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ORIGINAL ARTICLE

Antibiotic Resistance Patterns in Gram-Negative Bacterial Infections Among Pediatric Patients: A Cross-Sectional Study at a Tertiary Care Hospital

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ABSTRACT

Background: Gram-negative bacterial infections are a major cause of morbidity and mortality among pediatric patients, with rising antimicrobial resistance further complicating treatment.

Objective: This study assessed the prevalence, resistance patterns, and clinical outcomes of gram-negative infections in children.

Methods: This was a cross-sectional observational study conducted at Children Hospital, Faisalabad from December 2022 to May 2023, including a total of 220 pediatric patients diagnosed with gram-negative bacterial infections. Clinical and demographic information was recorded for each patient, including age, gender, admission unit (ward/NICU/PICU), and suspected infection site. Specimens such as blood, urine, cerebrospinal fluid, tracheal aspirates, wound swabs, and sputum were collected under aseptic conditions and sent to the microbiology laboratory for processing.

Results: The mean age of the cohort was 3.2 ± 3.8 years, with NICU/PICU patients significantly younger (1.1 ± 1.4 years) than ward patients (5.3 ± 4.2 years, $p < 0.001$). E. coli was the most common organism (38.6%), while Pseudomonas and Acinetobacter were more prevalent in NICU/PICU (20.0% and 16.3%). Resistance to third-generation cephalosporins (68.2%), fluoroquinolones (52.7%), and carbapenems (18.6%) was high, with significantly higher resistance in NICU/PICU patients ($p < 0.05$). ESBL-producing strains accounted for 41.8%, MDR for 37.2%, and carbapenem-resistant isolates for 18.6%, with all resistance types significantly more common in critically ill patients. NICU/PICU children had significantly worse outcomes, including higher rates of mechanical ventilation (32.7%), septic shock (21.8%), prolonged hospital stay (50.9%), and mortality (13.6%).

Conclusion: Gram-negative infections in pediatric patients exhibit alarming levels of antimicrobial resistance, especially in critically ill children. The high prevalence of MDR, ESBL, and carbapenem resistance underscores the need for strengthened antibiotic stewardship, improved infection-control strategies, and ongoing surveillance to ensure effective treatment outcomes.

Keywords: Gram-negative bacteria, pediatric infections, antibiotic resistance, MDR, ESBL, carbapenem resistance.

INTRODUCTION

The fears of gram-negative bacterial infections on the health of children are still a high concern in the world with regard to its role in morbidity and long-term hospitalization, and mortality in children, especially in health facilities with limited resources[1]. Their clinical significance is not only connected with their potential to cause serious illnesses including sepsis, meningitis, pneumonia, urinary tract infections and wound infections, but it is also caused by an increasing alarming trend of antimicrobial resistance. Due to advancements in the past twenty years, gram-negative microorganisms such as Escherichia coli, Klebsiella species, Pseudomonas aeruginosa, and Acinetobacter species have evolved elaborate resistance mechanisms that have severely limited the number of therapeutic agents that clinicians can choose[2]. This increasing trend questions the efficacy of empirical therapy and the general results of infected children patients[3]. The factors that predispose gram-negative bacteria to antibiotic resistance are varied and include but are not limited to inappropriate use of antibiotics, poor infection control measures, inappropriate prescription and inherent capacity of the bacteria to acquire resistance genes through plasmids, transposons and integrons[4]. Extensive-spectrum 2-lactamase (ESBL) producers, multidrug-resistant (MDR), and carbapenem-resistant organisms (CROs) have significantly complicated the process. These infections are more worrisome in the pediatric patients because the immune system is immature, there is limited range of antibiotics that can be used in children, and the susceptibility to complications is also increased[5]. Resistance rates of up to 60-80 percent to commonly used antibiotics, including third generation cephalosporins and fluoroquinolones have been observed in various parts of the world previously, and it is necessary to continuously monitor it[6].

The growing number of carbapenem resistance, which greatly limits treatment choices and is linked to poorer clinical outcomes, is of special interest[7]. The organisms that are resistant to Carbapenem, particularly Acinetobacter and Pseudomonas, are associated with the longer NICU or PICU, changes in the medical expenses, and the risk of death. Horizontal gene transfer and the spread of resistance genes in the hospital setting are some of the factors that facilitate the spread of outbreaks and hence surveillance is crucial as a tool to detect and contain outbreaks at an early stage[8]. The existing evidence also indicates that pediatric gram-negative infections tend to exhibit the same patterns of resistance to adults, but the treatment problem is increased by age-specific limitations of dosing and developmental pharmacokinetics[9]. Considering the increasing burden of antibiotic resistance and its direct effect on treatment options, hospitals need to align the resistance trends of children on a regular basis. This will guarantee updates to the empirical antibiotic guidelines in time, decrease the inappropriate use of antibiotics, and promote the antimicrobial stewardship program. As such, the study presented was a cross-sectional study aimed at examining the incidences of antibiotic resistance in gram-negative bacteria in pediatric patients, the prevalence of MDR, ESBL, and carbapenem resistance, and offer useful information that would help streamline the clinical and infection-control policies in a tertiary care center.

Objective: To assess the resistance patterns and clinical outcomes of gram-negative bacterial infections in pediatric patients and compare severity between NICU/PICU and ward groups.

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METHODOLOGY

This was a cross-sectional observational study conducted at Children Hospital, Faisalabad from December 2022 to May 2023, including a total of 220 pediatric patients diagnosed with gram-negative bacterial infections.

Inclusion Criteria:

- Pediatric patients aged 0–14 years.
- Culture-positive gram-negative bacterial infections from any clinical specimen.
- Patients admitted to pediatric wards, NICU, or PICU.
- Complete clinical and microbiological data available.

Exclusion Criteria:

- Culture reports showing gram-positive organisms, fungi, or contaminants.
- Patients already on long-term antibiotics (>72 hours) before culture sampling.
- Incomplete medical records or missing susceptibility data.
- Repeated isolates from the same patient (only the first isolate included).

Data Collection: Clinical and demographic information was recorded for each patient, including age, gender, admission unit (ward/NICU/PICU), and suspected infection site. Specimens such as blood, urine, cerebrospinal fluid, tracheal aspirates, wound swabs, and sputum were collected under aseptic conditions and sent to the microbiology laboratory for processing. Gram-negative organisms were identified using standard biochemical tests and automated identification systems where available. Antimicrobial susceptibility testing (AST) was performed according to Clinical and Laboratory Standards Institute (CLSI) guidelines using the Kirby–Bauer disk diffusion method. Antibiotics tested included penicillins, cephalosporins, aminoglycosides, carbapenems, fluoroquinolones, β-lactam/β-lactamase inhibitor combinations, and colistin. The presence of ESBL, MDR, and carbapenem-resistant organisms (CROs) was confirmed using phenotypic detection methods. All laboratory findings were recorded along with clinical outcomes such as length of stay, antibiotic use, and need for intensive care.

Statistical Analysis: Data analysis was performed using SPSS version 20.0. Continuous variables such as age and duration of hospital staywere expressed as mean ± standard deviation (SD) and compared using independent t-tests. Categorical variables such as type of organism, antibiotic resistance patterns, ESBL prevalence, MDR status, and carbapenem resistance were presented as frequencies and percentages and analyzed using the Chi-square test or Fisher's exact test, depending on data distribution. A p-value < 0.05 was considered statistically significant.

RESULTS

Data were collected from 220 patients, average age of the entire cohort was 3.2 ± 3.8 years, but children in NICU/PICU were much younger (1.1 ± 1.4 years) compared to those in the ward (5.3 ± 4.2 years, $p < 0.001$). Hospital stay was significantly longer in the NICU/PICU group (12.1 ± 4.9 days) versus the ward (6.8 ± 2.9 days, $p < 0.001$). Comorbidities were more frequent in severe cases (43.6%) than in ward patients (21.8%, $p = 0.001$). Prior antibiotic exposure was also higher in the NICU/PICU group (55.5%) compared with ward children (31.8%, $p = 0.001$).

Among the 220 gram-negative isolates, E. coli was the most common organism (38.6%), but its distribution differed significantly across settings: it was more common in the ward (51.8%) than in NICU/PICU (25.4%, $p < 0.001$). Conversely, Pseudomonas aeruginosa (20.0%) and Acinetobacter (16.3%) were far more prevalent in the NICU/PICU group compared to the ward (9.1% and 5.5%, respectively, $p < 0.05$).

Resistance to commonly used antibiotics was substantially higher in the NICU/PICU group. Third-generation cephalosporin resistance was highest overall at 68.2%, rising to 79.1% in NICU/PICU versus 57.3% in the ward ($p < 0.001$). Fluoroquinolone resistance followed a similar trend (60.9% vs. 44.5%, $p = 0.01$). Aminoglycoside resistance was 49.1% in NICU/PICU and 34.5% in the ward ($p = 0.02$). Carbapenem resistance was notably elevated in NICU/PICU (27.3%) compared with ward patients (10.0%, $p < 0.001$).

The prevalence of ESBL-producing strains was 41.8%, but disproportionately higher in NICU/PICU (50.9%) than ward patients (32.7%, $p = 0.006$). Multidrug-resistant (MDR) isolates were also more common among severe cases (43.6%) compared to the ward (30.9%, $p = 0.05$). Carbapenem-resistant organisms showed a striking difference: 27.3% in NICU/PICU versus 10.0% in the ward ($p = 0.001$). Colistin resistance remained low at 4.5%, with no statistical significance.

The need for oxygen therapy was 53.6% in NICU/PICU compared to 17.3% in ward patients ($p < 0.001$). Mechanical ventilation was required in 32.7% of NICU/PICU children but only 4.5% in the ward ($p < 0.001$). Septic shock occurred in 21.8% of severe cases versus 3.6%in the ward ($p < 0.001$). Prolonged hospital stay (>10 days) was more common in NICU/PICU (50.9%) than in the ward (14.5%, $p < 0.001$). Mortality was also significantly higher in NICU/PICU (13.6%) compared to the ward (1.8%, $p = 0.003$).

Table 1: Baseline Demographic and Clinical Characteristics (n = 220)

Variable	Total (n = 220)	NICU/PICU Group (n = 110)	Ward Group (n = 110)	p-value
Age (years), mean ± SD	3.2 ± 3.8	1.1 ± 1.4	5.3 ± 4.2	<0.001*
Male gender, n (%)	128 (58.2%)	67 (60.9%)	61 (55.5%)	0.41
Length of hospital stay (days), mean ± SD	9.4 ± 4.6	12.1 ± 4.9	6.8 ± 2.9	<0.001*
Presence of comorbidities, n (%)	72 (32.7%)	48 (43.6%)	24 (21.8%)	0.001*
Prior antibiotic use, n (%)	96 (43.6%)	61 (55.5%)	35 (31.8%)	0.001*
Site of infection (Respiratory/Urinary/Blood/Other)	84/66/48/22	55/18/28/9	29/48/20/13	<0.001*

Table 2: Distribution of Gram-Negative Organisms

Organism	Total (n = 220)	NICU/PICU (n = 110)	Ward (n = 110)	p-value
E. coli	85 (38.6%)	28 (25.4%)	57 (51.8%)	<0.001*
Klebsiella spp.	58 (26.3%)	34 (30.9%)	24 (21.8%)	0.13
Pseudomonas aeruginosa	32 (14.5%)	22 (20.0%)	10 (9.1%)	0.02*
Acinetobacter spp.	24 (10.9%)	18 (16.3%)	6 (5.5%)	0.01*
Enterobacter spp.	21 (9.7%)	8 (7.3%)	13 (11.8%)	0.26
Polymicrobial isolates	10 (4.5%)	7 (6.4%)	3 (2.7%)	0.20

Table 3: Antibiotic Resistance Patterns (%) to Major Drug Classes

Antibiotic Class	Total Resistance (%)	NICU/PICU Group	Ward Group	p-value
Third-gen cephalosporins	68.2%	79.1%	57.3%	<0.001*
Fluoroquinolones	52.7%	60.9%	44.5%	0.01*
Aminoglycosides	41.8%	49.1%	34.5%	0.02*
Piperacillin-tazobactam	36.4%	44.5%	28.2%	0.01*
Carbapenems	18.6%	27.3%	10.0%	<0.001*
Colistin	4.5%	7.3%	1.8%	0.08

Table 4: Prevalence of ESBL, MDR, and Carbapenem Resistance

Resistance Type	Total (n = 220)	NICU/PICU (n = 110)	Ward (n = 110)	p-value
ESBL-producing strains	92 (41.8%)	56 (50.9%)	36 (32.7%)	0.006*
MDR isolates	82 (37.2%)	48 (43.6%)	34 (30.9%)	0.05
Carbapenem-resistant GN bacteria	41 (18.6%)	30 (27.3%)	11 (10.0%)	0.001*
Colistin-resistant isolates	10 (4.5%)	7 (6.4%)	3 (2.7%)	0.20

Table 5: Clinical Outcomes of Infected Children

Outcome	Total (n = 220)	NICU/PICU (n = 110)	Ward (n = 110)	p-value
Need for oxygen therapy	78 (35.5%)	59 (53.6%)	19 (17.3%)	<0.001*
Need for mechanical ventilation	41 (18.6%)	36 (32.7%)	5 (4.5%)	<0.001*
Septic shock	28 (12.7%)	24 (21.8%)	4 (3.6%)	<0.001*
Length of stay >10 days	72 (32.7%)	56 (50.9%)	16 (14.5%)	<0.001*
Mortality	17 (7.7%)	15 (13.6%)	2 (1.8%)	0.003*

DISCUSSION

This paper presents the overall description of the dynamics of gram-negative bacterial infection antibiotic resistance in pediatric patients that discloses alarming statistics that have a substantial clinical value. The results indicate that critically ill children admitted to NICU/PICU had significantly greater burden of resisting organism, complication and poor clinical outcomes than children admitted to general pediatric wards. The demographic features of Table 1 present that children at a younger age, especially infants (mean age 1.1 + 1.4 years in NICU/PICU) were more severely infected, spend more time in hospital, and have a higher number of comorbid conditions. This trend is in line with past studies, which have also indicated the same fact that younger children have unsophisticated immune systems and are thus prone to serious gram-negative infections and extended hospital stay[10]. The high rate of the prior antibiotic use among NICU/PICU patients (55.5) also demonstrates the pressure of antimicrobial that similarly supports the selection of resistant strains, a tendency that is constantly replicated in the past literature[11]. Table 2 shows that E. coli was the most prevalent isolate over the entire sample (38.6), and mostly in ward patients (51.8). Pseudomonas aeruginosa, however, and Acinetobacter species were predominant in NICU/PICU cases (20.0 and 16.3, respectively), both of them being known hospital-acquired pathogens. This conforms to earlier studies, which more often than not, have reported such organisms to be the major causes of nosocomial infections in intensive care units as a result of their environmental persistence and resistance to disinfectants[12].

Table 3 of the patterns of antibiotic resistance indicated worrying proportions of resistance to the third generation cephalosporins (68.2%), fluoroquinolones (52.7%), and carbapenems (18.6%). The levels of resistance were considerably greater in NICU/PICU isolates, which proves that multidrug resistance develops under critical-care conditions. The results coincide with other studies, which had documented higher infection resistance rates in ICUs as a result of a high level of antibiotic exposure and high rates of invasive interventions[13]. The elevated resistance of NICU/PICU isolates to carbapenems (27.3%) is alarming in particular since carbapenems are typically the last-resort medication used in pediatric sepsis. Table 4 demonstrates that ESBL, MDR, and carbapenem-resistant strains are very common, supporting the issue of antimicrobial resistance growing more and more severe. Forty-nine percent of the isolates were found to produce ESBL, 37.2 percent MDR, and 18.6 percent carbapenem resistance. All these values are also reminiscent of the trends seen in prior studies, in which ESBL prevalence among children is frequently 3050 per cent, and MDR prevalence is more than 35 per cent in a tertiary setting[14]. The burden of resistance in NICU/PICU patients is considerably higher, which implies that antimicrobial stewardship interventions should be directed at the critical care environment. The poor clinical outcomes in Table 5 bring to light the actual clinical implications of resistant infections. The percentage of oxygen requirement (53.6%), mechanical ventilation (32.7%), septic shock (21.8%), and mortality (13.6) were significantly higher in NICU/PICU patients. These data represent the world tendencies which have been reported in the past studies, when resistant gram-negative infections are characterized by high morbidity, delaying recovery, and higher mortality among children due to the lack of medical options and quick deterioration of sepsis[15]. The cost of resistant organisms to the economy and healthcare can be highlighted with the long length of stay (>10 days) in 50% of NICU/PICU patients. Lastly, Table 6 antibiotic sensitivity pattern shows that despite the fact that some of the antibiotics are still effective, the sensitivity is much lower in NICU/PICU isolates. Meropenem with an overall sensitivity of 81.4 is one of the key agents but the lower efficacy in children, especially those who are critically ill (72.7), is a sign of increasing carbapenem resistance. Amikacin and piperacillin -tazobactam were moderately active, especially in the ward patients. Colistin had a high sensitivity of 95.5% which is aligned with other studies that have characterized colistin as one of the final agents that are always reliable with regard to acting on the extensively drug-resistant gram-negative bacteria[16]. The issue of high sensitivity to colistin has contributed to the continued relevance of colistin even though the effects of nephrotoxicity restrict its usage, particularly in children.

CONCLUSION

It is concluded that gram-negative bacterial infections among pediatric patients demonstrate a high burden of antimicrobial resistance, particularly in critically ill children admitted to NICU and PICU. Younger patients, those with comorbidities, and those previously exposed to antibiotics were more likely to develop infections with MDR, ESBL-producing, and carbapenem-resistant organisms. Critically ill children experienced significantly worse outcomes, including higher rates of mechanical ventilation, septic shock, prolonged hospitalization, and increased mortality. Although some antibiotics such as meropenem, amikacin, and colistin remained effective, their reduced sensitivity in severe cases highlights the narrowing therapeutic window.

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