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THE FIRST DAY LAST DEFENSE: EVALUATING THE IRRATIONAL USE OF ANTIBIOTICS IN NEONATAL INTENSIVE CARE UNITS (NICU)

Original Research

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ABSTRACT

Background: Antibiotics play a pivotal role in neonatal care, especially in Neonatal Intensive Care Units (NICUs), where newborns are highly susceptible to life-threatening infections such as sepsis. Despite their importance, antibiotics are frequently prescribed irrationally due to diagnostic uncertainty and fear of missing early infections. This irrational use not only disrupts neonatal microbial balance but also accelerates antimicrobial resistance (AMR), leading to long-term public health consequences.

Objective: To assess the patterns and prevalence of irrational antibiotic use in NICUs and identify clinical factors contributing to these practices.

Methods: A hospital-based, quantitative, cross-sectional study was conducted over a three-month period in the NICU of a public sector secondary care hospital. Data were retrospectively extracted from 180 neonates' medical records using a structured tool. A simple random sampling method was applied to ensure representative selection. Antibiotic use was evaluated against World Health Organization (WHO) guidelines and national neonatal protocols to determine rationality. Data analysis was performed using SPSS version 25, with descriptive statistics presented in frequencies and percentages, and chi-square tests applied to examine associations, considering $p < 0.05$ as statistically significant.

Results: Among 180 neonates, 48.8% received ampicillin + gentamicin, 22.2% were prescribed ceftriaxone, and 15.6% received meropenem. Only 13 neonates (7.2%) had blood cultures obtained prior to initiating antibiotics. Irrational antibiotic use was significantly more common in preterm neonates (57.1%, $p = 0.04$) and those who received antibiotic therapy beyond five days (70%, $p = 0.03$). Rational prescribing was strongly associated with the practice of sending cultures before treatment (60% rational vs. 40% irrational, $p = 0.01$).

Conclusion: The study highlights a high prevalence of irrational antibiotic use in NICUs, mainly driven by lack of culture diagnostics and unnecessarily prolonged therapy. Strengthening antimicrobial stewardship and improving diagnostic protocols are urgently needed to ensure safe and effective neonatal care.

Keywords: Anti-Bacterial Agents, Antimicrobial Stewardship, Drug Utilization Review, Infant, Newborn, Intensive Care Units, Neonatal Sepsis, Premature Birth.

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INTRODUCTION

Antibiotics have long been among the most vital tools in modern medicine, essential for reducing infectious disease-related mortality, particularly in critical care environments such as neonatal intensive care units (NICUs). In these specialized settings, vulnerable newborns—especially those born preterm or with low birth weight—are highly susceptible to infections, leading clinicians to often initiate antibiotic therapy within the first hours of life. This early administration is typically driven by the looming threat of neonatal sepsis, a severe and potentially fatal condition that remains a leading cause of neonatal death globally (1). However, while the instinct to act swiftly is rooted in concern for survival, it may also give rise to unintended consequences, including the widespread use of antibiotics without confirmed infections (2). The initial 24 hours of a neonate's life represent a crucial decision-making window. Empirical antibiotic therapy is frequently administered before microbiological confirmation due to the limited speed and sensitivity of current diagnostic tools. Blood cultures and other conventional investigations often fail to offer timely guidance, pushing clinicians toward a precautionary but indiscriminate use of antibiotics (3). These treatments, sometimes extended for days despite negative culture results and absent clinical signs of infection, may offer a sense of reassurance in the short term but contribute to long-term clinical challenges. These include the development of antimicrobial resistance (AMR), alterations in the neonatal microbiome, and heightened risks for conditions like necrotizing enterocolitis and invasive fungal infections (4).

This challenge is particularly pronounced in low- and middle-income countries (LMICs), where diagnostic infrastructure is often lacking, and standardized stewardship protocols are underdeveloped. In such environments, the misuse of antibiotics is not solely a function of medical necessity but also reflects systemic limitations and institutional cultures. Research indicates that between 50–70% of neonates in NICUs receive antibiotic treatment, frequently without a clear clinical indication (5,6). Overreliance on empirical treatment is compounded by factors such as limited laboratory capacity, staff shortages, and an ingrained clinical tendency to prioritize immediate intervention over diagnostic certainty. The dilemma is deeply complex—both ethically and logistically. Physicians are continually balancing the fundamental principle of "do no harm" against the very real danger of delayed treatment in sepsis cases. However, irrational antibiotic use has repercussions that extend beyond the individual patient. The emergence of multidrug-resistant organisms (MDROs) in NICUs, which are often densely populated and procedurally intensive environments, represents a mounting public health concern. Infections caused by these resistant strains are not only harder to treat but are associated with prolonged hospital stays and increased mortality (7,8). In addition, early exposure to broad-spectrum antibiotics can disrupt the natural development of an infant's gut microbiota, potentially affecting immune system maturation and predisposing the child to long-term health issues (9).

In response to these growing concerns, antimicrobial stewardship programs (ASPs) have been introduced to promote rational prescribing practices, focusing on appropriate initiation, timely de-escalation, and overall reduction in antibiotic exposure. High-income countries have reported encouraging outcomes following the implementation of ASPs in NICU settings, with evidence suggesting a decline in unnecessary antibiotic use without increased adverse outcomes. Nevertheless, translating these successes to resource-limited settings remains a formidable challenge. Local adaptation requires understanding specific institutional constraints, clinician behavior, and adherence barriers (10,11). Despite increased awareness, significant knowledge gaps persist regarding antibiotic use in neonatal care. The literature remains sparse on prescribing patterns, rationality of decision-making, and the clinical and psychological drivers that contribute to overtreatment in NICUs. These factors often stem not from negligence but from the immense pressure clinicians face in time-sensitive, high-stakes situations (12,13). As such, any solution must consider not only clinical guidelines and diagnostic algorithms but also the human factors shaping prescribing behavior. Given the urgency of the issue, it is imperative to investigate and understand the patterns of antibiotic use in NICUs and identify the clinical and systemic contributors to their irrational application. Therefore, the objective of this study is to evaluate the prevalence and nature of irrational antibiotic use in NICUs and to explore the clinical and institutional factors that drive such practices.

METHODS

A quantitative, cross-sectional study design was employed to investigate the prevalence and determinants of irrational antibiotic use in the Neonatal Intensive Care Unit (NICU) of a public sector secondary care hospital. The study was carried out over a three-month period

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and targeted neonates admitted to the NICU who were prescribed antibiotics during their hospitalization. The study population included all neonates admitted within the study timeframe; however, neonates with incomplete medical records or those who were transferred in or out of the unit before receiving any antibiotic treatment were excluded to ensure data consistency and reliability. A probability-based simple random sampling technique was utilized to draw a representative sample. From the total number of eligible neonates admitted during the study period, 180 participants were selected using a random number generator. The sample size was calculated using prevalence estimates from prior studies on neonatal antibiotic use in similar healthcare settings, with parameters set at a 95% confidence level and a 5% margin of error. This approach ensured unbiased selection while maintaining statistical power. Data were collected retrospectively through thorough review of patient medical records, antibiotic administration charts, and NICU logbooks.

A structured data collection tool was designed specifically for this study to capture relevant variables, including demographic characteristics (age, gestational age, birth weight), clinical indicators (diagnosis, lab results), and detailed information related to antibiotic prescribing practices. Each antibiotic prescription was systematically evaluated for rationality using standardized criteria derived from the World Health Organization (WHO) guidelines for rational drug use, as well as nationally endorsed neonatal antibiotic protocols. Prescriptions were categorized as either rational or irrational based on the appropriateness of indication, antibiotic spectrum, dosage, route, and duration, in context with the patient's clinical status and microbiological findings. Data were entered into Microsoft Excel and subsequently analyzed using SPSS version 25. Descriptive statistics, such as frequencies and percentages, were used to summarize categorical variables. To determine associations between antibiotic use and relevant clinical variables, chi-square tests were applied, and a p-value of less than 0.05 was considered statistically significant. Ethical approval for the study was obtained from the hospital's Institutional Review Board (IRB). As the study utilized retrospective data from existing records, informed consent was not required from the patients' guardians; however, data confidentiality and patient anonymity were strictly maintained throughout the research process in accordance with ethical standards.

RESULTS

The findings from this cross-sectional analysis revealed several critical insights into antibiotic prescribing practices in the NICU. A total of 180 neonates were included, of whom 41.7% were term (≥37 weeks gestation), 38.9% late preterm (32–36 weeks), and 19.4% extremely or very preterm (<32 weeks). In terms of birth weight distribution, 45.6% weighed between 1500–2499 grams, 22.2% were under 1500 grams, and 32.2% had normal birth weight (≥2500 grams). The male-to-female ratio was nearly balanced, with males accounting for 54.4% and females for 45.6% of the cohort. Regarding mode of delivery, 56.7% of neonates were born via cesarean section and 43.3% via vaginal birth. The most common admitting diagnosis was respiratory distress (36.1%), followed by birth asphyxia (23.3%), neonatal sepsis (21.1%), and other conditions including hypoglycemia and complications of prematurity (19.5%). Apgar scores recorded at 5 minutes post-delivery showed that 60% of neonates had scores between 7–10, indicating relatively stable early postnatal status, whereas 33.3% scored between 4–6, and 6.7% had critical scores of 0–3. A significant gap in diagnostic practices was observed, with only 7.2% of neonates having blood cultures sent before antibiotic initiation, and 92.8% receiving antibiotics without prior culture testing.

Empirical antibiotic use was common, with the combination of ampicillin and gentamicin prescribed in 48.8% of cases. Broad-spectrum agents were also frequently used, with ceftriaxone administered in 22.2%, meropenem in 15.6%, and vancomycin in 6.7% of neonates. Other antibiotic regimens accounted for the remaining 6.7%. The widespread use of broad-spectrum antibiotics, even in the absence of culture-confirmed infection, raised concerns about potential overtreatment. Evaluation of antibiotic rationality revealed that only 42.9% of prescriptions in preterm neonates were rational compared to 57.1% that were irrational, a statistically significant association ($p = 0.04$). Similarly, rational use was significantly more likely in cases where blood cultures were sent prior to therapy initiation (60% vs. 40%, $p = 0.01$). Prolonged antibiotic courses exceeding five days were associated with a higher rate of irrational use (70%, $p = 0.03$), indicating a trend toward unnecessary continuation of therapy. Although lower birth weight was more frequently associated with irrational prescribing, this relationship did not reach statistical significance ($p = 0.06$).

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Table 1: Demographic and Clinical Characteristics of Neonates (N = 180)

Variable	Category	Frequency (N)	Percentage (%)
Gestational Age	<32 weeks	35	19.4%
	32–36 weeks	70	38.9%
	≥37 weeks	75	41.7%
Birth Weight	<1500g	40	22.2%
	1500–2499g	82	45.6%
	≥2500g	58	32.2%
Sex	Male	98	54.4%
	Female	82	45.6%
Mode of Delivery	Caesarean Section	102	56.7%
	Vaginal Delivery	78	43.3%
Primary Diagnosis	Respiratory Distress	65	36.1%
	Birth Asphyxia	42	23.3%
	Sepsis	38	21.1%
	Other	35	19.5%
Apgar Score at 5 min	0–3	12	6.7%
	4–6	60	33.3%
	7–10	108	60.0%
Culture Sent	Yes	13	7.2%
	No	167	92.8%

Table 2: Patterns of Antibiotic Use in NICU (N = 180)

Antibiotic Regimen	Number Of Prescriptions	Percentage (%)
Ampicillin + Gentamicin	88	48.8%
Ceftriaxone	40	22.2%
Meropenem	28	15.6%
Vancomycin	12	6.7%
Others	12	6.7%

Table 3: Association Between Rationality of Antibiotic Use and Clinical Variables

Variable	Rational Use (%)	Irrational Use (%)	P-Value
Gestational Age	42.9%	57.1%	0.04
Birth Weight	40.2%	59.8%	0.06
Culture Sent	60.0%	40.0%	0.01
Duration >5 Days	30.0%	70.0%	0.03

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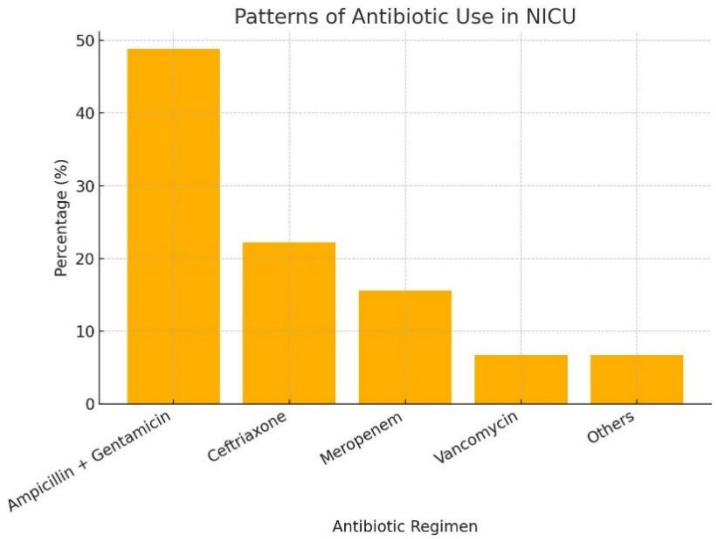

Figure 1 Patterns of Antibiotic Use in NICU

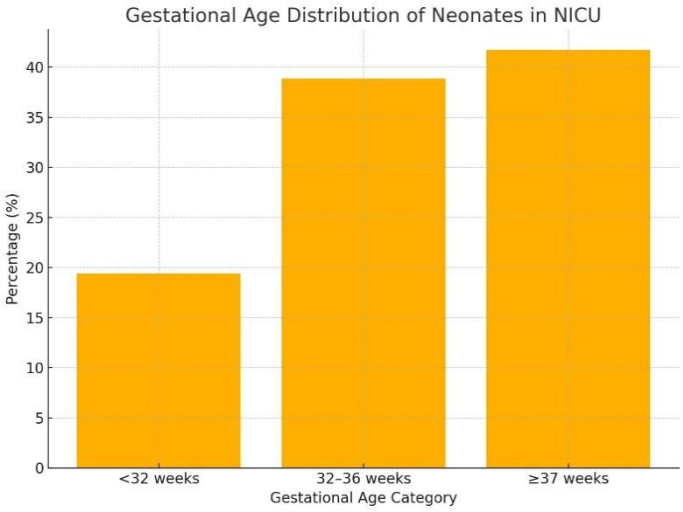

Figure 2 Gestational Age Distribution of Neonates in NICU

DISCUSSION

This study provides valuable insight into the patterns and clinical determinants of irrational antibiotic use in a Neonatal Intensive Care Unit (NICU) of a public sector secondary care hospital, contributing to the growing global discourse on antimicrobial stewardship in neonatal settings. The findings confirm widespread empirical antibiotic prescribing, often in the absence of culture confirmation, and a concerning reliance on broad-spectrum agents. These patterns are consistent with previous literature, particularly in low- and middle-income countries (LMICs), where diagnostic limitations, clinical uncertainty, and infrastructural constraints often shape prescribing behaviors (14,15). A key finding of this study was the extremely low rate (7.2%) of blood cultures being sent before antibiotic initiation, underscoring a significant diagnostic gap. This observation mirrors reports from various LMIC-based studies that have documented similar trends, attributing them to the unavailability or delayed turnaround of laboratory results (16,17). The high prevalence of empirical therapy, primarily involving ampicillin and gentamicin, reflects partial adherence to standard neonatal sepsis protocols. However, the frequent use of higher-generation antibiotics, such as ceftriaxone (22.2%) and meropenem (15.6%), raises concern. These agents, though life-saving in confirmed resistant infections, are often employed preemptively, contributing to antimicrobial resistance (AMR), disruption of the developing gut microbiome, and elevated risks of necrotizing enterocolitis and fungal infections in neonates (18,19).

This study adds to the evidence base by identifying clinical variables associated with irrational antibiotic use. A statistically significant association with lower gestational age ($p = 0.04$) suggests that prematurity may lead clinicians to adopt overly cautious prescribing practices. This aligns with prior studies where preterm infants were more frequently subjected to prolonged and empirically driven antibiotic regimens due to diagnostic uncertainty and perceived vulnerability (20). Similarly, the association between therapy durations exceeding five days and irrational use ($p = 0.03$) reflects the lack of timely review and de-escalation, a pattern well-documented in the literature (21). These results highlight systemic gaps in NICU antibiotic practices, where default continuation in the absence of clinical or microbiological justification may become normalized. Importantly, the significant association between sending cultures and rational antibiotic use ($p = 0.01$) reinforces the foundational role of diagnostic stewardship. These findings are consistent with international evidence demonstrating that structured stewardship programs—incorporating routine culture testing and biomarker-guided decision-making—can improve rational antibiotic prescribing without compromising neonatal outcomes (22,23). It suggests that strengthening diagnostic infrastructure and embedding culture-based protocols in NICU workflows could serve as pivotal strategies in addressing irrational prescribing patterns.

The implications of these findings are profound, particularly in the context of LMIC healthcare systems where resource constraints intersect with high infection burdens. There is an urgent need for the implementation of context-specific antimicrobial stewardship programs (ASPs) in NICUs. These programs must not only focus on guideline-based prescribing and diagnostic reinforcement but also

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provide training that addresses the clinical and psychological dimensions of decision-making in high-stakes neonatal care. Institutional policy revisions, capacity building, and routine monitoring of antibiotic use trends should be integral to such efforts. This study's strengths lie in its focus on a highly vulnerable patient population and its structured approach to defining and evaluating the rationality of antibiotic use against established international and national protocols. The use of random sampling minimized selection bias and enhanced the credibility of the findings. However, certain limitations must be acknowledged. Conducted in a single public sector facility, the findings may not be generalizable to other healthcare settings, especially tertiary or private institutions with differing clinical protocols and resource availability. The retrospective design inherently limits the ability to capture undocumented clinical reasoning or real-time decision-making, and there is potential for information bias due to reliance on medical record accuracy. Future research should aim to include multicenter settings, integrate prospective designs for real-time evaluation of prescribing behaviors, and assess the impact of targeted interventions on improving antibiotic use. Evaluating clinician knowledge, attitudes, and barriers to adopting stewardship practices could also offer insights into behavioral drivers of irrational use. A broader examination of antimicrobial resistance patterns linked to NICU prescribing practices would further contextualize the public health impact. In summary, the findings reinforce global concerns about the irrational use of antibiotics in neonatal care, particularly in resource-limited settings. The associations identified between clinical variables and irrational use offer direction for targeted interventions. Addressing diagnostic gaps, embedding stewardship principles, and supporting clinicians through education and policy reform are crucial steps toward safeguarding both neonatal health and antibiotic efficacy for future generations.

CONCLUSION

This study concludes that irrational antibiotic use remains a pervasive challenge in NICUs, largely fueled by diagnostic limitations, routine empirical prescribing, and unnecessarily extended treatment courses. These practices not only compromise the quality of neonatal care but also contribute to the growing threat of antimicrobial resistance. The findings underscore the pressing need for robust antimicrobial stewardship initiatives, better access to timely and accurate diagnostics, and adherence to evidence-based protocols. Addressing these issues is essential for promoting safer, more rational antibiotic use and ensuring improved health outcomes for vulnerable neonatal populations.

AUTHOR CONTRIBUTION

Author	Contribution
Bilal Mustafa	Substantial Contribution to study design, analysis, acquisition of Data Manuscript Writing Has given Final Approval of the version to be published
Abdul Razzaque Nohri*	Substantial Contribution to study design, acquisition and interpretation of Data Critical Review and Manuscript Writing Has given Final Approval of the version to be published
Sher Muhammad Nuhrio	Substantial Contribution to acquisition and interpretation of Data Has given Final Approval of the version to be published
Ahsan Ali Memon	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Hira Jamil	Contributed to Data Collection and Analysis Has given Final Approval of the version to be published
Asif Ali Soomro	Substantial Contribution to study design and Data Analysis Has given Final Approval of the version to be published

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