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CARBAPENEMASE-PRODUCING KLEBSIELLA PNEUMONIAE IN NEONATAL INTENSIVE CARE UNITS: THE OXA-48 CHALLENGE

Dr. Seema Gangar
Assistant Professor, Department of Microbiology,
M.M. Institute of Medical Sciences & Research, MM (DU), Ambala, India

Dr. Dibyashree Dibyashree
Assistant Professor, Department of Microbiology,
Santosh Medical College, Ghaziabad, UP, India

Dr. Nisha Goyal
Associate Professor, Department of Microbiology,
University College of Medical Sciences and Guru Teg Bahadur (GTB) hospital,
Delhi University, Delhi, India.

Dr.Narendra Pal Singh
Professor; Department of Microbiology,
Post Graduate Institute of Child Health (PGICH) Noida,
Uttar Pradesh, India

Abstract—**Background: Neonatal sepsis remains a leading cause of mortality in low- and middle-income countries, with rising multidrug-resistant (MDR) and extensively drug-resistant (XDR) pathogens threatening treatment outcomes. The carbapenemases producing Klebsiella pneumoniae especially oxacillinase-48 (OXA-48) producing strains yield misleading low carbapenem minimum inhibitory concentration (MIC), leading to inappropriate carbapenem use and emerging of drug resistance. This study investigates the prevalence, resistance patterns, and clinical implications of OXA-48 producing K. pneumoniae in bloodstream infections among neonates. Methods: A prospective observational study, conducted in a tertiary Neonatal intensive care unit (NICU) in Delhi, analyzing 100 non-duplicate K. pneumoniae blood isolates for production of OXA-48 and other carbapenemases via polymerase chain reaction (PCR). Their susceptibility patterns to various antimicrobial classes were tested by Kirby-bauer disk diffusion and MICs by epsilometer-test was done. Clinical data and potential risk factors were evaluated. Results: OXA-48 was detected in 12% of isolates, of which 75% were XDR and showed high resistance to aztreonam, third-generation cephalosporins, and meropenem. Two isolates co-harbored New Delhi metallo-β-lactamase-1 (NDM-1), resulting in elevated MICs. OXA-48 producers demonstrated broader resistance than non-producers. Statistically significant neonatal risk factors included vaginal delivery, prior antibiotic exposure, and ventilator support. Conclusion: OXA-48-producing K. pneumoniae represents a serious threat in neonatal sepsis, often masked by atypical resistance profiles and co-expressed resistance mechanisms. Routine molecular surveillance, early risk factor identification, and stringent NICU infection control are essential to mitigate its impact. The findings highlight an urgent need for targeted therapies and improved diagnostic strategies in neonatal care settings.**

Keywords—**OXA-48; Klebsiella pneumoniae; NICU; Carbapenemases; MIC**

I. INTRODUCTION

Neonatal sepsis is a life-threatening, systemic inflammatory response to infections in newborn, typically occurring within the first 28 days of life, accounting for over 550,000 deaths globally each year [1]. India contributing nearly a quarter of these. It remains a major barrier to reducing neonatal mortality in low- and middle-income countries (LMICs). As of 2022, the global neonatal mortality rate (NMR) stands at 17 deaths per 1,000 live births [2]. India has made significant progress, reducing its NMR from 28 per 1,000 live births in 2015 to 17 in 2023 with a 39% decline over eight years. However, achieving the Sustainable Development Goal (SDG) target of

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12 per 1,000 live births by 2030 requires an additional 29.4% reduction within the next few years [3].

While this goal is attainable, it presents significant challenges. The decline may slow as remote and underserved populations continue to face unequal access to healthcare. Moreover, a key contributor to neonatal sepsis is the rise of multidrug-resistant (MDR; resistant to at least one agent in ≥ 3 antimicrobial classes) and extensive drug resistant (XDR; Non susceptibility to all but 1 or 2 antimicrobial classes) pathogens such as Klebsiella pneumoniae. This gram-negative bacterium (GNB) from the Enterobacteriaceae family, is commonly present in the human microbiome. It can cause severe infections in critically ill patients such as newborns, especially in healthcare settings [4]. In neonatal intensive care units (NICU), blood stream infections by K. pneumoniae are a leading hospital-acquired infection, often resulting in poor clinical outcomes and prolonged hospital stays [5,6].

K. pneumoniae is a high-risk pathogen, its clinical threat is amplified by its ability to produce carbapenemases and carry multiple resistance genes, leading to widespread drug resistance and high mortality rates. Carbapenem-producing Klebsiella pneumoniae (CP-KPN) has threat emerged as a major global health concern, frequently causing outbreaks in NICUs affecting nations across the economic spectrum [6,7].

Carbapenemases, key enzymes behind carbapenem resistance, are classified into three main classes A, B, and D as per Ambler classification. Class A and D are serine-β-lactamases (SBLs), while Class B are metallo-β-lactamases (MBLs) containing a zinc ion at the active site. The most clinically significant and widely disseminated carbapenemases in K. pneumoniae include Klebsiella pneumoniaecarbapenemase (KPC, Class A), New Delhi metallo-β-lactamase (NDM, Class B), Verona integron-encoded metallo-β-lactamase (VIM, Class B), Imipenemase (IMP, Class B), and oxacillinase-48-like enzymes (OXA-48, Class D) [8]. Notably, both OXA 48 and NDM are endemic in the Indian subcontinent, contributing significantly to the region's burden of carbapenem-producing Enterobacteriales (CPE) [9].

OXA 48 like carbapenemases, first detected in K. pneumoniae in Turkey in 2001, have gained attention due to their silent global spread primarily via IncL/M plasmids carrying the Tn1999.2 transposon, with occasional chromosomal integration. Key variants include OXA 48, OXA 181, OXA 232, OXA 204, OXA 162, and OXA 244, with over a dozen others later reported. These class D β lactamases efficiently hydrolyze penicillins, modestly impact carbapenems (especially ertapenem), spare extended spectrum cephalosporins, and resist most β lactamase inhibitors except avibactam. Although they typically raise carbapenem MICs only moderately, they pose significant therapeutic challenges, particularly when co-expressed with extended-spectrum β-lactamase (ESBLs), AmpC enzymes or other resistance mechanisms like membrane permeability defects. Surveys assessing the global prevalence of CPE isolates consistently identify OXA 48–like variants among the top three carbapenemases, highlighting both their widespread presence and clinical significance [8,9,10].

Unlike other major carbapenemases like KPC, NDM, VIM, and IMP, OXA-48 are often missed in routine screening, especially when carried on a single epidemic plasmid without other resistance genes. These strains yield misleading low carbapenem MICs, leading to inappropriate carbapenem use. However, resistance may rapidly emerge during treatment, suggesting its spread is linked to antibiotic pressure and more to undetected transmission [11].

Transmission of CP-KPN in hospital settings is often driven by lapses in infection control, particularly hygiene protocols, inadequate disinfection of medical devices, and contaminated equipment. Additionally, these bugs thrive persistently as gut colonizers in NICU admitted patients and in environmental reservoirs like sinks, drains, and faucets. Healthcare workers can also serve as carriers through contact with contaminated clothing or protective gear. According to CDC guidelines, effective containment strategies include stringent infection control practices, judicious use of invasive devices, early identification, continuous surveillance, and robust antimicrobial stewardship programs [12,13].

Treatment options for neonatal infections caused by XDR Klebsiella are extremely limited. Colistin, often used alone or in combination with meropenem, amikacin, or ciprofloxacin, has shown moderate success but carries toxicity concerns. High-dose meropenem is sometimes used despite resistance. Ceftazidime-avibactam has emerged as a promising salvage therapy, showing efficacy and tolerability in small pediatric case series. However, comprehensive safety and efficacy data in neonates are still lacking, underscoring the urgent need for targeted clinical studies [14,15].

Given the growing threat of OXA-48-like CP-KPN in NICUs, this study seeks to explore the antimicrobial susceptibility patterns of these isolates and their clinical impact in neonates. The study provides crucial insights into treatment challenges and guide more effective management strategies for neonatal infections.

II. METHODS

A. Sample Size and study design –

A prospective observational study was conducted from July 2019 to June 2020. A total of 100 non-duplicate Klebsiella pneumoniae blood isolates were collected from confirmed neonatal sepsis cases in the NICU of a tertiary care hospital in Delhi.

B. Ethical Considerations–

Ethical approval was obtained from the Institutional Ethics Committee-Human Research (IEC-HR), University College of Medical Sciences, prior to the initiation of the study.

C. Culture, Isolation and Identification of Isolates

Blood samples were cultured on Blood and MacConkey agar and incubated overnight at 37°C under aerobic conditions.

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Isolates were identified based on by exploring their gram staining, cultural and biochemical characteristics.

D. Antibiotic Susceptibility Tests

Antimicrobial susceptibility testing of non-duplicate K. pneumoniae isolates was performed using the Kirby-Bauer disc diffusion method on Mueller-Hinton agar, following 0.5 McFarland standard inoculum preparation. Antibiotics tested included aminoglycosides (amikacin 30 µg, gentamicin 10 µg), β-lactam/β-lactamase inhibitors (piperacillin-tazobactam 100/10 µg), third-generation cephalosporins (cefotaxime 30 µg, cefixime 5 µg, ceftazidime 30 µg), fluoroquinolones (ciprofloxacin 5 µg), carbapenems (imipenem 10 µg, meropenem 10 µg), and monobactams (aztreonam 30 µg). Disks were sourced from HiMedia Laboratories, India. Plates were incubated at 35°C for 16–18 hours. Quality control was ensured using E. coli ATCC 25922, S. aureus ATCC 25923, and P. aeruginosa ATCC 27853 [16].Minimum inhibitory concentrations (MICs) for imipenem and meropenem were determined using Ezy MIC™ strips (range: 0.002–32 µg/mL) from HiMedia Laboratories, India. Klebsiella pneumonia ATCC BAA-1705 was used as the positive control and ATCC BAA-1706 as the negative control.Results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) M100 guidelines [16].

E. Detection of blaOXA and other Carbapenemases Genes

DNA extraction : Genomic DNA was extracted from all isolates using the HiPurA™ Bacterial Genomic DNA Purification Kit (HiMedia, India), and purity was assessed at 260/280 nm using a NanoDrop spectrophotometer (Thermo Scientific, UK). Gene Amplification**:** For detection of the blaOXA-48 gene, PCR was performed using a 281 bp primer set: Forward Primer (FP): GCTTGATCGCCCTCGATT and Reverse Primer (RP): GATTTGCTCCGTGGCCGAAA (Sigma-Aldrich). PCR (Polymerase chain reaction) conditions included initial denaturation at 94°C for 10 minutes, followed by 30 cycles of 94°C for 40 seconds, 60°C for 40 seconds, and 72°C for 1 minute, with a final extension at 72°C for 7 minutes. The optimal annealing temperature was 57°C [17]. Further, isolates were screened for other carbapenemase genes blaNDM-1, blaKPC, blaIMP, and blaVIM, using multiplex PCR. The primers used were: for blaNDM-1 (237 bp), FP: GCATAAGTCGCAATCCCCG and RP: CTTCCTATCTCGACATGCCG; for blaKPC (201 bp), FP: TCGAACAGGACTTTGGCG and RP: GGAACCAGCGCATTTTTGC; for blaIMP (578 bp), FP: GAAGGCGTTTATGTTCATAC and RP: GTAAGTTTCAAGAGTGATGC; and for blaVIM (382 bp), FP: GTTTGGTCGCATATCGCAAC and RP: AATGCGCAGCACCAGGATAG (all from Sigma-Aldrich). Cycling conditions for multiplex PCR involved 30 cycles at 94°C for 1 minute, 54°C for 1 minute, and 72°C for 1.5 minutes, followed by a final extension at 72°C for 5 minutes (18). Amplified products were subjected to gel electrophoresis on 1.5% agarose gel (HiMedia, India) stained with ethidium bromide (0.5 µg/mL) at 100 V for 45–60 min, visualized under UV light (G:BOX, SynGene), and photographed using GeneSnap (SynGene).

F. Data Entry and Statistical Analysis

Results were expressed as percentages, and graphs were generated using Microsoft Excel. Statistical analysis was performed using Fisher's Exact Test, with a p-value < 0.05 considered statistically significant.

III. RESULTS

Among 100 K. pneumoniae isolates, 27% were susceptible to all the tested antimicrobials, while 37% were MDR and 19% were XDR (Figure 1). The blaOXA-48 gene was detected in 12 isolates. Of these, 75% (9/12) were XDR, 16.7% (2/12) were MDR, and one isolate (8.3%) was susceptible to all the tested antimicrobials by disk diffusion method. On further testing, two OXA-48 producers also co-harboured the blaNDM-1 gene, and four additional isolates carried NDM-1 alone, resulting in a total carbapenemase prevalence of 16%. No KPC, IMP, or VIM genes were detected by PCR.

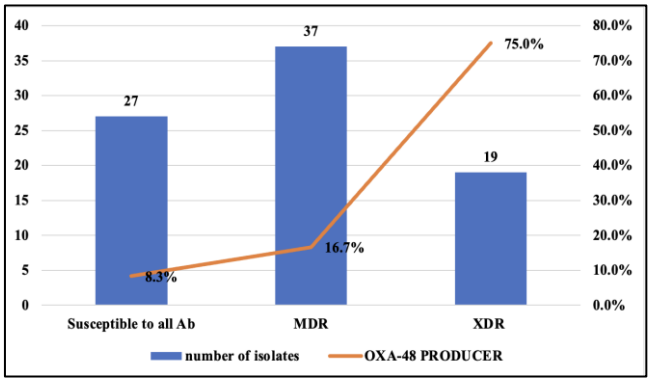

Fig. 1. Distribution of multidrug and extensive drug resistance among Klebsiella pneumoniae isolates.

Figure 2 illustrates the antimicrobial resistance patterns of OXA-48-producing and non-OXA-48-producing K. pneumoniae isolates. Overall, OXA-48 producers exhibited significantly higher resistance levels. Resistance to aztreonam and cephalosporins exceeded 90% among OXA-48 producers, compared to less than 60% in non-producers. OXA-48 producers showed 83% resistance to meropenem, and 75% to both piperacillin-tazobactam and gentamicin, while non-producers exhibited resistance rates below 30% for these antimicrobial agents. Ciprofloxacin resistance increased from 51% in non-producers to 83% in OXA-48 producers. Imipenem remained the most effective agent against both groups.

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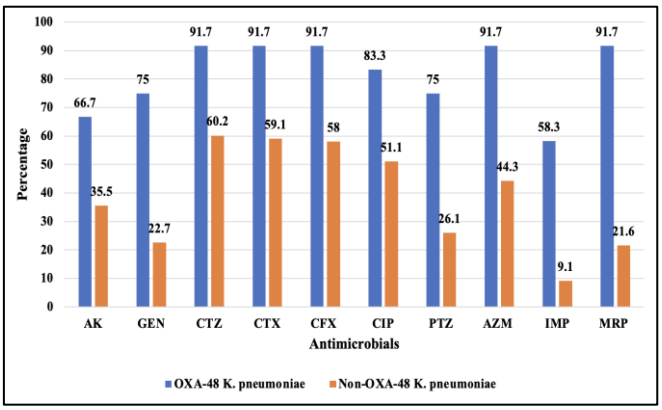


Fig. 2. Antimicrobial resistance among OXA-48 producers and non-OXA-48 producer Klebsiella pneumoniae.

AK: Amikacin; GEN: Gentamicin; CTZ: Ceftazidime; CTX: Ceftriaxone; CFX: Cefixime; CIP: Ciprofloxacin; PTZ: Piperacillin-tazobactam; AZM: Aztreonam; IMP: Imipenem; MRP: Meropenem.

Figure 3 presents the MIC values of imipenem and meropenem for OXA-48-producing isolates. In all cases, meropenem MICs were equal to or higher than those of imipenem. According to CLSI guidelines, MIC values >4 µg/mL indicate resistance. The first three isolates showed low imipenem MICs (0.19, 0.25, and 0.75 µg/mL) (Image 1), while one isolate had an intermediate MIC (2 µg/mL). Despite this, all four were resistant to meropenem, with MICs ranging from 4 to 16 µg/mL. Isolates 6 and 7, co-producing OXA-48 and NDM-1, exhibited the highest MICs (32 µg/mL) for both carbapenems.

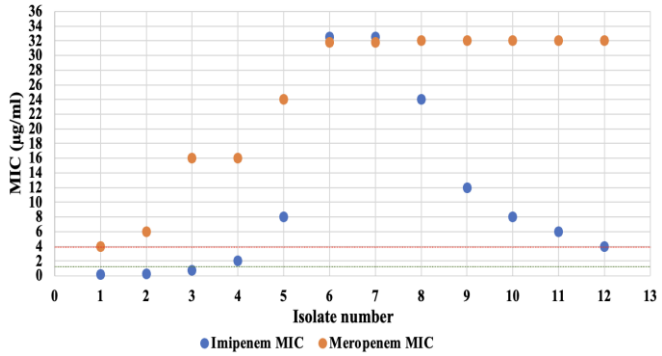
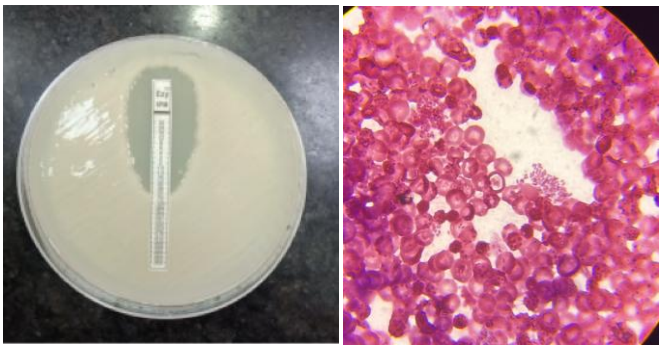


Fig. 3. MIC values of imipenem and meropenem among OXA-48-producing isolates.

MIC: Minimum Inhibitory Concentration



(a) (b)

Fig. 4. (a) Imipenem MIC of an OXA-48 producing Klebsiella pneumoniae; (b) Direct blood gram stain showing gram-negative bacilli.

Table 1 summarizes the socio-demographic characteristics and potential risk factors for bloodstream infections caused by carbapenemase-producing (both OXA-48 and NDM-1) Klebsiella pneumoniae in neonates. Affected neonates were predominantly male, with a higher incidence of early-onset sepsis (EOS) compared to late-onset sepsis (LOS). Half of the cases involved low birth weight (LBW) infants, and 71% were preterm. Most deliveries occurred via normal vaginal delivery (NVD), with GTB Hospital being the primary place of birth. Ventilator support was required in 9% of cases. No significant antenatal history wasnoted in 90% of neonates, and only 16% had prior antibiotic exposure. Notably, 98% had no other medical or surgical interventions.

IV. DISCUSSION

The study focused on OXA-48-producing K. pneumoniae strains from neonatal sepsis patients. As one of the most prevalent carbapenemases reported in India, OXA-48 poses unique diagnostic and therapeutic challenges due to its subtle resistance profile and frequent co-occurrence with other resistance mechanisms [10]. More than half of the isolates in our study were either multidrug-resistant (37%) or extensively drug-resistant (19%), with only 44% isolates remaining susceptible to most of the tested antibiotics by routine disk diffusion, underscoring the alarming rate of drug-resistant bloodstream infections among neonates. Resistance was particularly high among OXA-48-producing isolates, with 75% (9/12) classified as XDR. These findings align with recent studies showing a significant shift in the distribution of neonatal sepsis pathogens over the past two years, with GNB emerging as predominant causative agents. More than half of sepsis cases in hospitalized neonates involved MDR organisms, consistent with our results. Notably, 15.6% of Klebsiella pneumoniae isolates were resistant to carbapenems [12]. In a recent NICU outbreak in a tertiary care hospital in India, 14 K. pneumoniae isolates from neonatal sepsis were found to be resistant to all tested antibiotics, including carbapenems and colistin. Similarly, 17 of 18 K. pneumoniae isolates sepsis or pneumonia showed pan-resistance, while non-ICU isolates

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were largely susceptible [19]. In another study from India, GNB accounted for 70% of isolates, with K. pneumoniae (22.9%) and E. coli (14.8%) being most common; notably, 75–88% of these isolates were multidrug-resistant [5]. These patterns highlight the critical and escalating threat of MDR/ XDR infections in this vulnerable population.

Table -1 Socio-Demographic Characteristics and possible risk factors.

Risk factors (total)	CP-Kps **(16) n (%)**	Non CP-Kps **(84) n (%)**	**p-value**
Gender			0.157
Female (40)	5 (31.2%)	35(41.6%)	
Males (60)	11(68.7%)	49(58.3%)	
Onset of sepsis			1
EOS (71)	12(75%)	59(70.2%)	
LOS (29)	4 (25%)	25(29.7%)	
Birth weight			
LBW (50)	8 (50%)	42(50%)	0.67
VLBW (31)	4 (25%)	27(32.1%)	1
ELBW (6)	3 (18.7%)	3(3.57%)	0.079
Normal birth weight (13)	1(6.25%)	12(14.3%)	
Gestational age			0.38
Preterm (71)	13 (81.2%)	58(69%)	
Term (29)	3 (18.7%)	26(30.9%)	
Post-term (0)	0	0	
Mode of delivery			**0.022**
NVD (88)	11 (68.7%)	77(91.6%)	
LSCS (12)	5 (31.2%)	7(8.3%)	
Place of delivery			
GTBH (97)	16 (100%)	81(96.4%)	1
-other hospital (3)	0	3(3.57%)	
Type of feed			
NPO (69)	7 (43.75%)	62(73.8%)	
Breast milk (29)	8 (50%)	21 (25%)	0.061
Top milk (2)	1(6.25%)	1(1.19%)	0.214
Intervention			NA
IV cannula (100)	16(100%)	84(100%)	
NG tube			0.28
Present (84)	12 (75%)	72(85.7%)	
Absent (16)	4(25%)	12(14.2%)	
Ventilator			**0.0172**
Required (9)	5(31.2%)	4(4.7%)	
Not required (91)	11(68.7%)	80(95.2%)	
Maternal history			
PROM (9)	3(18.7%)	6(7.1%)	0.157
Chorioamnionitis (1)	0	1(1.19%)	
UTI (0)	0	0	
No significant history (90)	13(81.2%)	77(91.6%)	
Past history of similar illness			0.29
Present (2)	1(6.25%)	1(1.19%)	
Absent (98)	15(93.7%)	83(98.8%)	
Antibiotics			**0.003**
Administered (16)	7(43.7%)	9(10.7%)	
Not administered (84)	9(56.2%)	75(89.2%)	

Other medical/ surgical interventions			0.29
Present (2)	1(6.25%)	1(1.19%)	
Absent (98)	15(93.7%)	83(98.8%)	
History of antenatal steroids			1
Administered (48)	8(50%)	40(47.6%)	
Not administered (52)	8(50%)	44(52.3%)	
Duration of hospital stay			NA
3 days (1)	0	1(1.19%)	
4 days (12)	0	12(14.2%)	
5 days (17)	1(6.25%)	16(19%)	
6 days (39)	5(31.2%)	34(40.4%)	
7 days (11)	2(12.5%)	9(10.7%)	
8 days (11)	2(12.5%)	9(10.7%)	
9 days (8)	5(31.2%)	3(3.57%)	
>=10 days (1)	1(6.25%)	0	

(Key words : EOS = early onset sepsis (age< 1week); LOS = late onset sepsis (age > 1 week) ; LBW = low birth weight; VLBW= very low birth weight; ELBW = extremely low birth weight; NVD= normal vaginal delivery; LSCS= lower segment caesarean section; NPO= nil per orally; NG = naso-gastric; PROM= Premature rupture of membranes; UTI= urinary tract infection; NA= not applicable.)

Although OXA-48 carbapenemases typically exhibit low-level carbapenem hydrolysis and may not always confer high-level resistance, pattern was not reflected in our study. Strikingly, only one OXA-48-producing isolate was susceptible to all tested antibiotics by disk diffusion, representing the classical resistance profile attributed solely to OXA-48. In contrast, the remaining isolates exhibited high-level resistance, strongly suggesting the involvement of additional resistance mechanisms beyond OXA-48 alone. Notably, two of the XDR isolates co-produced NDM-1 carbapenemases, while none of the K. pneumoniae isolates carried other carbapenemases such as KPC, IMP, or VIM, indicating that OXA-48 is the predominant carbapenemase circulating in our NICU setting. This is consistent with other studies where K. pneumoniae was also the most prevalent neonatal pathogen. In one such study, OXA-48 and NDM-1 were identified in 60.8% and 52.2% of carbapenemase-producing isolates, respectively, with over half showing coexistence of both [20]. Similarly, another Indian study reported blaOXA-48 in 56.2% and blaNDM in 21.9% of CRKP isolates from ICU/NICU settings [19]. Notably, like our study, neither KPC, IMP, nor VIM genes were detected in these cohorts. These findings collectively highlight the dominance of OXA-48 and the frequent co-occurrence of other resistance determinants in neonatal care settings reinforcing the urgent need for molecular surveillance to guide effective antimicrobial strategies.

OXA-48-producing bacteria shows highly variable β-lactam resistance profiles. Some isolates remain susceptible to broad-spectrum cephalosporins or carbapenems, or both, resulting in a wide range of phenotypic presentations that complicating reliable detection and interpretation [8,10,11]. However, in our study, over 90% of OXA-48 producers show resistance to third-generation cephalosporins, aztreonam, and meropenem. This contrasts with the typically variable resistance profiles of OXA-48 producers and suggests the presence of additional resistance mechanisms, particularly ESBLs (e.g., CTX-M, SHV, TEM). A study reported frequent detection of ESBL genes such as blaSHV and blaCTX-M along with blaOXA-48 and blaNDM in CPKPN isolates from ICU/NICU settings [19]. Although aztreonam is generally stable against most β-lactamases except MBLs (as seen in two isolates co-harbouring NDM-1 and OXA-48), its efficacy may be compromised when combined with porin loss, even in the absence of efficient hydrolysis by ESBLs. The high aztreonam and ceftazidime resistance observed also indicates the likely absence of OXA-48 variants like OXA-163 or OXA-405, which hydrolyze ceftazidime but usually spare aztreonam, reinforcing the role of co-existing ESBLs in driving resistance.

Comparison of MIC values revealed that meropenem consistently showed higher MICs than imipenem across all tested isolates. Three isolates displayed low imipenem MICs (0.19, 0.25, and 0.75 µg/mL) and one had an intermediate MIC (2 µg/mL), all within the susceptible range. However, these isolates were resistant to meropenem (MIC > 4 µg/mL) despite being susceptible to imipenem. These findings suggest that meropenem MICs are more reliable predictor of OXA-48-mediated resistance compared to imipenem. Notably, two isolates (isolate no 6 &7) co-producing NDM-1 and OXA-48 exhibited the highest MICs (32 µg/mL) for both meropenem and imipenem, highlighting the potent additive effect of multiple carbapenemases, particularly a metallo-β-lactamases (MBLs). These markedly elevated MICs in NDM-1 co-producers emphasize that MBLs contribute significantly to high-level carbapenem resistance. Even though undetected resistance mechanisms may exist, their comparatively lower

MICs suggest a lesser impact than that of MBLs. Even if a bacterial strain appears susceptible at first, resistance can develop during treatment, particularly in carbapenemase-producing strains. A study found that NDM producers showed the highest increase in meropenem MIC at high bacterial loads, while OXA-48 producers had the smallest increase. Interestingly, strains with lower initial MICs showed a stronger inoculum effect (increase in MIC at high bacterial densities) likely due to increased enzyme activity under antibiotic pressure [21]. This suggests that strains with low initial MICs, such as OXA-48 produces identified in our study, may still carry a risk for treatment failure due to their potential for enzyme upregulation enzyme-inducing potential. Identifying the type of carbapenemase and the initial MIC can help predict resistance development and guide more effective therapy.

Statistically significant neonatal risk factors in our study were normal vaginal delivery, prior antibiotic exposure, and need for ventilator support, suggesting possible vertical transmission or early hospital-acquired infections. Our findings were supported by evidence from univariate analysis of other studies, where mechanical ventilation and prior exposure to carbapenems were also identified as significant risk factors [12,13]. While no significant association with risk of infections was found in other demographic variable such as gender, onset of sepsis, birth weight, gestational age and prior medical or surgical interventions etc. However, other studies have identified ICU admission, LBW to ELBW, prematurity, low, and maternal factors like antenatal steroid use and chorionic inflammation as significant risk factors for neonatal sepsis [12]. These non-significant findings in our study may reflect underlying clinical patterns, but the lack of statistical significance suggests that a larger sample size or more targeted analysis may be needed to confirm their role in infection risk. While certain neonatal risk factors were identified, further large-scale, multi-centric studies with broader genotypic profiling can provide a more comprehensive picture of resistance dynamics and guide effective treatment strategies in this vulnerable population.Given these risk factors, stringent infection control in NICUs is vital to curb CP-KPN spread. Key measures include strict hand hygiene, equipment and surface disinfection, and contact precautions. Routine rectal screening for CRE helps identify carriers early, enabling prompt isolation. Combined with staff education, adequate staffing, and strong antimicrobial stewardship, these actions are essential for safeguarding neonates in this high-risk setting and breaking chain of transmission.

V. CONCLUSION

Our study highlights the alarming prevalence of OXA-48-producing K. pneumoniae in neonatal sepsis, with a majority of isolates exhibiting multidrug or extensively drug-resistant profiles. The high resistance rates, particularly among OXA-48 co-producers, underscore the complexity of β-lactam resistance driven by additional mechanisms like MBLs and ESBLs. The observed phenotypic variability reinforces the limitations of conventional susceptibility testing and the urgent need for molecular diagnostics to ensure targeted intervention. The identification of key neonatal risk factors further emphasizes the likelihood of early transmission and the critical need for strengthened infection control and antimicrobial stewardship in NICU settings.

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VI. REFERENCE

[1]. Hayes R, Hartnett J, Semova G, Murray C, Murphy K et al. (2023) Neonatal sepsis definitions from randomised clinical trials. Pediatric research.(Vol 93(5): pp 1141-8).

[2]. UNICEF. Neonatal mortality. UNICEF data; 2023. Available from: https://data.unicef.org/topic/child-survival/neonatal-mortality [Last accessed on 2025 December 09].

[3]. Ministry of Health & Family welfare. India witnesses a steady downward trend in maternal and child mortality towards achievement of SDG 2030 targets. Available from: https://www.mohfw.gov.in/?q=en/pressrelease/india-witnesses-steady-downward-trend-maternal-and-child-mortality-towards-achievement#:~:text=India's%20Progress%20Outpaces%20Global%20Averages,of%20child%20mortality%20indicators%20continued. [Last accessed on 2025 June 21].

[4]. Reyes J, Aguilar AC, Caicedo A.(2019). Carbapenem-resistant Klebsiella pneumoniae: microbiology key points for clinical practice. International journal of general medicine. (28: pp437-46).

[5]. Jain K, Kumar V, Plakkal N, Chawla D, Jindal A, Bora R et al. (2025) Multidrug-resistant sepsis in special newborn care units in five district hospitals in India: a prospective cohort study. The Lancet Global Health.(13(5):pp e870-8).

[6]. Pathak A, Tejan N, Dubey A, Chauhan R, Fatima N, Jyoti et al. (2023). Outbreak of colistin resistant, carbapenemase (bla NDM, bla OXA-232) producing Klebsiella pneumoniae causing blood stream infection among neonates at a tertiary care hospital in India. Frontiers in Cellular and Infection Microbiology.(13:pp1051020).

[7]. Hassuna N. A., AbdelAziz R. A., Zakaria A., Abdelhakeem, M.(2020) Extensively-drug resistant Klebsiella pneumoniae recovered from neonatal sepsis cases from a major NICU in Egypt. Front. Microbiol. (pp11).

[8]. Alvisi G, Curtoni A, Fonnesu R, Piazza A, Signoretto C, Piccinini G et al. (2025) Epidemiology and Genetic Traits of Carbapenemase-Producing Enterobacterales: A Global Threat to Human Health. Antibiotics.(14(2):pp141).

[9]. Filgona J, Banerjee T, Anupurba S. (2018). Endemicity of OXA-48 and NDM-1 Carbapenemase producing Klebsiella pneumoniae and Escherichia coli from a tertiary hospital in Varanasi, India. JAMB;(12:pp1-8).

[10]. Pitout JD, Peirano G, Kock MM, Strydom KA, Matsumura Y. (2019). The global ascendency of OXA-48-type carbapenemases. Clinical microbiology reviews. (33(1):pp10-128).

[11]. Poirel L, Potron A, Nordmann P. (2012). OXA-48-like carbapenemases: the phantom menace. Journal of Antimicrobial Chemotherapy.(67(7):pp1597-606).

[12]. Zou H, Jia X, He X, Su Y, Zhou L, Shen Y et al. (2021). Emerging threat of multidrug resistant pathogens from neonatal sepsis. Frontiers in Cellular and Infection Microbiology. (11:pp694093).

[13]. Wei X, Liang J, Zhang H, Yan C, Lu X, Chen Y et al. (2024). Clinical features and risk factors of Klebsiella pneumoniae infection in premature infants: a retrospective cohort study. BMC Infectious Diseases.24(1):1311.

[14]. Chiusaroli L, Liberati C, Caseti M, Rulli L, Barbieri E, Giaquinto C et al. (2022). Therapeutic options and outcomes for the treatment of neonates and preterms with Gram-negative multidrug-resistant bacteria: a systematic review. Antibiotics.(11(8):pp1088).

[15]. Iosifidis E, Chorafa E, Agakidou E, Kontou A, Violaki A, Volakli E et al. (2019). Use of ceftazidime-avibactam for the treatment of extensively drug-resistant or pan drug-resistant Klebsiella pneumoniae in neonates and children< 5 years of age. The Pediatric infectious disease journal.(38(8):pp812-5).

[16]. CLSI. (2020). Performance standards for antimicrobial susceptibility testing; Thirith informational supplement. CLSI document M100-S30. Wayne, PA. Clinical and Laboratory Standards Institute.

[17]. Dallenne C, da Costa A, Decré D, Favier C, Arlet G.(2010) Development of a set of multiplex PCR assays for the detection of genes encoding important β-lactamases in Enterobacteriaceae.J Antimicrob Chemother. (65:pp490-5).

[18]. Solanki R, Vanjari L, Subramanian S, Aparna B, Lakshmi V. (2014). Comparative evaluation of multiplex PCR and routine laboratory phenotypic methods for detection of carbapenemases among gram negative bacilli. J Clin Diagn Res.(8:DC23-6).

[19]. Sharma S, Banerjee T, Kumar A, Yadav G, Basu S. (2022). Extensive outbreak of colistin resistant, carbapenemase (bla OXA-48, bla NDM) producing Klebsiella pneumoniae in a large tertiary care hospital, India. Antimicrobial Resistance & Infection Control.(11(1):pp1).

[20]. Ghaith DM, Zafer MM, Said HM, Elanwary S, Elsaban S, Al-Agamy MH et al.(2020) Genetic diversity of carbapenem-resistant Klebsiella Pneumoniae causing neonatal sepsis in intensive care unit, Cairo, Egypt. European Journal of Clinical Microbiology & Infectious Diseases.(39:583-pp91).

[21]. Golikova MV, Strukova EN, Alieva KN, Ageevets VA, Avdeeva AA, Sulian OS et al.(2023). Meropenem MICs at standard and high inocula and mutant prevention concentration inter-relations: comparative study with non-carbapenemase-producing and OXA-48-, KPC-and NDM-producing Klebsiella pneumoniae. Antibiotics. (12(5):pp872).