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## Original Research Article

# Drug utilisation pattern among neonates admitted to a tertiary care neonatal intensive care unit: a prospective observational study

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## ABSTRACT

**Background:** Neonates in NICUs frequently require numerous medications because of severe illnesses and immature physiology. Drug utilization studies help identify prescribing trends and potential areas for enhancing rational pharmacotherapy. This research assessed drug utilization patterns among neonates in a tertiary care NICU, utilising World Health Organization (WHO) prescribing indicators.

**Methods:** A prospective study over eight months (May–December 2025) was conducted in a NICU at a tertiary hospital in Gujarat, India. Neonates receiving at least one therapeutic medication and meeting eligibility criteria were enrolled. Demographic, clinical data, prescribed medications, therapeutic classes, and antibiotic use were recorded. Prescribing practices were assessed using WHO indicators, and drugs classified via the WHO ATC system.

**Results:** A total of 302 neonates received 1581 prescribed medications, with an average of  $5.23 \pm 2.93$  drugs per encounter. Generic drugs made up 67.17%, and 79.32% of the medications were from the National List of Essential Medicines 2022. Antibiotics were prescribed in 85.10% of cases, and injections in all cases. Antibiotics represented the largest therapeutic category at 49.40%. The most frequently prescribed drugs were calcium gluconate (81.13%), piperacillin–tazobactam (73.51%), and gentamicin (66.89%). No significant differences were found between preterm and full-term neonates regarding the average number of medications, antibiotic use, or length of hospital stay.

**Conclusions:** The prescribing pattern reflected the clinical complexity of neonates requiring intensive care, with substantial use of antibiotics and supportive medications. Regular drug utilisation monitoring and antimicrobial stewardship may help promote rational and safe pharmacotherapy in NICUs.

**Keywords:** Drug utilisation study, Neonates, Neonatal intensive care unit, WHO prescribing indicators, Prescription pattern, Antibiotic utilisation

## INTRODUCTION

A neonate is a live-born infant within the first 28 days of life. This group is especially vulnerable due to immature organ systems and rapid physiological changes that influence their responses to medications.<sup>1</sup> Neonates admitted to neonatal intensive care units (NICUs) often need multiple drugs to treat critical conditions such as prematurity, sepsis, respiratory distress syndrome, and

birth asphyxia.<sup>2</sup> As a result, these infants are frequently exposed to several medications during their relatively brief hospital stay, highlighting the importance of rational prescribing.<sup>3</sup> Analysing drug use patterns in this setting provides valuable insights into prescribing practices, medication exposure, antibiotic administration, adherence to essential medicine guidelines, and potential areas for enhancing pharmacotherapy quality.<sup>4,5</sup> Neonatal treatment poses distinct challenges due to limited clinical evidence for this age group. Many medications are prescribed based

on experience or data from older children and adults.<sup>1</sup> Critically ill neonates often receive multiple drugs simultaneously, including antibiotics, IV fluids, respiratory medications, and other supportive therapies. Although these treatments are frequently lifesaving, ongoing review of prescribing practices is essential to ensure safe and appropriate medication use.<sup>6</sup> Previous research indicates that drug use patterns in NICUs differ significantly, influenced by patient characteristics, disease types, hospital protocols, resistance patterns, and local prescribing habits.<sup>7</sup> Antibiotics are the most frequently prescribed medications in most NICUs, owing to the high infection rates.<sup>8</sup> Utilising WHO prescribing indicators provides a standardised method to evaluate and compare prescribing practices across different hospitals.<sup>9</sup>

The problem of inappropriate antimicrobial use is particularly acute in NICUs. A recent meta-analysis of over 350,000 neonates provides compelling evidence that implementing Antimicrobial Stewardship Programs (ASPs) can significantly reduce the initiation and duration of antimicrobial therapy without increasing adverse events.<sup>10</sup> However, a 2025 national survey of Indian neonatologists found that despite 91% of institutions reporting ASP initiatives, there is significant variation in practice, with the use of sepsis screening tests often leading to prolonged antibiotic courses.<sup>11</sup> This highlights the gap between policy and practice, underscoring the need for ongoing local drug utilization studies like ours to guide effective stewardship.

Given the limited contemporary data from western Indian tertiary NICUs, the high antibiotic utilisation reported in previous studies, and the growing concern about antimicrobial resistance, we conducted this prospective observational study to evaluate drug utilisation patterns in our NICU using WHO core prescribing indicators. Specifically, we sought to address three questions: What is the current medication burden and prescribing quality in our NICU?; What therapeutic classes predominate, and do they align with essential medicines recommendations? and; Does gestational age predict medication exposure, or are other factors such as clinical diagnosis more influential? By answering these questions, we aimed to generate evidence to inform rational pharmacotherapy and antimicrobial stewardship in our setting.

## METHODS

### *Study design and setting*

This prospective observational study was conducted in the Neonatal Intensive Care Unit (NICU) of the Department of Pediatrics at Medical College and SSG Hospital, Vadodara, Gujarat, India, a tertiary-care teaching hospital and referral center providing comprehensive neonatal care for both inborn and outborn neonates. The study was conducted over eight months, from May 2025 to December 2025.

### *Study population*

All neonates admitted to the NICU during the study period who met the eligibility criteria were enrolled after obtaining written informed consent from their parents or legal guardians. Neonates who received at least one medication during their NICU stay were included. Neonates with major congenital anomalies, those admitted for less than 48 hours, those receiving only prophylactic interventions (vitamin K, vaccines, prophylactic eye medication) those receiving blood or blood products, those receiving intravenous fluids without any therapeutic medications, and those discharged against medical advice before completion of treatment were excluded from the study.

### *Sample size*

The minimum sample size was calculated using the single-population proportion formula,  $n = Z^2P(1-P)/d^2$ , with a prevalence of 25%, a 95% confidence level, and a 5% absolute precision. The resulting minimum sample size was 288 neonates. Consecutive sampling was used, and eligible neonates were enrolled consecutively until the calculated sample size was achieved. A total of 302 neonates were enrolled in the study.

### *Data collection*

Demographic characteristics, maternal details, clinical diagnoses, duration of hospital stay, and survival status were recorded using a predesigned case record form. Details of all prescribed medications, including generic name, dosage form, dose, route, frequency, duration, and indication, were collected prospectively until discharge or transfer from the NICU. All prescribed medications were classified according to the WHO Anatomical Therapeutic Chemical (ATC) Classification System using the 2025 edition.<sup>12</sup>

### *Drug utilization assessment*

Drug utilisation was evaluated using the World Health Organization (WHO) core prescribing indicators, (Average number of drugs per encounter, percentage prescribed by generic name, percentage of encounters with an antibiotic, percentage with an injection) with prescribing from National Essential Medicines List (NLEM) 2022<sup>13</sup> additionally addressed as an institutionally relevant indicator.<sup>9</sup> The frequency of use of different therapeutic classes and the most commonly prescribed medications was also analysed.

### *Ethical issues*

The study protocol was approved by the Institutional Ethics Committee (Approval No. IECBHR/Certi/6/84-2025) before the study commenced. Written informed consent was obtained from the parents or legal guardians of all enrolled neonates before data collection.

## Statistical analysis

Data were entered into Microsoft Excel and analysed using jamovi (version 2.6), an open-source statistical software (the jamovi project, 2025). Continuous variables were reported as mean±standard deviation (SD) or median, as appropriate. Categorical variables were summarized as frequencies and percentages. Missing or incomplete data were reviewed by cross-checking with primary case record forms; if discrepancies remained unresolved, the affected data points were excluded from the specific analyses. The proportion of missing data for the main variables was minimal and did not affect the overall analysis. Comparisons between categorical variables were performed using the Chi-square test or Fisher's exact test, as appropriate. Continuous variables were compared using the independent-samples t-test or the Mann–Whitney U test, depending on the distribution of the data. A two-tailed  $p < 0.05$  was considered statistically significant.

## RESULTS

During the study, 605 neonates were admitted to the Neonatal Intensive Care Unit (NICU). Of these, 590 underwent eligibility screening. Fifteen neonates were not screened because eligibility assessment was not conducted for them. Among the 590 screened, 288 were excluded due to predefined exclusion criteria, leaving 302 neonates who met the eligibility criteria and were enrolled. All enrolled neonates completed follow-up, and data from all 302 participants were included in the final analysis.

### Demographic and clinical characteristics

Among 302 neonates, males accounted for 180 (59.6%) and females for 122 (40.4%). The mean birth weight was  $2168.4 \pm 677.3$  g, mean gestational age was  $36.3 \pm 3.4$  weeks, and mean age at admission was  $3.9 \pm 6.1$  days, indicating that most neonates were admitted during the early neonatal period. The mean duration of hospital stay was  $13.8 \pm 10.1$  days. Low birth weight (1500–2499 g) was observed in 43.4% of neonates, while 52.0% were term and 47.7% were preterm. Caesarean section was the predominant mode of delivery (64.2%) (Table 1).

### Clinical diagnoses

Among 634 recorded diagnoses, neonatal sepsis was the most common (179, 28.24%), followed by neonatal jaundice (161, 25.39%) and respiratory distress syndrome (99, 15.62%). Other diagnoses included transient tachypnoea of the newborn (41, 6.47%), low birth weight (38, 5.99%), hyaline membrane disease (35, 5.52%), hypoglycemia (33, 5.21%), asymptomatic hypoglycemia

(25, 3.94%), and meconium aspiration syndrome (23, 3.63%). The total percentage exceeds 100%, indicating that multiple diagnoses were recorded for the same neonate, a common occurrence in NICU studies. Neonatal sepsis, neonatal jaundice, and respiratory distress syndrome accounted for the majority of NICU diagnoses (Table 2).

### Prescription pattern and WHO prescribing indicators

A total of 1581 drugs were prescribed to all enrolled neonates in the study. The mean number of drugs per patient was  $5.2 \pm 2.9$ , with a median of 5. The number of drugs per patient ranged from 1 to 15. This evidence indicates that neonates admitted to the NICU were exposed to multiple medications during hospitalization. Overall, the majority of neonates received 4–6 drugs, accounting for 121 (40%) neonates. A total of 92 (30.5%) neonates received 1–3 drugs, while 62 (20.5%) received 7–9 drugs. More than nine drugs were prescribed to 27 (8.9%) neonates. Overall, approximately 29.5% of neonates received seven or more drugs during their NICU stay.

Assessment of prescribing practices using WHO core prescribing indicators revealed an average of  $5.23 \pm 2.93$  drugs per encounter. Of the 1581 drugs prescribed, 1062 (67.17%) were prescribed by their generic names. A total of 1254 (79.32%) drugs were prescribed from the National List of Essential Medicines (NLEM) 2022. Antibiotics were prescribed in 257 (85.10%) encounters, indicating high utilisation of antimicrobial agents in the NICU. Injectable formulations were prescribed in all encounters (302, 100%) (Table 3).

### Therapeutic classes

Antibiotics accounted for nearly half of all prescriptions (49.4%), followed by supportive medications (27.9%), cardiovascular drugs (10.8%), CNS drugs (4.2%), NSAIDs/analgesics (3.9%), and respiratory drugs (3.0%). Among antibiotics, piperacillin–tazobactam and gentamicin were the most frequently prescribed. Calcium gluconate, potassium chloride, sodium bicarbonate, and caffeine citrate were the most commonly prescribed supportive medications (Table 4 and Figure 1). Calcium gluconate was the most frequently prescribed drug, used in 245 (81.13%) neonates. Piperacillin–tazobactam (73.51%) and gentamicin (66.89%) were the most commonly prescribed antibiotics. Caffeine citrate was used in 73 (24.17%) neonates, while dobutamine was the most common cardiovascular drug (25.50%). Overall, calcium gluconate, piperacillin–tazobactam, and gentamicin were the three most frequently prescribed drugs in the NICU (Figure 2).

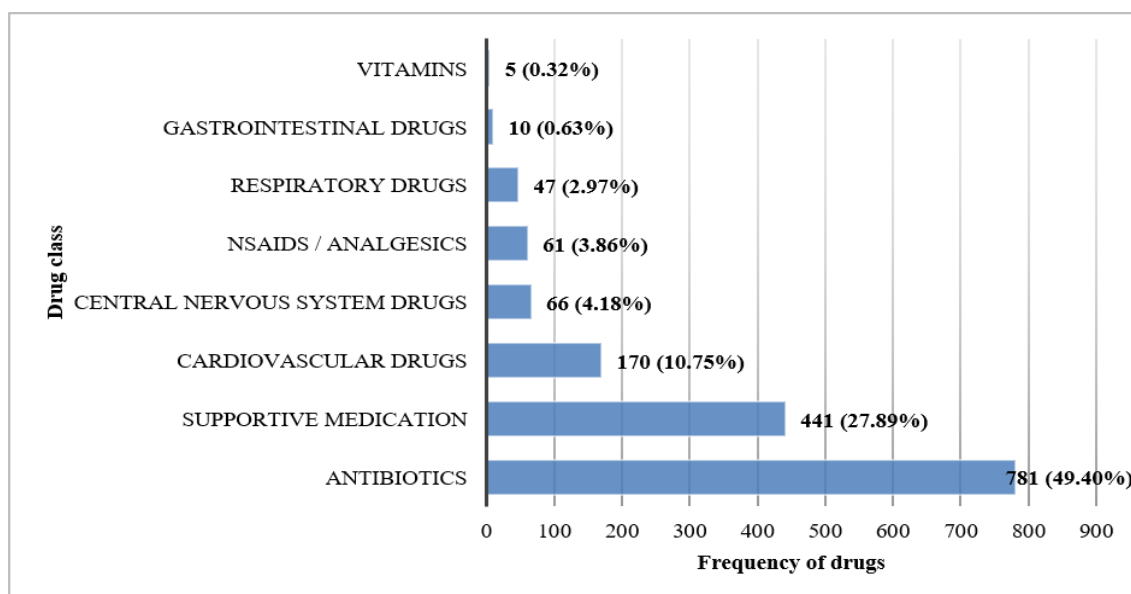


**Figure 1: Distribution of prescribed drugs by therapeutic class.**

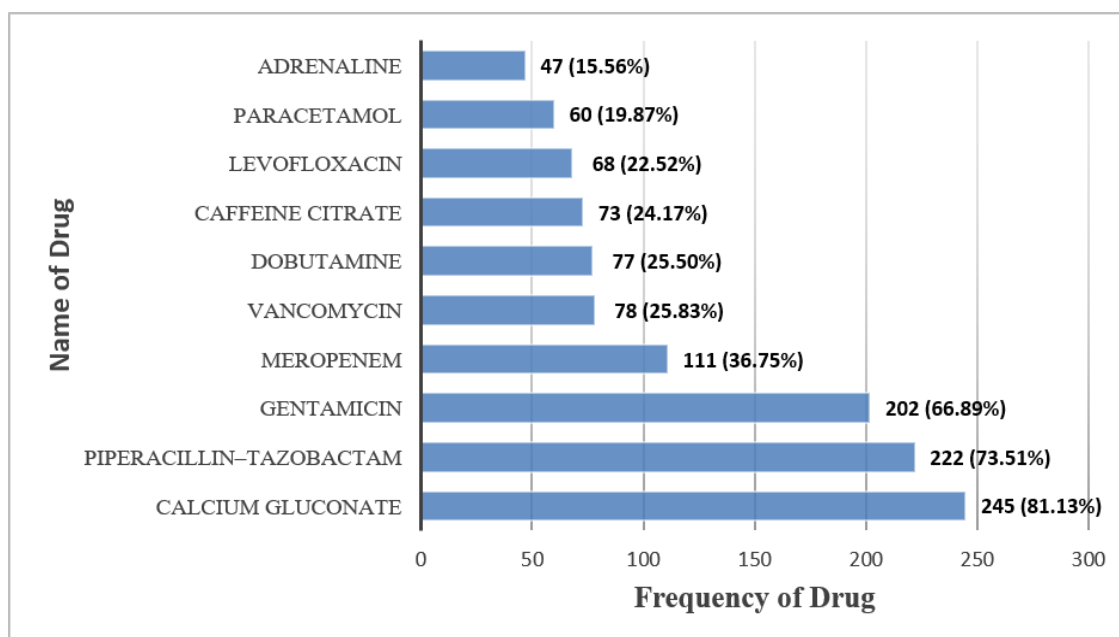


**Figure 2: Top 10 prescribed drugs in neonates.**

### ***Antibiotic utilisation pattern***

Of the 302 neonates included in the study, 257 (85.10%) received at least one antibiotic during their NICU stay, whereas 45 (14.90%) did not receive any antibiotic therapy. The mean number of antibiotics prescribed per patient was  $2.66 \pm 1.70$ . The maximum number of antibiotics prescribed to a single neonate was eight. These findings indicate high utilisation of antimicrobial agents in the NICU (Table 5).

Among the 781 antibiotics prescribed during the study period, piperacillin-tazobactam was the most frequently prescribed antibiotic, accounting for 222 (28.43%)

prescriptions. Gentamicin was the second most commonly prescribed antibiotic, with 202 (25.86%) prescriptions, followed by meropenem with 111 (14.21%) prescriptions. Vancomycin and levofloxacin accounted for 78 (9.99%) and 68 (8.71%) prescriptions, respectively. Piperacillin-tazobactam and gentamicin together constituted more than half of all antibiotics prescribed, indicating their predominant role in empirical and targeted antimicrobial therapy in the NICU. The most commonly prescribed antibiotic combination was piperacillin-tazobactam plus gentamicin ( $n=201$ ). Other frequently used combinations were piperacillin-tazobactam plus meropenem ( $n=84$ ), meropenem plus vancomycin ( $n=76$ ), and gentamicin plus meropenem ( $n=71$ ) (Table 6).

**Clinical outcome**

Among all neonates in the study, 217 (71.9%) showed clinical improvement and were discharged. 11 (3.6%) were referred to higher centers for further care, and 29

(9.6%) left against medical advice (LAMA). Deaths were recorded in 45 neonates, accounting for 14.9% of the total, which is the overall mortality rate observed in the study population.

**Table 1: Baseline demographic and clinical characteristics (n=302).**

| Characteristics         | N (%) / Mean±SD |
|-------------------------|-----------------|
| Male sex                | 180 (59.6)      |
| Birth weight (g)        | 2168.4±677.3    |
| <1500 g                 | 57 (18.9)       |
| 1500–2499 g             | 131 (43.4)      |
| ≥2500 g                 | 114 (37.7)      |
| Gestational age (weeks) | 36.3±3.4        |
| Pre-term                | 144 (47.7)      |
| Term                    | 157 (52.0)      |
| Post-term               | 1 (0.3)         |
| Caesarean delivery      | 194 (64.2)      |
| Vaginal delivery        | 106 (35.1)      |
| Instrumental delivery   | 2 (0.7)         |
| Age at admission        | 3.9 ± 6.1       |
| Hospital stay           | 13.8 ± 10.1     |

**Table 2: Distribution of clinical diagnoses among enrolled neonates (n=634).**

| Diagnosis                       | N (%)        |
|---------------------------------|--------------|
| Neonatal sepsis                 | 179 (28.24%) |
| Neonatal jaundice               | 161 (25.39%) |
| Respiratory distress syndrome   | 99 (15.62%)  |
| Transient tachypnoea of newborn | 41 (6.47%)   |
| Low birth weight                | 38 (5.99%)   |
| Hyaline membrane disease        | 35 (5.52%)   |
| Hypoglycaemia                   | 33 (5.21%)   |
| Asymptomatic hypoglycaemia      | 25 (3.94%)   |
| Meconium aspiration syndrome    | 23 (3.63%)   |

\*Percentages are based on the total number of recorded diagnoses because multiple diagnoses were recorded for individual neonates.

**Table 3: WHO core prescribing indicators and NLEM 2022 prescribing.**

| WHO prescribing indicator                                                  | Value         |
|----------------------------------------------------------------------------|---------------|
| Average number of drugs per encounter                                      | 5.23±2.93     |
| Drugs prescribed by generic name                                           | 1062 (67.17%) |
| Drugs prescribed from the National List of Essential Medicines (NLEM) 2022 | 1254 (79.32%) |
| Encounters with antibiotics prescribed                                     | 257 (85.10%)  |
| Encounters with injections prescribed                                      | 302 (100%)    |

**Comparison between preterm and term neonates**

The mean number of drugs prescribed was 5.26 among preterm neonates and 5.13 among term neonates. Similarly, the mean number of antibiotics prescribed was 2.62 and 2.69 among preterm and term neonates,

respectively. The mean duration of hospital stay was 13.75 days in preterm neonates and 13.91 days in term neonates. No, statistically significant differences were observed between preterm and term neonates in the mean number of drugs prescribed ( $p=0.687$ ), mean number of antibiotics prescribed ( $p=0.700$ ), or mean duration of hospital stay ( $p=0.891$ ) (Table 7).

**Table 4: Distribution of drugs according to therapeutic class.**

| Drug Class                   | Frequency   | Percentage  |
|------------------------------|-------------|-------------|
| Antibiotics                  | 781         | 49.40%      |
| Supportive medications       | 441         | 27.89%      |
| Cardiovascular drugs         | 170         | 10.75%      |
| Central nervous system drugs | 66          | 4.18%       |
| NSAIDs / Analgesics          | 61          | 3.86%       |
| Respiratory drugs            | 47          | 2.97%       |
| Gastrointestinal drugs       | 10          | 0.63%       |
| Vitamins                     | 5           | 0.32%       |
| <b>Total</b>                 | <b>1581</b> | <b>100%</b> |

\* Following ATC classification, drugs were grouped into clinically relevant therapeutic classes for descriptive analysis.

**Table 5: Antibiotic utilisation and most commonly prescribed antibiotics**

| Parameters                            | Value           |
|---------------------------------------|-----------------|
| Patients receiving antibiotics        | 257             |
| Mean antibiotics per patient $\pm$ SD | 2.66 $\pm$ 1.70 |
| Maximum antibiotics prescribed        | 8               |
| Most commonly prescribed antibiotics  |                 |
| Piperacillin–Tazobactam               | 222 (28.43 %)   |
| Gentamicin                            | 202 (25.86 %)   |
| Meropenem                             | 111 (14.21 %)   |
| Vancomycin                            | 78 (9.99 %)     |
| Levofloxacin                          | 68 (8.71 %)     |

**Table 6: Top 10 most frequently prescribed drugs.**

| Drugs                   | Frequency | Exposure rate (%) |
|-------------------------|-----------|-------------------|
| Calcium Gluconate       | 245       | 81.13%            |
| Piperacillin–Tazobactam | 222       | 73.51%            |
| Gentamicin              | 202       | 66.89%            |
| Meropenem               | 111       | 36.75%            |
| Vancomycin              | 78        | 25.83%            |
| Dobutamine              | 77        | 25.50%            |
| Caffeine Citrate        | 73        | 24.17%            |
| Levofloxacin            | 68        | 22.52%            |
| Paracetamol             | 60        | 19.87%            |
| Adrenaline              | 47        | 15.56%            |

**Table 7: Comparison of drug utilisation between pre-term and term neonates.**

| Variables                    | Pre-term          | Term              | P value |
|------------------------------|-------------------|-------------------|---------|
| Mean drugs prescribed        | 5.26 $\pm$ 2.98   | 5.13 $\pm$ 2.88   | 0.687   |
| Mean antibiotics prescribed  | 2.62 $\pm$ 1.54   | 2.69 $\pm$ 1.49   | 0.700   |
| Mean duration of stay (days) | 13.75 $\pm$ 10.21 | 13.91 $\pm$ 10.05 | 0.891   |

## DISCUSSION

This prospective observational study offers a detailed assessment of drug use patterns among neonates admitted to a tertiary care neonatal intensive care unit (NICU), utilizing WHO prescribing indicators. The study identified neonatal sepsis, neonatal jaundice, and respiratory distress syndrome as the leading conditions requiring NICU

admission. Neonates were treated with multiple medications, with an average of 5.2 $\pm$ 2.9 drugs per patient, reflecting the complexity of pharmacotherapy in critically ill newborns. Nearly half of all prescribed medications were antibiotics, administered in 85.1% of encounters, highlighting the central role of antimicrobial therapy in neonatal care, consistent with numerous Indian and international studies.<sup>7,13</sup> Although most drugs were

prescribed from the National List of Essential Medicines (79.3%) and by generic names (67.2%), there is room to enhance adherence to rational prescribing practices, especially regarding generic medications. Calcium gluconate, piperacillin–tazobactam, and gentamicin were the most commonly prescribed drugs, indicating the combined need for supportive and empirical antimicrobial therapy. Additionally, no significant differences were found between preterm and term neonates concerning the number of drugs prescribed, antibiotic exposure, or length of hospital stay, suggesting similar prescribing patterns across these groups within the study.

The demographic profile of our cohort predominantly male (59.6%), with mean birth weight of  $2168.4 \pm 677.3$  g and mean gestational age of  $36.3 \pm 3.4$  weeks reflects the typical high-risk population requiring tertiary neonatal care. The higher proportion of male neonates aligns with several drug utilisation studies from India and other countries, indicating that this trend is common across neonatal intensive care units.<sup>15-17</sup> The predominance of male infants requiring care has been linked to their increased biological susceptibility to conditions such as respiratory distress syndrome, sepsis, and complications from prematurity. Additionally, socio-cultural factors affecting healthcare-seeking behavior in certain regions may lead to more male infants being admitted.

The substantial proportion of low-birth-weight (43.4%) and preterm (47.7%) infants highlights the ongoing challenge of prematurity and low birth weight in neonatal healthcare in India, consistent with earlier studies from tertiary NICUs.<sup>18,19</sup>

Neonatal sepsis, neonatal jaundice, and respiratory distress syndrome were the most common clinical conditions observed in this study. These findings align with earlier Indian research, where neonatal sepsis consistently was the primary reason for NICU admission and use of antibiotics.<sup>20,21</sup> The high prevalence of infectious and respiratory conditions in this study explains the widespread use of antibiotics and supportive medications, which made up most of the prescriptions. Therefore, the demographic and clinical profile of the study group reflects the typical disease spectrum seen in tertiary NICUs and offers a relevant context for understanding the patterns of drug use observed.

The average of  $5.23 \pm 2.93$  medications per neonate observed in our study represents a substantial medication burden that warrants careful interpretation. This figure is higher than the 3.57 drugs per neonate reported in a recent Indian study focusing specifically on neonates with sepsis, and higher than the 3.8–4.5 drugs per encounter reported in several other Indian NICUs.<sup>22,16-18</sup> The higher polypharmacy in our cohort likely reflects the inclusion of neonates with a broader range of clinical conditions not just sepsis and the intensive supportive care required for preterm and low-birth-weight infants. Polypharmacy is frequently unavoidable in neonatal intensive care due to the

presence of conditions such as prematurity, sepsis, respiratory issues, metabolic imbalances, and other co-occurring health problems that require multiple simultaneous treatments. Although the current medication exposure reflects the complexity of NICU cases, regular review of prescriptions is crucial to promote rational drug use and avoid unnecessary medications.

Using the WHO core prescribing indicators to evaluate prescribing practices offers an objective way to measure drug utilisation quality and compare different healthcare settings.<sup>9</sup> While this represents a majority of prescriptions, this rate is notably lower than the 78–91% generic prescribing reported in other Indian tertiary NICU studies.<sup>5,21-24</sup> This discrepancy is noteworthy because our institution is a government teaching hospital where generic prescribing is institutionally mandated. We hypothesize that this gap may reflect institutional prescribers' habits, availability of certain formulations with proprietary labels, documentation practices where brand names are recorded even when generic equivalents are available and lack of awareness about WHO guidelines for generic prescribing practices. This finding suggests that policy enforcement alone may be insufficient to achieve universal generic prescribing, and targeted educational interventions such as regular prescription audits and feedback to prescribers may be warranted to promote generic prescribing behavior.

This study also found that 79.3% of prescribed drugs were part of the National List of Essential Medicines (NLEM) 2022, showing notable adherence to evidence-based prescribing. This proportion is comparable to the 78–91% adherence reported in other Indian studies.<sup>16,19,21,22</sup> Essential medicines are chosen for their proven efficacy, safety, quality, and cost-effectiveness, forming the basis of rational pharmacotherapy. While this proportion is promising, full adherence may not always be possible in tertiary care NICUs, as critically ill neonates often need newer broad-spectrum antimicrobials, inotropic agents, and specialized supportive medications that may not be in the essential medicines list. Nevertheless, maximizing the use of essential medicines whenever clinically appropriate should remain a key institutional goal. The 100% rate of injection prescribing should be interpreted in the context of an inpatient NICU population, in which parenteral administration is frequently required because of critical illness, limited enteral tolerance, and the need for reliable drug delivery.

Antibiotics were prescribed in 85.1% of cases, with injectable forms used in all hospitalized neonates. The high antibiotic utilization may partly reflect the substantial burden of suspected or documented neonatal infection in the study population. This prescribing pattern aligns with other studies in India and internationally.<sup>18,25-28</sup> While a 2025 national survey found that most Indian institutions report having antimicrobial stewardship initiatives, the impact of these programs on clinical practice may be limited, with fewer than 10% of clinicians willing to discontinue antibiotics by 72 hours based on clinical

improvement alone.<sup>11</sup> This suggests that our observed antibiotic use is not just a local phenomenon but reflects a national pattern driven by diagnostic uncertainty and reliance on sepsis screening tests, rather than a lack of awareness of stewardship principles. In light of these findings, the implementation of a formal antimicrobial stewardship program in our NICU is a critical next step. The effectiveness of such programs in reducing unnecessary antibiotic exposure in neonates is now supported by high-level evidence.<sup>10</sup> The universal use of injectables is typical in critically ill NICU patients, as parenteral administration ensures quick drug delivery, reliable bioavailability, and accurate dosing- especially since neonates often cannot tolerate enteral therapy. These findings differ from prescribing patterns reported by various Indian tertiary care NICUs.<sup>17,19,23</sup> They also emphasize the importance of regular drug utilisation reviews, antimicrobial stewardship programmes, and adherence to evidence-based guidelines to optimize neonatal pharmacotherapy and minimise unnecessary antimicrobial use.

The distribution of therapeutic classes in our study antibiotics (49.4%), supportive medications (27.9%), cardiovascular drugs (10.8%), CNS drugs (4.2%), and respiratory medications (3.0%) reflects the range of conditions encountered in the NICU. Similar findings have been reported in multiple Indian NICU drug utilisation studies, where anti-infective agents are consistently the most frequently prescribed class.<sup>18,25</sup> The considerable use of supportive medications such as calcium gluconate, potassium chloride, sodium bicarbonate, and caffeine citrate highlights the importance of correcting electrolyte imbalances, maintaining metabolic stability, and managing prematurity-related issues like apnoea of prematurity. Cardiovascular drugs, especially inotropic agents, were often used to treat neonatal shock and haemodynamic instability, while anticonvulsants like phenobarbitone and levetiracetam were administered to control neonatal seizures. Respiratory medications were less common, mainly indicated for apnoea of prematurity and bronchospasm. Overall, the distribution of therapeutic classes reflects the range of conditions encountered in the NICU and aligns with current neonatal treatment guidelines. However, the prominence of antibiotics underscores the need for ongoing monitoring of prescribing practices, regular prescription audits, and antimicrobial stewardship programmes to ensure appropriate antibiotic use, improve treatment outcomes, and reduce the risk of antimicrobial resistance.

The predominance of piperacillin-tazobactam and gentamicin as the first-line empirical combination (used in 201/257 antibiotic-exposed neonates, 78.2%) reflects our institutional protocol for suspected early-onset sepsis. However, this combination raises two clinically significant concerns. First, the widespread use of piperacillin-tazobactam an antipseudomonal agent in the absence of microbiological confirmation suggests potential overuse of broad-spectrum therapy. Second, the concurrent use of

meropenem and vancomycin in 76 neonates (29.6%) indicates rapid escalation to second-line agents, which may reflect either appropriate response to clinical deterioration or a low threshold for escalation. Without microbiological susceptibility data a limitation of this study, we cannot determine which scenario predominates. Nonetheless, the 85.1% antibiotic exposure rate (range: 1-8 antibiotics per neonate) and the substantial use of combination therapy underscore the urgent need for systematic antimicrobial stewardship in our NICU.<sup>29</sup> We propose that empirical therapy should be regularly reviewed, with de-escalation or discontinuation based on culture results and clinical progress and implement strategies like antimicrobial stewardship, prepare institutional level evidence-based guidelines and regular conducting prescription audits.<sup>30,31</sup> There is clear evidence that stewardship interventions are effective. A recent study from a Kanpur NICU demonstrated that implementing an antimicrobial stewardship program, including a "No Antibiotic Zone," reduced antimicrobial utilisation by 42% and significantly shortened hospital stays without increasing mortality.<sup>32</sup> These findings confirm that our recommendation for a formal stewardship program is not only justified but has a proven evidence base within the Indian context.

Most neonates (71.9%) showed clinical improvement and were discharged, indicating positive outcomes in NICU. However, the 14.9% mortality rate observed in our cohort is higher than the 7-12% range reported in several Indian tertiary NICUs.<sup>19,21</sup> While this likely reflects the high acuity of our referral population evidenced by the predominance of sepsis (28.2%) and respiratory distress (15.6%) we believe it also raises questions about modifiable factors. Specifically, the substantial antibiotic burden (85.1% exposure) and high rate of combination therapy may contribute to adverse outcomes through mechanisms such as disruption of gut microbiome, increased risk of fungal sepsis, or nephrotoxicity, though causality cannot be established from this study. The 9.6% LAMA (left against medical advice) rate also warrants attention, as it may reflect socioeconomic barriers to prolonged hospitalization, a factor that is frequently overlooked in drug utilisation studies but has profound implications for treatment completion and outcomes. We recommend that future research in our setting include qualitative assessment of barriers to treatment adherence and exploration of the relationship between antimicrobial stewardship and clinical outcomes.

We found no significant differences in medication exposure or hospital stay between preterm and term neonates. This finding challenges the assumption that prematurity is the primary driver of medication burden in NICUs. We interpret this as evidence that, in our setting, clinical diagnosis particularly the high prevalence of neonatal sepsis in both groups may be a more powerful determinant of prescribing than gestational age itself. A significant finding from the Iranian study was that neonates with a gestational age of less than 32 weeks, a birth weight under 1500g, or an antibiotic course longer than seven days

had significantly higher consumption of Watch group antibiotics.<sup>33</sup> This provides a crucial context for our own comparison, which found no significant differences in medication exposure between preterm and term neonates. The discrepancy suggests that while preterm neonates are globally recognized as being at higher risk for receiving broad-spectrum therapy, in our setting, the high illness severity among term neonates primarily driven by conditions like neonatal sepsis may be the more influential factor driving prescribing decisions, effectively masking the gestational age-related differences observed elsewhere. Notably, the term neonates in our study had substantial illness severity as evidenced by diagnoses of sepsis, respiratory distress, and birth asphyxia, which may have offset the expected differences. Some studies align with these findings, while others show more medication use in preterm infants, possibly due to longer stays and more morbidity.<sup>16,24</sup> This observation has practical implications: risk-stratification models for medication exposure in NICUs should prioritize clinical diagnosis over gestational age alone. However, we acknowledge that our study was not powered to detect subgroup differences, and these findings warrant confirmation in larger cohorts.

A significant finding from the Iranian study was that neonates with a gestational age of less than 32 weeks, a birth weight under 1500g, or an antibiotic course longer than seven days had significantly higher consumption of Watch group antibiotics. This provides a crucial context for our own comparison, which found no significant differences in medication exposure between preterm and term neonates. The discrepancy suggests that while preterm neonates are globally recognized as being at higher risk for receiving broad-spectrum therapy, in our setting, the high illness severity among term neonates primarily driven by conditions like neonatal sepsis may be the more influential factor driving prescribing decisions, effectively masking the gestational age-related differences observed elsewhere.

### Limitations

Several limitations should be considered when interpreting our findings. First, as a single-centre study, our results may not be generalisable to other NICUs with different patient populations, protocols, or resources. Second, we did not assess the appropriateness of individual antibiotic prescriptions (e.g., concordance with culture results or de-escalation practices), which limits our ability to judge the quality of antimicrobial use. Third, we did not evaluate adverse drug events or medication errors, which are important safety endpoints in neonatal pharmacotherapy. Fourth, the study was conducted over eight months, and seasonal variations in disease patterns may affect prescribing. Finally, we did not adjust for disease severity in comparing preterm and term neonates, which may confound the observed similarities. Despite these limitations, our study provides a robust baseline for ongoing monitoring and stewardship efforts.

## CONCLUSION

This prospective observational study demonstrates a substantial medication burden and high antibiotic utilisation among neonates admitted to a tertiary care NICU. Although prescribing practices showed considerable use of generic medicines and drugs listed in the NLEM, the high use of antibiotics, particularly broad-spectrum and combination therapy, highlights the need for continued monitoring of antimicrobial prescribing. No significant differences were observed in medication exposure or hospital stay between preterm and term neonates, suggesting that clinical conditions and illness severity may have an important influence on prescribing patterns. The findings provide a useful baseline for strengthening antimicrobial stewardship, conducting regular prescription audits, and promoting evidence-based and rational drug use in neonatal care. Further multicentre studies incorporating disease severity, microbiological data, antibiotic appropriateness, and clinical outcomes are warranted to guide targeted stewardship interventions.

### Recommendations

Building on this baseline, we have identified three priority areas for future research and quality improvement in our NICU: a point-prevalence study of antibiotic appropriateness, incorporating microbiological data to distinguish empirical from culture-directed therapy; a qualitative study exploring factors contributing to LAMA (left against medical advice) and their impact on treatment outcomes; and implementation of an antimicrobial stewardship programme with pre- and post-intervention drug utilisation assessments to evaluate its impact on prescribing quality. Additionally, we plan to conduct a follow-up study in 2027 to assess whether the patterns observed here have changed over time, particularly in response to evolving antimicrobial resistance patterns.

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