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CLINICAL OUTCOMES OF MULTIDRUG-RESISTANT KLEBSIELLA SEPSIS IN NEONATES: A PROSPECTIVE OBSERVATIONAL STUDY IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: *Klebsiella pneumoniae* is a major cause of neonatal sepsis in NICUs, often associated with multidrug resistance (MDR) and poor outcomes. Local epidemiological data are essential to guide empirical therapy and infection control. **Objective:** To evaluate the incidence, antimicrobial resistance patterns, and clinical outcomes of culture-positive *Klebsiella* sepsis among neonates admitted to a tertiary care NICU. **Methods:** Retrospective analysis of 85 neonates (52 inborn, 33 outborn) with culture-positive *Klebsiella* sepsis. Demographic, clinical, and microbiological data were collected. Statistical comparisons were performed using Chi-square, Fisher's exact, and Mann–Whitney U tests. **Results:** The majority were preterm (65.9%) and male (55.3%), with no significant differences between inborn and outborn groups ($\chi^2 = 0.013–0.019$, $p > 0.05$). Meningitis occurred in 26 cases (30.6%), with similar prevalence across groups (Fisher's exact = 0.65, p = 0.65). Overall, 63 neonates (74.1%) were discharged, 17 (20%) died, and 5 (5.9%) left against medical advice. Mortality was higher in outborn neonates (27.3% vs 15.4%), though not statistically significant (Fisher's exact = 0.18, p = 0.18). Treatment duration was significantly longer in meningitis cases (median 21 vs 14 days; Mann–Whitney U = 42, $p < 0.001$). Resistance rates were high for ampicillin (70–92%) and cephalosporins (58–86%). Outborn isolates showed higher resistance to cephalosporins ($\chi^2 = 3.81$, p = 0.051), carbapenems ($\chi^2 = 2.19$, p = 0.139), and colistin ($\chi^2 = 0.88$, p = 0.348), though differences were not statistically significant. **Conclusion:** MDR *Klebsiella* sepsis remains a significant challenge in NICUs. Meningitis cases require prolonged therapy, and outborn isolates demonstrate higher resistance trends, particularly to cephalosporins. These findings underscore the need for strengthened antimicrobial stewardship and infection control measures in tertiary care settings.

INTRODUCTION

Neonatal sepsis remains one of the leading causes of neonatal morbidity and mortality worldwide, particularly in low- and middle-income countries.(1) Despite advances in neonatal intensive care, the burden of sepsis continues to be substantial due to factors such as prematurity, low birth weight, invasive procedures, prolonged hospital stay, and irrational antibiotic use.(2) Among the causative organisms, Gram-negative bacteria, especially Klebsiella species, have emerged as predominant pathogens in neonatal intensive care units (NICUs).(3)

Klebsiella pneumoniae is a significant opportunistic pathogen responsible for early- and late-onset neonatal sepsis. (4)Over the past decade, the increasing emergence of multidrug-resistant (MDR) Klebsiella strains has posed serious challenges to neonatal care. These organisms often exhibit resistance to multiple antibiotic classes, including third-generation cephalosporins, aminoglycosides, fluoroquinolones, and increasingly, carbapenems. The rise of carbapenem-resistant Klebsiella has further limited therapeutic options, frequently leaving last-resort drugs such as colistin as the only effective agents.(5-7)

Neonates are particularly vulnerable to MDR infections due to their immature immune systems and frequent exposure to invasive interventions such as mechanical ventilation, central venous catheters, and prolonged antibiotic therapy. (8) In NICUs, MDR Klebsiella infections are associated with higher mortality rates, prolonged hospital stays, increased healthcare costs, and long-term neurodevelopmental sequelae. The transmission of MDR organisms is often facilitated by overcrowding, inadequate infection control practices, and antibiotic overuse. (9)

Although several studies have documented the prevalence of MDR Klebsiella infections in NICUs, data on incidence, antimicrobial resistance patterns, and clinical outcomes remain limited, particularly from tertiary care centres in eastern India. Local epidemiological data are crucial to guide empirical antibiotic policies, strengthen antimicrobial stewardship programmes, and implement effective infection prevention strategies. (10-13)

In this context, the present study was undertaken to evaluate the incidence, antimicrobial resistance pattern, and clinical outcome of multidrug-resistant culture-positive Klebsiella sepsis among neonates admitted to the NICU of a tertiary care centre.

Objectives

Primary objective: Estimate the incidence and describe the clinical outcomes (mortality, length of stay, complications) of culture-positive multidrug-resistant Klebsiella sepsis among neonates admitted to the NICU of a tertiary care centre.

Secondary Objective: Characterize the antimicrobial resistance pattern of Klebsiella isolates causing neonatal sepsis, including resistance to key antibiotic classes and identification of multidrug resistance profiles.

METHODOLOGY

Study Design And Setting

This was a prospective observational study conducted in the Neonatal Intensive Care Unit (NICU) of a tertiary care teaching hospital in Bhubaneswar, Odisha, India. The study was carried out over a period of 10 months.

Study Population

All neonates admitted to the NICU during the study period and clinically suspected to have neonatal sepsis were screened for eligibility.

Inclusion Criteria

1. Neonates (≤28 days of life) admitted to the NICU
2. Clinical features suggestive of neonatal sepsis
3. Blood culture positive for Klebsiella species
4. Isolates confirmed as multidrug resistant (MDR), defined as resistance to at least one agent in three or more antimicrobial classes

Exclusion Criteria

1. Neonates with culture-negative sepsis
2. Neonates with sepsis caused by organisms other than Klebsiella
3. Neonates with major congenital anomalies incompatible with life
4. Neonates whose parents declined consent

Sample Size

A total of 100 neonates at risk for sepsis were enrolled during the study period. Among them, 45 neonates had blood culture-positive MDR Klebsiella sepsis and were included in the final analysis.

Data Collection

Detailed clinical and demographic data were collected using a pre-designed structured proforma. Information recorded included:

1. Gestational age
2. Birth weight
3. Gender
4. Place of birth (inborn or outborn)
5. Risk factors for sepsis
6. Clinical presentation
7. Duration of NICU stay
8. Need for ventilatory support
9. Antibiotic therapy received
10. Final outcome (survived/discharged or expired)

Laboratory Methods

Blood samples were collected aseptically prior to initiation of antibiotics and sent for culture and sensitivity testing. Blood cultures were processed using standard microbiological techniques. Identification of Klebsiella species and antimicrobial susceptibility testing were performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

Multidrug resistance was determined based on resistance to multiple antibiotic classes. Antibiotic susceptibility patterns for commonly used drugs, including third-generation cephalosporins, carbapenems, aminoglycosides, and colistin, were documented.

Outcome Measures

The primary outcomes assessed were:

1. Incidence of culture-positive MDR Klebsiella sepsis
2. Antimicrobial resistance pattern
3. Mortality among affected neonates

Statistical Analysis

Data was entered into Microsoft Excel and analyzed using the Statistical Package of Social Sciences Version 26. Categorical variables were expressed as frequencies and percentages. Descriptive analyses were computed in terms of mean and standard deviation for continuous variables and frequency with percentage for ordinal and nominal variables. Chi square test was performed to find comparison and level of significance between two or more than two variables, when the data is categorical. Correlations between the variables were assessed using Pearson's test. Pearson's correlation coefficient of +1 indicates perfect positive correlation (both values rise together) whereas correlation coefficient -1 indicates perfect negative correlation (When one value rises, the other Value decreases). All tests were 2 tailed and p value less than 0.05 was considered statistically significant (95% confidence interval). isher's exact test for categorical comparisons (mortality, meningitis prevalence). Mann–Whitney U test for treatment duration.

Operational Definitions

Neonatal sepsis case: Neonate ≤28 days with clinical signs of sepsis and positive blood culture for Klebsiella spp.

MDR Klebsiella: Resistance to at least one agent in three or more antimicrobial classes, per standardized criteria.

Incidence proportion: Number of culture-positive MDR Klebsiella sepsis cases divided by total neonates evaluated for sepsis during the study period.

Clinical outcomes: Mortality (in-hospital), NICU length of stay, ventilator requirement, shock, NEC, IVH, seizures, and discharge status.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from legal guardians of all enrolled neonates. Confidentiality of patient information was maintained throughout the study.

RESULTS

A total of **85 neonates** with culture-positive *Klebsiella* sepsis were included, comprising **52 inborn** and **33 outborn** cases. The majority were **preterm (65.9%)** and **male (55.3%)**, with no significant differences in sex distribution, prematurity, or growth status between groups (χ^2 = 0.013–0.019, $p > 0.05$; Table 1). **Meningitis** was documented in 26 cases (30.6%), with similar prevalence across inborn and outborn neonates (Fisher's exact = 0.65, $p = 0.65$; Table 1).

Clinical outcomes are summarized in **Table 2**. Overall, **63 neonates (74.1%) were discharged**, **17 (20%) died**, and **5 (5.9%) left against medical advice**. Mortality was higher among outborn neonates (27.3%) compared to inborn (15.4%), though this difference was not statistically significant (Fisher's exact = 0.18, $p = 0.18$). Treatment duration was significantly longer in meningitis cases, with a median of 21 days compared to 14 days in non-meningitis cases (Mann–Whitney U = 42, $p < 0.001$; Table 3, Figure 1).

Antimicrobial resistance patterns are detailed in **Table 4** and illustrated in **Figure 2**. Resistance to ampicillin was uniformly high (70–92%), while cephalosporin resistance ranged from 58% in inborn to 86% in outborn isolates ($\chi^2 = 3.81$, $p = 0.051$). Carbapenem resistance was 23% in inborn and 49% in outborn isolates ($\chi^2 = 2.19$, $p = 0.139$), and colistin resistance was 10% versus 23% respectively ($\chi^2 = 0.88$, $p = 0.348$). Although these differences did not reach statistical significance, the consistent trend of higher resistance in outborn isolates is noteworthy. Ampicillin-sulbactam resistance was also high across both groups (60–69%).

Taken together, these findings highlight a substantial burden of MDR *Klebsiella* sepsis in neonates. Meningitis cases required significantly prolonged therapy, and outborn isolates demonstrated a trend toward higher resistance, particularly to cephalosporins, underscoring the need for vigilant antimicrobial stewardship and infection control in NICUs.

Table 1. Demographic And Clinical Characteristics (N= 85)

Variable	Inborn (n=52)	Outborn (n=33)	Total (n=85)	Chu-square (χ^2)	p-Value
Male	29 (55.8%)	18 (54.5%)	47 (55.3%)	0.013	0.91

Preterm (<37w)	34 (65.4%)	22 (66.7%)	56 (65.9%)	0.019	0.89
IUGR/ SGA	16 (30.8%)	10 (30.3%)	26 (30.6%)	0.002	0.96
Meningitis	15 (28.8%)	11 (33.3%)	26 (30.6%)	0.65*	0.65

*Fischer's exact test

Table 2. Clinical Outcomes (N= 85)

Outcome	Inborn (n=52)	Outborn (n=33)	Total (n=85)	Chi-square (χ^2)	p-Value
Discharged	41 (78.8%)	22 (66.7%)	63 (74.1%)	1.56	0.21
Death	8 (15.4%)	9 (27.3%)	17 (20.0%)	0.18*	0.18
DAMA	3 (5.8%)	2 (6.1%)	5 (5.9%)	–	–

*Fischer's exact test

Table 3.Treatment Duration (LOS Proxy) [N=85]

Group	Median Days	Range (days)	Mann–Whitney U test (U)	p-Value
Meningitis	21	21–21	42	< 0.001
Non-Meningitis	14	7–18	42	

Table 4. Antimicrobial Resistance Patterns Of Klebsiella Isolates (N= 85)

Antibiotic Class	Inborn Resistance (%)	Outborn Resistance (%)	p-Value
Cephalosporins	58	86	0.051
Carbapenems	23	49	0.139
Colistin	10	23	0.348
Ampicillin	70	92	–
Ampicillin-Sulbactam	60	69	–

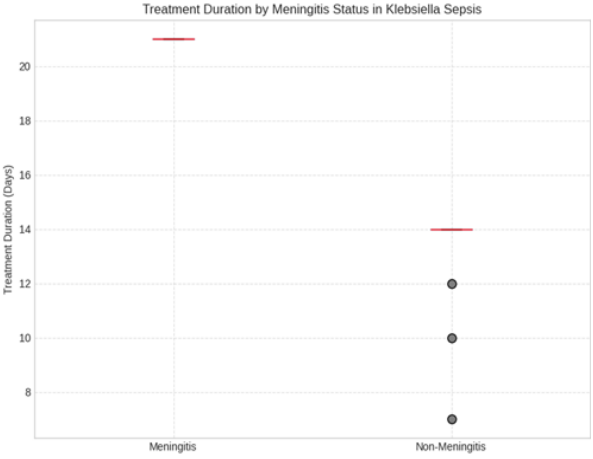

Figure-1: Box-and-whisker plot showing treatment duration (days) in neonates with Klebsiella sepsis, stratified by meningitis status.

DISCUSSION

This study of 85 neonates with culture-positive *Klebsiella* sepsis provides important insights into the burden of multidrug-resistant (MDR) infections in a tertiary care NICU. We observed a **mortality rate of 20%**, meningitis in nearly one-third of cases, and significantly longer treatment duration in meningitis compared to non-meningitis cases ($U = 42$, $p < 0.001$). Outborn isolates demonstrated numerically higher resistance to cephalosporins, carbapenems, and colistin, though differences were not statistically significant. These findings highlight both the clinical severity of *Klebsiella* sepsis and the growing challenge of antimicrobial resistance.

Our mortality rate is comparable to that reported in other Indian NICU studies. Chauhan et al. (2023) documented mortality of 22% among neonates with *Klebsiella* sepsis, with resistance dominated by cephalosporins and aminoglycosides. (14) Similarly, Patel et al. (2024) in a multicenter cohort across five district hospitals in India found mortality exceeding 25% in MDR Gram-negative sepsis, with *Klebsiella* as the leading pathogen. Although our mortality was slightly lower, the trend of higher mortality in outborn neonates (27.3% vs 15.4%) mirrors their findings, suggesting that referral-related exposure and prior antibiotic use may contribute to worse outcomes. (15)

International studies echo these concerns. Ma et al. (2024) reported that *Klebsiella pneumoniae* was a predominant cause of neonatal septicemia in Shanghai, with resistance to third-generation cephalosporins exceeding 60% and carbapenem resistance emerging as a major threat. (16) Our carbapenem resistance rates (23% in inborn vs 49% in outborn) are consistent with this global trend, underscoring the narrowing therapeutic options available for neonates. Mukherjee et al. (2021) further highlighted the devastating impact of carbapenem-resistant and hypervirulent *Klebsiella pneumoniae* in Eastern India, noting higher mortality and prolonged hospital stays. (17) While our cohort showed modest mortality, the presence of carbapenem resistance in nearly half of outborn isolates raises concern for future outcomes if resistance continues to escalate.

Another important finding was the **significantly longer treatment duration in meningitis cases** (median 21 vs 14 days). This is consistent with prior reports that neonatal meningitis requires extended therapy due to poor antibiotic penetration into the cerebrospinal fluid and the risk of long-term neurological sequelae. Gupta et al. (2025) similarly observed prolonged hospital stays and extended antibiotic courses in neonates with *Klebsiella* meningitis. Our data reinforce the need for early recognition and aggressive management of CNS involvement in neonatal sepsis.

The resistance profile in our study is particularly alarming. High resistance to ampicillin (70–92%) and cephalosporins (58–86%) reflects widespread antibiotic pressure in NICUs. Outborn isolates consistently showed higher resistance trends, especially to cephalosporins ($\chi^2 = 3.81$, $p = 0.051$), suggesting that neonates referred from peripheral centers may already have been exposed to broad-spectrum antibiotics. (18) This observation emphasizes the importance of **antimicrobial stewardship programs** and strict infection control practices, particularly in referral hospitals where empirical antibiotic use is common.

Taken together, our findings contribute to the growing body of evidence that MDR *Klebsiella* is a persistent and escalating threat in NICUs. The clinical implications are clear: empiric therapy must be guided by local resistance surveillance, infection control measures must be strengthened to prevent nosocomial transmission, and stewardship programs must be implemented to curb irrational antibiotic use. Future research should focus on multicenter surveillance to better understand regional variations in resistance and outcomes, as well as on evaluating novel therapeutic strategies for carbapenem-resistant infections.

CONCLUSION

This study highlights the significant burden of multidrug-resistant *Klebsiella* sepsis in neonates admitted to a tertiary care NICU. With an overall mortality of 20% and meningitis complicating nearly one-third of cases, the clinical impact is substantial. Treatment duration was significantly longer in meningitis cases, underscoring the need for early recognition and aggressive management of central nervous system involvement. Although differences in resistance between inborn and outborn isolates did not reach statistical significance, the consistent trend of higher resistance in outborn neonates-particularly to cephalosporins-suggests referral-related antibiotic exposure as a contributing factor.

The high rates of resistance to ampicillin, cephalosporins, and emerging carbapenem and colistin resistance reflect the narrowing therapeutic options available for neonatal sepsis. These findings reinforce the urgent need for **strengthened antimicrobial stewardship programs, strict infection control practices, and continuous surveillance of resistance patterns** to guide empiric therapy. Multicenter studies are warranted to better understand regional variations and to develop standardized treatment protocols.

In summary, MDR *Klebsiella* remains a formidable challenge in neonatal care. Addressing this threat requires coordinated efforts in infection prevention, rational antibiotic use, and policy-driven stewardship strategies to improve neonatal survival and long-term outcomes

REFERENCES

1. Liu L, Oza S, Hogan D, Chu Y, Perin J, Zhu J, et al. Global, regional, and national causes of under-5 mortality in 2000–15: an updated systematic analysis with implications for the Sustainable Development Goals. *Lancet*. 2016;388(10063):3027-35.
2. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. *Lancet*. 2017;390(10104):1770-80.
3. Folgori L, Bielicki J, Heath PT, Sharland M. Antimicrobial-resistant Gram-negative infections in neonates: burden of disease and challenges in treatment. *Curr Opin Infect Dis*. 2017;30(3):281-8.
4. Dong Y, Speer CP. *Klebsiella* species as emerging pathogens in neonatal sepsis: epidemiology, clinical features, and antimicrobial resistance. *Infect Drug Resist*. 2015;8:123-30.
5. Mukherjee S, Mitra S, Dutta S, Basu S. Neonatal sepsis: the impact of carbapenem-resistant and hypervirulent *Klebsiella pneumoniae*. *Front Med*. 2021;8:634349.
6. Logan LK, Weinstein RA. The epidemiology of carbapenem-resistant Enterobacteriaceae: the impact and evolution of a global threat. *J Infect Dis*. 2017;215(suppl_1):S28-36.
7. Kumar S, Verma A, Singh A, Naranje KM, Misra R. Colistin-resistant *Klebsiella pneumoniae* sepsis in neonates and infants: an alarming crisis in an Indian NICU. *J Trop Pediatr*. 2025;71(2):fmae044.
8. Hornik CP, Fort P, Clark RH, Watt K, Benjamin DK Jr, Smith PB, et al. Early and late onset sepsis in very-low-birth-weight infants from a large group of neonatal intensive care units. *Early Hum Dev*. 2012;88 Suppl 2:S69-74.
9. Zaidi AKM, Huskins WC, Thaver D, Bhutta ZA, Abbas Z, Goldmann DA. Hospital-acquired neonatal infections in developing countries. *Lancet*. 2005;365(9465):1175-88.
10. Allegranzi B, Bagheri Nejad S, Combescure C, Graafmans W, Attar H, Donaldson L, et al. Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. *Lancet*. 2011;377(9761):228-41.
11. Chauhan A, Kachhwaha C, Kamle A, Singer M, Prajapati J. Bacteriological profile, antibiotic susceptibility and outcome of neonatal sepsis in a tertiary care hospital in Central India. *Res J Med Sci*. 2023;49-54.
12. Gupta AK, Joha S, Era N, Mukherjee S. Treatment outcomes, antibiotic use, and resistance patterns among neonatal sepsis patients: a prospective observational study in Eastern India. *J Med Sci Health*. 2025;11(3):335-42.
13. Ma H, Xu J, Zhang Y, Zhang R, Wu J. Relevance and antimicrobial resistance profile of *Klebsiella pneumoniae* in neonatal sepsis. *J Matern Fetal Neonatal Med*. 2024;37(1). doi:10.1080/14767058.2024.2327828
14. Patel A, et al. Multidrug-resistant sepsis in special newborn care units in five district hospitals in India: a prospective cohort study. *Lancet Glob Health*. 2024;12(10):e1567-76.
15. Chauhan A, Kachhwaha C, Kamle A, Singer M, Prajapati J. Bacteriological profile, antibiotic susceptibility and outcome of neonatal sepsis in a tertiary care hospital in Central India. *Res J Med Sci*. 2023;49-54.
16. Mukherjee S, Mitra S, Dutta S, Basu S. Neonatal sepsis: the impact of carbapenem-resistant and hypervirulent *Klebsiella pneumoniae*. *Front Med*. 2021;8:634349.
17. Ma H, Xu J, Zhang Y, Zhang R, Wu J. Relevance and antimicrobial resistance profile of *Klebsiella pneumoniae* in neonatal sepsis. *J Matern Fetal Neonatal Med*. 2024;37(1). doi:10.1080/14767058.2024.2327828
18. Gupta AK, Joha S, Era N, Mukherjee S. Treatment outcomes, antibiotic use, and resistance patterns among neonatal sepsis patients: a prospective observational study in Eastern India. *J Med Sci Health*. 2025;11(3):335-42.