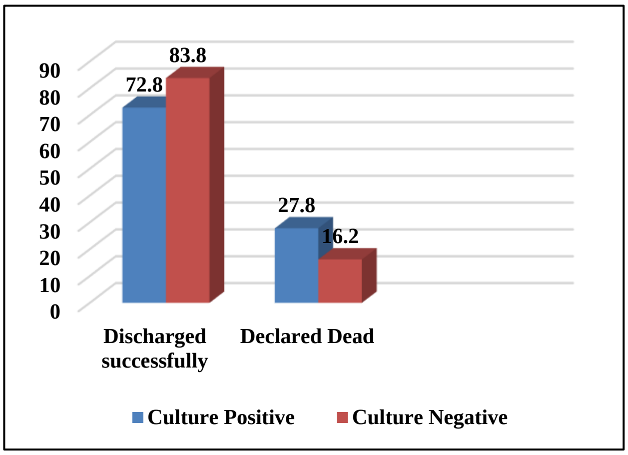

Figure 3: Mortality and discharge outcomes in neonatal sepsis.

DISCUSSION

In the present study, clinical sepsis was confirmed in 28.5% of cases with isolation of organisms in blood culture which is similar to other studies.[10-12] As the majority of referral centers do not have facilities for blood cultures, the start of empirical treatment before taking a blood culture in more than 50% of cases may be the reason for sterile culture in most of the cases.

In more than 72% of cases of clinical sepsis, neonates presented with LOS which is consistent with other studies.[13,14] Preterm low birth weight babies may be 3-10 times more prone to developing sepsis than term neonates.[16]

Gram-negative organisms are most commonly found in the majority of studies done in tertiary care centers in India, similar to present study.[21,22] As per NNPD data, *K. pneumoniae* was the most common pathogen (32.5%) of neonatal sepsis, followed by *S. aureus* (13.6%) and *E. coli* (10.6%).[23] Whereas in present study *K. pneumoniae* is the most common pathogen (33.9%) of neonatal sepsis, followed by *E. coli* (18.1%) and *Staphylococcus aureus* (17.7%).

Newly emerging pathogens of tertiary care NICUs like non-fermenting Gram-negative bacilli are also found in our study just like other studies.[24] In present study, *S. aureus* was found to be the most common Gram-positive organism followed by CONS.[17,19,25] Isolation of CONS in only 5.7% of cases in our study is due to aseptic sample collection technique and proper handling of culture bottles. Infection with S. aureus was isolated in the majority of cases in both EOS and LOS.[14,26] It could be due to poor personal hygiene. Isolation of *S. aureus* in inborn cases may be the result of a lack of strict hand washing, infrequent or improper sterilization, and cleaning of ICU.

Symptoms like respiratory distress, lethargy, and poor cry are common in EOS and LOS which are similar to other studies.[24,27,28]

In our study, Gram-negative and Gram-positive organisms were resistant to Amoxyclav in 98% cases. Most of the organisms showed sensitivity to Colistin, Cefepime+ Tazobactam, Cefoperazone+sulbactam, and Piperacillin+ Tazobactam.

Acienetobacter showed sensitivity to Aztreonam in 100% cases.

Due to gradually increasing resistance to ongoing empirical antibiotics there is a need to change the choice of empirical antibiotics policy.

The limitations include as it is a level III NICU, many critically ill neonates are referred cases in whom empirical antibiotic therapy has already started. So proper growth of microorganisms might not take place leading to falsely negative culture reports.

CONCLUSION

It is important to analyze the blood culture report and its sensitivity pattern as well as to formulate local antibiotic usage for better clinical outcomes. A high degree of resistance of organisms to penicillins and aminoglycosides calls for a re-evaluation of antibiotic policy and protocols for empirical treatment in neonatal sepsis. High prevalence of Staphylococcus aureus warrants urgent need for strict hand washing and hygiene policies. Infection control guidelines and education of healthcare staff about maintenance of strict asepsis should be reinforced. Strict antibiotic stewardship should be practiced to save the babies from the development of multidrug resistance in the future.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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