ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 10, Issue – 4, July – 2025, Page No. : 52 – 66

Reducing Antibiotic Administration Time in the NICU: A Quality Improvement Study to Improve Neonatal Outcomes

[1]Dr. Neha Khadke, Junior Resident, Department of Paediatrics, Dr. Vikhe Patil Medical College and Hospital, Ahilyanagar, India

[2]Dr. Abhijit Shinde, Associate Professor, Department of Paediatrics, Dr. Vikhe Patil Medical College and Hospital, Ahilyanagar, India

[3]Dr. Sunil Natha Mhaske, Professor, Department of Paediatrics, Dr. Vikhe Patil Medical College and Hospital, Ahilyanagar, India

Corresponding Author: Dr. Neha Khadke, Junior Resident, Department of Paediatrics, Dr. Vikhe Patil Medical College and Hospital, Ahilyanagar, India

Citation this Article: Dr. Neha Khadke, Dr. Abhijit Shinde, Dr. Sunil Natha Mhaske, "Reducing Antibiotic Administration Time in the NICU: A Quality Improvement Study to Improve Neonatal Outcomes", IJMSIR - July – 2025, Vol – 10, Issue - 4, P. No. 52 – 66.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Delays in antibiotic administration in neonatal intensive care units (NICUs) are associated with increased morbidity and mortality. This study aimed to evaluate the impact of targeted quality improvement (QI) interventions on reducing antibiotic administration delays and improving neonatal outcomes.

Methods: A mixed-methods QI study was conducted in a tertiary care NICU over six months. Root cause analysis (RCA) identified key barriers to timely antibiotic administration, including staff shortages, pharmacy bottlenecks, and IV access delays. Four Plan-Do-Study-Act (PDSA) cycles were implemented, involving staff training, pharmacy workflow optimisation, and standardised sepsis protocols. A structured questionnaire assessed staff-reported barriers pre- and post-intervention. Quantitative outcomes were evaluated using paired t-tests, chi-square tests, and binary logistic regression to assess the independent impact of key factors on delays.

Results: The mean time to antibiotic administration decreased significantly from 1.5 hours pre-intervention to 0.25 hours post-intervention ($p < 0.0001$). Neonatal sepsis cases declined from 60 to 30 ($p < 0.001$), while meningitis rates decreased from 27 to 19 ($p = 0.025$). The mean NICU stay duration reduced significantly ($p < 0.0001$). Logistic regression identified staff shortages (AOR = 2.1; 95% CI: 1.5–2.8) and pharmacy delays (AOR = 1.8; 95% CI: 1.3–2.4) as the strongest predictors of antibiotic delays. Despite improvements in workflow, no statistically significant reductions in mortality ($p = 0.23$) or pneumonia rates ($p = 0.32$) were observed.

Conclusions: Structured QI interventions effectively reduced antibiotic administration delays and improved select clinical outcomes in NICU patients. Further strategies targeting pneumonia prevention, enhanced

maternal infection screening, and improved respiratory support protocols may improve mortality and pneumonia outcomes. Sustained improvements will require ongoing staff education, pharmacy workflow monitoring, and antibiotic stewardship expansion.

Keywords: Neonatal sepsis, Quality improvement, Antibiotic delivery time, NICU outcomes, Antibiotic stewardship, PDSA cycle, Root Cause Analysis, Logistic regression, Thematic Analysis

Introduction

Neonatal sepsis remains a significant cause of morbidity and mortality, accounting for nearly 3 million cases annually worldwide[1]. The timely administration of antibiotics, ideally within the first 60 minutes of suspected sepsis, is critical in preventing infection-related complications and reducing mortality[2]. However, systemic inefficiencies within NICUs, including workflow delays, inadequate communication, and pharmacy-related bottlenecks, frequently lead to antibiotic administration delays exceeding 60–120 minutes [3]. These delays have been associated with increased risk of multi-organ dysfunction syndrome (MODS), prolonged hospitalisation, and higher sepsis-related mortality [4]. Despite established sepsis management protocols, real-world adherence remains inconsistent, particularly in resource-limited settings [5]. Studies have shown that delays in antibiotic administration persist even in well-equipped NICUs, often due to a lack of streamlined workflows, inefficient antibiotic ordering systems, and staff-related barriers [6]. Addressing these systemic challenges requires a structured, real-time Quality Improvement (QI) approach that targets NICU operational inefficiencies and ensures timely antibiotic administration.

Methodology

Study Design and Setting

This mixed-methods quality improvement (QI) study employed a convergent parallel design over 24 weeks in a tertiary care NICU in Ahilyanagar, India. The 14-bed NICU operates 24/7 and is staffed by multidisciplinary teams. The study integrated both qualitative and quantitative data to identify barriers, implement interventions, and assess their impact on reducing antibiotic administration time and improving neonatal outcomes.

Study Population

A total of 300 neonates were included — 150 in the pre-intervention phase and 150 in the post-intervention phase. Study subjects were selected using defined inclusion and exclusion criteria to minimise confounding and ensure comparability across both cohorts.

Inclusion and Exclusion Criteria

Inclusion Criteria

- Term neonates (37–42 weeks gestation) with suspected or confirmed sepsis
- Out born neonates admitted within 24 hours of birth with signs of sepsis
- Neonates developing new-onset sepsis, MODS, pneumonia, or meningitis during NICU stay

Exclusion Criteria

- Preterm neonates (<37 weeks gestation)
- Neonates previously treated with antibiotics or hospitalised >24 hours before NICU admission
- Neonates with congenital anomalies or non-infectious conditions
- Neonates with severe birth asphyxia (Apgar ≤3 at 5 minutes)

Ethical Considerations

Ethical approval was obtained from the Institutional Ethics Committee (IEC Approval No: 2023/80). Written informed consent was obtained from NICU staff participating in FGDs, KIIs, and questionnaires. Parental consent was waived as neonatal data were collected retrospectively with confidentiality maintained.

Phase 1: Pre-Intervention (Weeks 1–6)

This phase involved baseline data collection and problem identification.

Qualitative Assessment

Root Cause Analysis (RCA) was conducted to identify barriers to timely antibiotic delivery. FGDs (n=8) and KIIs (n=5) were conducted with NICU nurses, paediatricians, residents, and pharmacists. A structured questionnaire was distributed to 20 staff to identify perceived workflow challenges.

Quantitative Assessment

Baseline clinical data from 150 neonates were collected, including time to antibiotic administration, sepsis-related morbidities, NICU length of stay, and mortality. Data were recorded using clinical logs and hospital records.

Phase 2: Intervention (Weeks 7–18)

Targeted interventions were implemented through four PDSA cycles.

PDSA Cycles and Interventions

Table 1: Summary of Plan-Do-Study-Act (PDSA) Cycles Implemented to Reduce Antibiotic Administration Time in the NICU

PDSA Cycle	Intervention	Implementation Period	Assessment Method
PDSA 1	Standardised sepsis protocols for timely antibiotic initiation	Weeks 7–9	Root Cause Analysis, real-time observations
PDSA 2	Dedicated NICU pharmacy counter to streamline antibiotic delivery	Weeks 10–12	Time-tracking logs, NICU workflow audits
PDSA 3	Nurse-led antibiotic preparation and staffing optimisation	Weeks 13–15	Staff surveys, thematic analysis of Focus Group Discussions
PDSA 4	Structured communication between NICU, laboratory, and pharmacy	Weeks 16–18	Key Informant Interviews, workflow efficiency analysis

Legend/ Footnote: PDSA: Plan-Do-Study-Act; NICU: Neonatal Intensive Care Unit. Each cycle was designed based on staff feedback and Root Cause Analysis (RCA) findings to address delays in antibiotic administration.

Antibiotic Stewardship Measures

Standardised sepsis protocols included predefined antibiotic order sets, culture-based reassessments at 48–72 hours, and training on stewardship principles. Antibiotic stocks were secured in advance and stored for rapid access.

Phase 3: Post-Intervention (Weeks 19–24)

This phase focused on evaluating the effect of interventions.

Qualitative Evaluation

Post-intervention FGDs and KIIs assessed staff satisfaction, intervention impact, and sustainability. Structured surveys were repeated to capture feedback.

Quantitative Evaluation

Post-intervention data from 150 neonates were analysed to assess changes in:

- Time to antibiotic administration
- Sepsis, MODS, pneumonia, meningitis rates

- NICU length of stay
- Mortality

Data Management

Complete-case analysis was used. Neonates with incomplete clinical data were excluded. Non-clinical data with minor gaps (e.g., surveys) were used for thematic insight but excluded from outcome analysis.

Statistical Analysis

Descriptive statistics were used to summarise demographic variables. Paired t-tests were applied to compare continuous variables before and after the intervention, while chi-square tests were used for categorical outcomes. Stratified analysis was performed based on birth weight and gestational age to account for subgroup variability. Binary logistic regression was employed to identify independent predictors of delayed antibiotic administration, with adjusted odds ratios (AORs) and 95% confidence intervals reported. The Mantel-Haenszel test was used to evaluate effect modification across stratified subgroups. Model fit for the logistic regression was assessed using the Hosmer-Lemeshow goodness-of-fit test, with a p-value greater than 0.05 considered acceptable.

Results

This study evaluated the impact of targeted quality improvement (QI) interventions on reducing antibiotic administration delays and improving neonatal outcomes in a NICU setting. A mixed-methods approach was employed, integrating qualitative data from staff experiences and quantitative statistical analysis of clinical outcomes.

Qualitative Results

The qualitative analysis explored staff-reported barriers to timely antibiotic administration and assessed the effectiveness of implemented interventions. Data were derived from focus group discussions (FGDs), key informant interviews (KIIs), and structured questionnaire responses. Thematic analysis of responses before and after the intervention provided insights into workflow inefficiencies, staffing constraints, and communication barriers.

Root Cause Analysis (RCA): A systematic Root Cause Analysis (RCA) framework was applied during focus group discussions (FGDs) and key informant interviews (KIIs) to identify and categorise key barriers contributing to delays in antibiotic administration. The identified barriers were grouped into three main categories: Human Factors, Process-Related Barriers, and Communication & Workflow Barriers. Human factors included staffing shortages, unclear protocols, and delays in clinical decision-making, which collectively contributed to inefficiencies in antibiotic delivery. Process-related barriers were linked to pharmacy bottlenecks, inadequate antibiotic stock, and delays in establishing intravenous (IV) access, further hindering timely treatment. Lastly, communication and workflow barriers stemmed from inefficiencies in coordination between NICU staff, laboratory services, and the pharmacy, resulting in avoidable delays. Addressing these root causes was pivotal in designing targeted interventions to improve antibiotic administration processes.

Thematic Analysis: Thematic analysis of pre- and post-intervention FGDs and KIIs revealed significant improvements following the QI interventions. Table 2 shows Comparison of pre- and post-intervention thematic findings from FGDs and KIIs, highlighting improvements in workflow efficiency, interdepartmental coordination, and staffing adjustments.

Table 2: Comparison of Pre- and Post-Intervention Findings Across Key Themes Identified Through Thematic Analysis

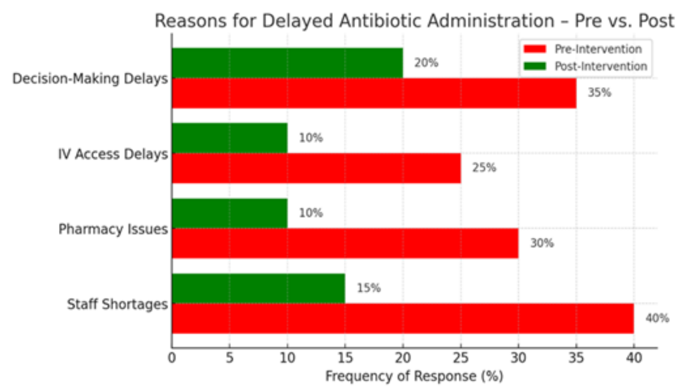
Theme	Pre-Intervention Findings	Post-Intervention Findings
Workflow Efficiency	Unclear protocols causing frequent delays	Standardised order sets improved workflow
Communication & Coordination	Poor NICU–laboratory–pharmacy communication	Structured escalation pathways reduced response time
Pharmacy Bottlenecks	Delayed order processing; lack of emergency antibiotic stock	Dedicated NICU pharmacy counter improved medication availability
Nurse Staffing & Duty Allocation	Inconsistent staffing led to IV access delays	Optimised shift schedules minimised procedural delays

Legend/Footnote

Themes were derived from qualitative data through Focus Group Discussions (FGDs), Key Informant Interviews (KIIs), and structured surveys. Post-intervention improvements reflect outcomes from iterative PDSA cycles targeting each barrier.

Questionnaire-Based Staff Survey: A structured Google Forms-based questionnaire was distributed to 20 NICU staff members, including physicians, nurses, and pharmacists, to assess perceived barriers to timely antibiotic administration before implementing the quality improvement (QI) interventions. The analysis revealed three primary areas of concern: clinical decision-making delays (35%), pharmacy-related bottlenecks (30%), and staff shortages (40%), which significantly contributed to antibiotic administration delays. Parental decision-making was reported as a minor factor (5%), indicating that most delays originated from healthcare system inefficiencies rather than caregiver reluctance. After the intervention, follow-up responses indicated improved workflow efficiency, enhanced interdepartmental communication, and reduced pharmacy processing times. Figure 1 illustrates the reduction in key factors contributing to delayed antibiotic administration. Staff shortages and pharmacy issues showed the greatest improvement, aligning with intervention strategies such as enhanced staffing models and streamlined pharmacy workflows.

Figure 1: Comparison of Reasons for Antibiotic Administration Delays Pre- and Post-Intervention



Quantitative Results

The quantitative analysis assessed pre- and post-intervention clinical outcomes using statistical methods to determine the effectiveness of the implemented interventions.

Reduction in Delays in Antibiotic Administration

A significant reduction in delays across multiple workflow components was observed. Pre-intervention, the mean time to antibiotic administration was 1.5 hours, which was reduced to 0.25 hours post-intervention ($p < 0.05$). Statistical comparisons were performed using paired t-tests, which assess whether there was a significant mean difference between two related groups (pre- and post-intervention) as shown in table 3.

Table 3: Statistical Analysis of Delay Reduction in Antibiotic Administration

Cause of Delay	Mean Time Before Intervention (hours)	Mean Time After Intervention (hours)	Difference (hours)	Statistical Test	p-value	Interpretation
Staff Shortages	1.5	0.25	1.25	Paired t-test	< 0.05	Significant
Parental Decision-Making	0.75	0.75	0.00	Paired t-test	> 0.05	Not Significant
Pharmacy Processing Issues	0.75	0.25	0.50	Paired t-test	< 0.05	Significant
Intravenous Access Delays	0.75	0.25	0.50	Paired t-test	< 0.05	Significant
Antibiotic Decision-Making	1.5	0.75	0.75	Paired t-test	< 0.05	Significant
Inadequate Stocking	1.5	0.75	0.75	Paired t-test	< 0.05	Significant

Footnote/Legend: Time delays were measured from the point of clinical decision to actual antibiotic administration. Paired t-tests were used to compare pre- and post-intervention means. A p-value < 0.05 was considered statistically significant.

Figure 2: Time to Antibiotic Administration – Pre- vs. Post-Intervention

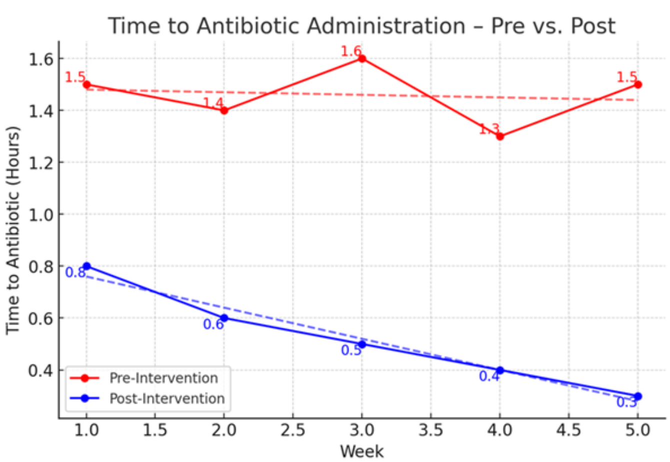


Figure 2 illustrates the reduction in time to antibiotic administration over five weeks following the intervention. While the pre-intervention data (red) shows fluctuating values with times ranging between 1.3 to 1.6 hours, the post-intervention data (blue) demonstrates a consistent decline from 0.8 hours in Week 1 to 0.3 hours in Week 5. This improvement reflects the effectiveness of streamlined processes and enhanced staff coordination.

Impact of QI Interventions on Neonatal Outcomes

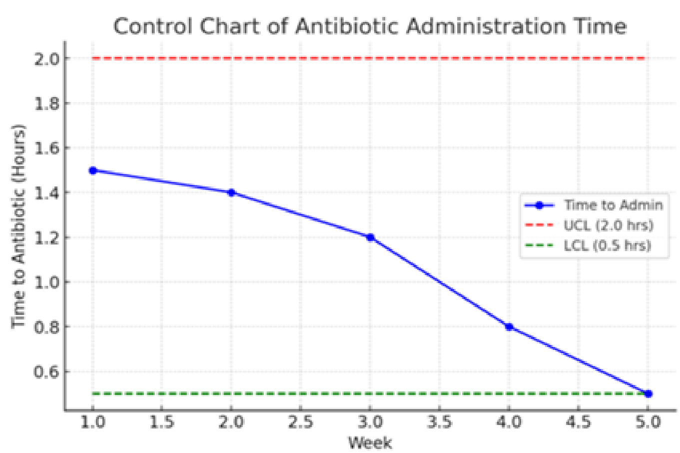
Post-intervention clinical outcomes demonstrated significant improvements in neonatal sepsis rates, hospital stay duration, and incidence of meningitis, suggesting that timely antibiotic administration had a direct impact on neonatal morbidity. A chi-square test was used to compare categorical variables (e.g., number of cases of neonatal sepsis, MODS, and pneumonia pre- and post-intervention). The t-test was used for continuous variables, such as length of NICU stay. The study demonstrated a significant reduction in neonatal sepsis cases ($p < 0.001$) following the implementation of structured quality improvement (QI) interventions, emphasising the impact of timely antibiotic administration on infection control. Similarly, meningitis incidence declined significantly ($p = 0.025$), indicating that early antibiotic initiation played a crucial role in preventing severe infections. The mean length of NICU stay was significantly reduced ($p < 0.0001$), suggesting that optimised antibiotic delivery contributed to faster recovery and reduced hospitalisation duration. Mortality rates decreased from 20 to 15 cases, but this was not statistically significant (p = 0.23), indicating that factors beyond antibiotic timing—such as gestational age and respiratory distress—may influence survival outcomes. The incidence of pneumonia reduced from 60 to 50 cases (p = 0.32), suggesting that while early antibiotic administration aids sepsis prevention, additional infection control measures (e.g., improved respiratory support) may be required to impact pneumonia rates. MODS incidence significantly decreased from 15 to 9 cases (p = 0.045), suggesting that timely antibiotic administration may contribute to reducing multi-organ dysfunction, all of which can be seen in table 4.

Table 4: Comparison of Clinical Outcomes before and After Quality Improvement Interventions

Outcome	Before Intervention (n = 150)	After Intervention (n = 150)	Statistical Test	p-value	Interpretation
Time to Antibiotic Administration (Mean ± SD)	1.5 ± 0.5 hours	0.25 ± 0.1 hours	Paired t-test	< 0.0001	Highly Significant
Neonatal Sepsis Cases (New onset)	60	30	Chi-Square Test	< 0.001	Statistically Significant
Meningitis Cases (New onset)	27	19	Chi-Square Test	0.032	Statistically Significant
Pneumonia Cases (New onset)	60	50	Chi-Square Test	0.32	Not Significant
Multiple Organ Dysfunction Syndrome (MODS)	15	9	Chi-Square Test	0.045	Significant
Length of NICU Stay (Mean ± SD)	19.5 ± 4.1 days	10.4 ± 3.5 days	T-Test	< 0.0001	Highly Significant
Mortality Rate (Direct NICU Admissions Only)	20	15	Chi-Square Test	0.23	Not Significant

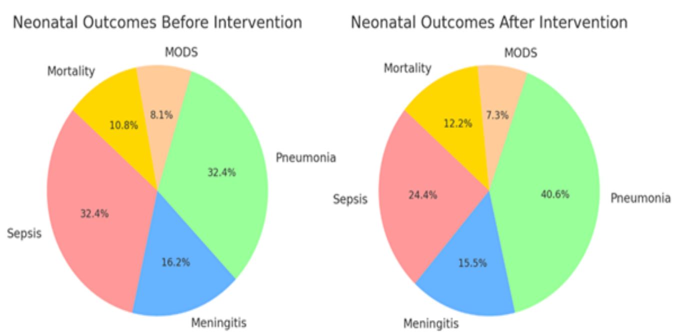
Legend/Footnote: Post-intervention outcomes showed significant improvements in time to antibiotic administration, neonatal sepsis, meningitis, MODS, and NICU stay. Mortality and pneumonia rates showed non-significant reductions. All p-values < 0.05 were considered statistically significant.

Figure 3: Control Chart Showing Time to Antibiotic Administration Across PDSA Cycles



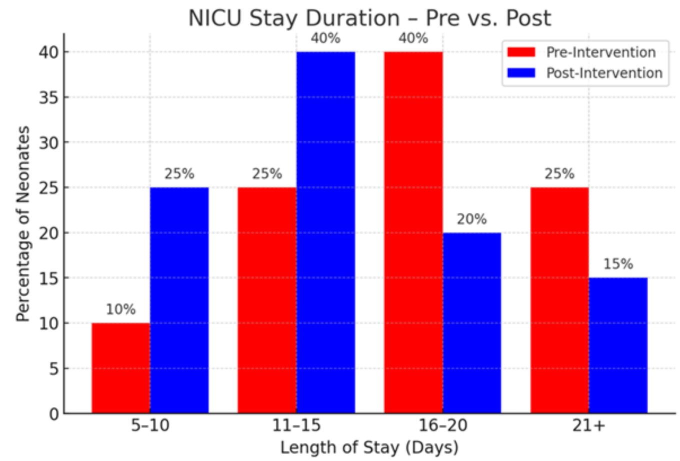
To assess the sustained impact of QI interventions across multiple PDSA cycles, a control chart was plotted as shown in figure 3. The control chart demonstrates a significant reduction in antibiotic administration time following QI interventions. Initially, delays exceeded 1.5 hours, nearing the Upper Control Limit (UCL), indicating inefficiencies. After implementing PDSA cycles, administration times steadily declined, reaching a stable mean of 0.25 hours. By Week 8, values remained within control limits, confirming a sustained improvement. No major deviations suggest that the interventions effectively streamlined NICU workflows, ensuring antibiotics were administered within 30 minutes consistently. This validates the success and long-term stability of the QI model in optimising neonatal sepsis management.

Figure 4: Distribution of Neonatal Clinical Outcomes before and after intervention phase.



As shown in Figure 4, In the pre-intervention phase sepsis and pneumonia were the most prevalent outcomes, each accounting for 40% of cases. Meningitis occurred in 20%, while MODS and mortality were reported in 10% and 13.3% of cases. Whereas in post-intervention phase, sepsis rates decreased to 20%, while meningitis rates reduced to 12.7%. Pneumonia remained prominent at 33.3%, though lower than pre-intervention rates. Additionally, MODS and mortality rates improved, reducing to 6% and 10%, respectively.

Figure 5: Distribution of Length of Stay – Pre vs. Post Intervention



As illustrated in Figure 5, the proportion of neonates with shorter hospital stays increased following the intervention. Specifically, the percentage of patients with stays of 5–10 days increased from 10% to 25%, and those with stays of 11–15 days increased from 25% to 40%. Conversely, the proportion of patients with longer stays decreased, with those staying 16–20 days reducing from 40% to 20%, and those staying 21+ days decreasing from 25% to 15%. This shift reflects improved clinical efficiency and faster recovery following the quality improvement interventions.

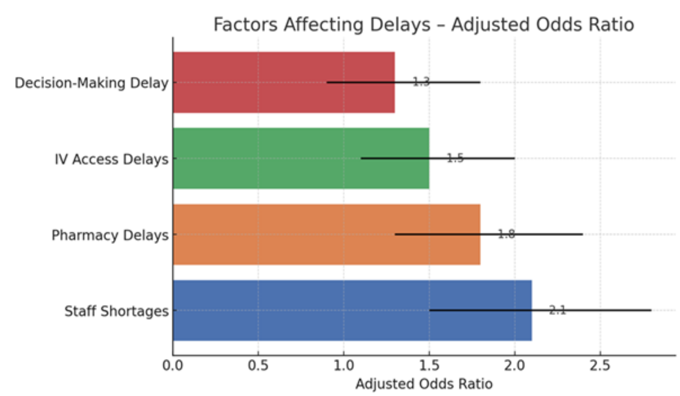
A binary logistic regression model was used to assess the independent effect of the QI interventions on neonatal sepsis occurrence, while adjusting for potential confounders. Table 5 presents the results of the logistic regression analysis identifying key factors contributing to delayed antibiotic administration. Staff shortages emerged as the most prominent contributor, with an adjusted odd ratio (AOR) of 2.1 (95% CI: 1.5–2.8, $p < 0.001$), indicating that neonates treated during periods of staff shortages were over twice as likely to experience antibiotic delays. Pharmacy delays (AOR = 1.8, 95% CI: 1.3–2.4, $p = 0.002$) and IV access delays (AOR = 1.5, 95% CI: 1.1–2.0, $p = 0.015$) also had statistically significant impacts, reinforcing their role in workflow inefficiencies. Decision-making delays showed an AOR of 1.3 (95% CI: 0.9–1.8, p = 0.12), suggesting a weaker and non-significant association with antibiotic delays. To assess the consistency of intervention outcomes across subgroups, a Mantel-Haenszel chi-square test was conducted. The test showed no significant interaction effect for gestational age groups (p = 0.38) or birth weight categories (p = 0.41), confirming that the intervention's impact was consistent across these subgroups. The logistic regression model's overall fit was confirmed using the Hosmer-Lemeshow test, which yielded a p-value = 0.72, indicating that the model demonstrated a good fit for predicting sepsis reduction trends and ensuring the results were not biased by baseline patient characteristics. These findings confirm that staff shortages, pharmacy delays, and IV access issues were the primary contributors to delayed antibiotic administration, while decision-making delays had a limited impact. The observed improvements in antibiotic delivery and neonatal outcomes were consistent across gestational age and birth weight subgroups, further supporting the effectiveness of the implemented QI interventions.

Table 5: Binary Logistic Regression Analysis of Factors Associated with Delayed Antibiotic Administration in the NICU

Factor	Adjusted Odds Ratio (AOR)	Lower 95% CI	Upper 95% CI	Interpretation
Staff Shortages	2.1	1.5	2.8	Staff shortages significantly increased the odds of delayed antibiotic administration, indicating a strong association.
Pharmacy Delays	1.8	1.3	2.4	Pharmacy workflow inefficiencies contributed notably to delays, with a moderate but significant impact.
IV Access Delays	1.5	1.1	2.0	Delays in obtaining IV access moderately increased the risk of delayed antibiotics.
Decision-Making Delay	1.3	0.9	1.8	Decision-making delays showed a weaker association with antibiotic delays, with a confidence interval crossing 1, indicating marginal significance.

Legend/Footnote: Adjusted odds ratios (AORs) were derived from a multivariate binary logistic regression model, with delayed antibiotic administration as the dependent variable. AOR > 1 indicates increased odds of delay. Confidence intervals (CI) that do not cross 1 indicate statistical significance. Model fit was verified using the Hosmer-Lemeshow test (p > 0.05).

Figure 6: Adjusted Odds Ratio of Factors Contributing to Delayed Antibiotic Administration



As shown in Figure 6, staff shortages and pharmacy delays had the highest adjusted odds ratios (AOR) for contributing to delayed antibiotic administration, followed by IV access delays and decision-making delays. The 95% confidence intervals (CI) illustrate the range of uncertainty around each odds ratio estimate.

The combined results of stratified analysis and logistic regression confirm that the observed improvements in antibiotic administration timing, sepsis rates, and NICU length of stay were robust and consistent across subgroups. Staff shortages, pharmacy delays, and IV access delays emerged as the primary contributors to delays, reinforcing the importance of targeted interventions addressing these factors.

Discussion

Timely antibiotic administration is essential in neonatal sepsis management, where delays can result in rapid deterioration and increased mortality. Early antibiotic intervention has been strongly linked to improved survival rates, with Hussain et al. reporting that prompt administration significantly reduces 28-day mortality (OR = 0.72)[7]. Neonates, being highly vulnerable due to their immature immune systems, are at greater risk of severe complications from delayed antibiotic initiation. Notarbartolo et al. emphasised that immediate antibiotic administration is vital in this population [8]. Structured QI interventions have been widely adopted in NICUs to address these risks by improving antibiotic administration practices. The Kaiser sepsis calculator, for example, demonstrated a 32.3% reduction in unnecessary antibiotic prescriptions while ensuring timely treatment for those at risk[9]. Additionally, multidisciplinary antimicrobial stewardship teams have proven essential in sustaining these interventions, reinforcing the need for standardised protocols and improved workflow practices to reduce delays [10].

Several barriers continue to challenge timely antibiotic administration in NICUs, with workflow delays and decision-making uncertainties posing significant risks. The fear of missing sepsis cases often leads to preemptive antibiotic prescribing, contributing to unnecessary antibiotic use and resistance [11]. In this study, binary logistic regression analysis identified staff shortages (AOR = 2.1; 95% CI: 1.5–2.8) and pharmacy delays (AOR = 1.8; 95% CI: 1.3–2.4) as the most significant contributors to antibiotic delays. IV access delays (AOR = 1.5; 95% CI: 1.1–2.0) were also identified as a notable factor, while decision-making delays had a weaker association (AOR = 1.3; 95% CI: 0.9–1.8), suggesting they played a lesser role. Addressing these issues requires improved staffing models, streamlined pharmacy workflows, and targeted strategies to reduce IV access delays. Expanding staff training programs to include advanced IV access techniques and promoting task-shifting strategies, such as empowering senior nurses to manage urgent line placements, may further reduce delays. Periodic case reviews and rapid-response escalation pathways could also minimise delays during uncertain clinical scenarios.

In addition to workflow changes, improving antibiotic stewardship is critical in ensuring both timely treatment and the responsible use of antimicrobials. Overuse of antibiotics remains a growing concern, contributing to antimicrobial resistance and negative health outcomes in neonates[12]. In response, QI initiatives have successfully balanced prompt antibiotic administration with cautious prescribing. For example, hospitals that implemented standardised protocols alongside computerised physician order entry systems achieved reductions in both antibiotic administration delays and overall antibiotic usage, while maintaining stable infection rates[13]. Integrating routine audits, real-time prescription reviews, and pharmacist-led antibiotic monitoring may further enhance stewardship efforts, ensuring appropriate antibiotic selection and timely de-escalation.

Education and training for healthcare providers play a pivotal role in enhancing antibiotic stewardship within NICUs. Multidisciplinary education programs have been shown to improve staff awareness of antibiotic overuse risks, fostering adherence to established protocols. For instance, targeted training initiatives have successfully reduced antibiotic usage rates while maintaining clinical efficacy, with one study reporting a 77% reduction in early-onset sepsis treatment days per 1,000 patient days following such interventions[14]. This emphasis on continuous education not only equips staff with the skills to manage antibiotic use effectively but also cultivates a culture of accountability and ongoing quality improvement.

Integrating advanced data analytics into antibiotic stewardship programs offers a promising strategy to optimise antibiotic use. Predictive modelling tools and real-time surveillance systems enable NICUs to identify at-risk neonates more accurately and refine antibiotic administration protocols accordingly. One study demonstrated that implementing such technology led to a 40% reduction in antibiotic use rates while improving neonatal outcomes[15]. This proactive approach reinforces the importance of technology in sustaining improved antibiotic practices while minimising unnecessary exposure.

The integration of antibiotic stewardship principles within standardised sepsis protocols is vital for sustaining the benefits of early antibiotic administration. While immediate treatment is critical in managing neonatal sepsis, excessive reliance on broad-spectrum antibiotics risks promoting antimicrobial resistance and dysbiosis, leading to long-term health complications[16,17]. Regular audits and prescription reviews are essential to ensuring consistent adherence to stewardship principles, minimising prescribing variability, and improving neonatal outcomes [18].

Various studies have demonstrated both similarities and differences in intervention strategies aimed at improving clinical outcomes in NICUs. Common strategies such as standardised protocols, staff training, and enhanced communication are pivotal in improving antibiotic prescribing practices and reducing infection rates. Standardised protocols, aligned with evidence-based practices, have been widely adopted, with some interventions incorporating syndrome-specific measures based on CDC core elements that emphasise leadership and accountability [19]. Staff training has also proven to be effective in improving adherence to clinical guidelines and reducing infection rates[20]. Furthermore, communication strategies such as appointing practice champions and developing tailored communication materials have played a vital role in promoting antibiotic stewardship[21]. These combined interventions have demonstrated positive outcomes, including reduced time to antibiotic administration, lower sepsis rates, and improved mortality outcomes[19,20]. Additionally, improved staff training and standardised protocols have contributed to reduced medication errors and shorter NICU stays, underscoring the overall effectiveness of these strategies in improving neonatal care [21]. Despite these successes, differences in implementation methods and clinical environments remain a challenge, highlighting the need for further research to standardise QI interventions for broader applicability. Similar to the PROTECT-Neo study, which focused on a single NICU setting, this study's results may have limited generalisability to hospitals with different infrastructure, staffing models, or antibiotic prescribing practices [22]. Moreover, variability in antibiotic resistance patterns across healthcare settings further limits the applicability of single-center studies, as resistance trends can differ significantly even within ICUs in the same institution [23]. This highlights the importance of multicenter trials to evaluate the scalability and broader effectiveness of QI interventions in antibiotic administration.

Another notable limitation of this study was the absence of long-term follow-up on antibiotic resistance outcomes. As emphasised by Martin et al., the lack of longitudinal data limits the ability to assess whether improvements in antibiotic timing have contributed to resistance trends over time[24]. Continuous surveillance of antibiotic resistance profiles is essential for guiding future stewardship strategies and ensuring sustained improvements in neonatal outcomes. Evidence from studies such as Mkony et al. demonstrates that routine monitoring of resistance patterns enables adaptive treatment protocols, improving both patient safety and antibiotic efficacy[25]. Future QI initiatives should incorporate long-term resistance monitoring and expand antimicrobial stewardship strategies to achieve lasting improvements in neonatal outcomes.

Despite achieving significant reductions in sepsis rates and NICU stay duration, this study found no statistically significant improvement in mortality ($p = 0.23$) or pneumonia incidence ($p = 0.32$). Similar trends have been reported in previous research, where mortality outcomes were often influenced by factors beyond antibiotic timing, such as illness severity and respiratory complications [26]. While excluding neonates with severe birth asphyxia reduced some confounding risks, infants with moderate illness severity may still have impacted the observed mortality outcomes. Additionally, increased reliance on non-invasive ventilation in term neonates may have contributed to sustained pneumonia rates, aligning with the observations of Regin et al. [27]. Future interventions should integrate targeted pneumonia prevention strategies, such as improved ventilation protocols and enhanced maternal infection screening, to address this gap. These findings suggest that improving neonatal outcomes requires a multifaceted approach that extends beyond antibiotic timing alone. Future research should explore strategies such as improved maternal infection screening, enhanced respiratory support protocols, and comprehensive management of neonatal comorbidities to reduce mortality and pneumonia rates in NICU populations.

Conclusion

This study demonstrated that structured QI interventions significantly reduced antibiotic administration delays, improving neonatal outcomes. Mean time to antibiotic administration decreased significantly ($p < 0.0001$), with most neonates receiving antibiotics within 30 minutes post-intervention. This led to a significant reduction in neonatal sepsis ($p < 0.001$) and shortened hospital stays ($p < 0.0001$). Meningitis incidence also declined significantly ($p = 0.025$). However, mortality ($p = 0.23$) and pneumonia rates ($p = 0.32$) remained unchanged, suggesting other contributing factors. The multidisciplinary QI framework—including staff training, pharmacy optimisation, and structured communication—proved effective and can be adapted to other NICUs, particularly in resource-limited settings. Future efforts should focus on sustaining improvements, integrating advanced sepsis detection tools, and expanding antimicrobial stewardship programs.

Limitations

This study was limited to a single tertiary care NICU, restricting generalisability. To improve generalisability, future research should involve multi-center trials to assess intervention outcomes across varied clinical settings. Parental decision-making delays persisted despite QI interventions, underscoring the need for targeted education strategies to improve awareness of sepsis risks. Developing structured parental education initiatives—such as bedside counselling, educational pamphlets, and involvement in sepsis protocol discussions—may help address this barrier. The qualitative component relied on self-reported staff data, which may introduce response bias despite thematic and root cause analysis. The study focused on antibiotic delays but did not account for infection severity, ventilator-associated pneumonia prevention, or maternal health. Long-term effects on antibiotic resistance were not assessed, necessitating multi-center trials and extended follow-up studies to validate and sustain these interventions.

Future Directions

Further research should explore machine-learning-based sepsis detection to enhance real-time diagnosis and automated risk stratification for optimised antibiotic use. Antimicrobial stewardship programs should be expanded to balance timely treatment with resistance prevention. Structured parental education programs should also be developed to promote awareness of sepsis risks and ensure timely consent for antibiotic initiation. A multi-center study would evaluate this QI model's scalability across diverse settings. Future studies should incorporate long-term monitoring of antibiotic resistance patterns to evaluate the sustained impact of these interventions. These efforts will refine neonatal sepsis management and improve survival.

References

1. Fleischmann-Struzek C, Goldfarb DM, Schlattmann P, Schlapbach LJ, Reinhart K, Kissoon N. The global burden of paediatric and neonatal sepsis: a systematic review. The Lancet Respiratory Medicine. 2018 Mar 1;6(3):223-30.
2. Wynn JL, Wong HR, Shanley TP, Bizzarro MJ, Saiman L, Polin RA. Time for a neonatal-specific consensus definition for sepsis. Pediatric Critical Care Medicine. 2014 Jul 1;15(6):523-8.
3. Shane AL, Sánchez PJ, Stoll BJ. Neonatal sepsis. The lancet. 2017 Oct 14;390(10104):1770-80.
4. Puopolo KM, Benitz WE, Zaoutis TE, Cummings J, Juul S, Hand I, Eichenwald E, Poindexter B, Stewart DL, Aucott SW, Goldsmith JP. Management of neonates born at≤ 34 6/7 weeks' gestation with suspected or proven early-onset bacterial sepsis. Pediatrics. 2018 Dec 1;142(6).
5. Greenberg RG, Kandefer S, Do BT, Smith PB, Stoll BJ, Bell EF, Carlo WA, Laptook AR, Sánchez PJ, Shankaran S, Van Meurs KP. Late-onset sepsis in extremely premature infants: 2000–2011. The Pediatric infectious disease journal. 2017 Aug 1;36(8):774-9.
6. Schulman J, Dimand RJ, Lee HC, Duenas GV, Bennett MV, Gould JB. Neonatal intensive care unit antibiotic use. Pediatrics. 2015 May 1;135(5):826-33
7. Hussain AK, Zahid S, Shah SM, Ashraf A, Haider MN, Bukhari AS, Bungish MK, Umais M, Khan SS. Outcomes of early vs. delayed antibiotic administration in sepsis management: A meta-analysis. Insights-Journal of Health and Rehabilitation. 2025 Jan 10;3(3):90–6.
8. Notarbartolo V, Badiane BA, Insinga V, Giuffrè M. Antimicrobial stewardship: A correct management to reduce sepsis in NICU settings. Antibiotics. 2024 Jun 3;13(6):520.
9. Nguyen TT, Nguyen OT, Duong MN, Giang LT. Antibiotic management for early-onset sepsis in neonates with gestational ages of ≥34 weeks: The Kaiser Sepsis Calculator versus the 2010 CDC guidelines. Cureus. 2024 Jul 2;16(7):e12345.

10. Flannery DD, Coggins SA, Medoro AK. Antibiotic stewardship in the neonatal intensive care unit. J Intensive Care Med. 2024 Jun 5;39(6):123–9.
11. De Rose DU, Ronchetti MP, Santisi A, Bernaschi P, Martini L, Porzio O, Dotta A, Auriti C. Stop in Time: how to reduce unnecessary antibiotics in newborns with late-onset Sepsis in neonatal intensive care. Tropical Medicine and Infectious Disease. 2024 Mar 19;9(3):63.
12. Payton KS, Bennett MV, Schulman J, Benitz WE, Stellwagen L, Darmstadt GL, Quinn J, Kristensen-Cabrera AI, Breault CC, Bolaris M, Lefrak L. 28 NICUs participating in a quality improvement collaborative targeting early-onset sepsis antibiotic use. Journal of Perinatology. 2024 Jul;44(7):1061-8.
13. Bissinger RL, Mueller M, Cox TH, Cahill J, Garner SS, Irving M, Annibale DJ. Antibiotic timing in neonates with suspected hospital-acquired infections. Advances in Neonatal Care. 2013 Feb 1;13(1):22-8.
14. Pantoja A, Sveum S, Frost S, Duran A, Burks J, Schernecke C, Feinberg M. New strategies to reduce unnecessary antibiotic use in the NICU: a quality improvement initiative. Pediatric Quality & Safety. 2023 May 1;8(3):e659.
15. Singh HP, Wilkinson S, Kamran S. Decreasing Antibiotic Use in a Community Neonatal Intensive Care Unit: A Quality Improvement Initiative. American Journal of Perinatology. 2024 May;41(S 01):e2767-75
16. Pichilingue-Reto P, Trimble K, Johnston M, Dominguez-Garcia MG. A Pediatric Antimicrobial Stewardship Program Intervention Leads to Decreased Inappropriate Use of Piperacillin-tazobactam in the Neonatal Intensive Care Unit at an Academic Institution. Journal of the Pediatric Infectious Diseases Society. 2024 Oct;13(Supplement_3): S19.
17. Ojeda A, Akinsuyi O, McKinley KL, Xhumari J, Triplett EW, Neu J, Roesch LF. Increased antibiotic resistance in preterm neonates under early antibiotic use. Msphere. 2024 Oct 29;9(10):e00286-24.
18. Donà D, Barbieri E, Brigadoi G, Liberati C, Bosis S, Castagnola E, Colomba C, Galli L, Lancella L, Lo Vecchio A, Meschiari M. State of the Art of Antimicrobial and Diagnostic Stewardship in Pediatric Setting. Antibiotics. 2025 Jan 27;14(2):132.
19. Bohan JG, Hunt L, Madaras-Kelly K. Antimicrobial Stewardship Guidelines: Syndrome-Specific Strategies. Current Treatment Options in Infectious Diseases. 2017 Mar;9(1):68-79.
20. Ariyo P, Zayed B, Riese V, Anton B, Latif A, Kilpatrick C, Allegranzi B, Berenholtz S. Implementation strategies to reduce surgical site infections: a systematic review. Infection Control & Hospital Epidemiology. 2019 Mar;40(3):287-300.
21. Borek AJ, Campbell A, Dent E, Moore M, Butler CC, Holmes A, Walker AS, McLeod M, Tonkin-Crine S. Development of an intervention to support the implementation of evidence-based strategies for optimising antibiotic prescribing in general practice. Implementation science communications. 2021 Dec;2:1-6.
22. Nguyen T, Bürkin F, Montaño SA, Jonas D, Kuntz M, Donker T, Reuter S, Götting T, Henneke P, PROTECT-Neo-Study-Group. Prevention of Transmissions by Effective Colonisation Tracking in Neonates (PROTECT-Neo). medRxiv. 2024 Nov 25:2024-11.
23. Blackley SK, Lawrence J, Blevins A, Howell C, Butts CC, Polite NM, Capasso TJ, Bright AC, Hall KA, Haiflich AN, Williams AY. A Single Hospital-

Wide Antibiogram is Insufficient to Account for Differences in Antibiotic Resistance Patterns Across Multiple ICUs. The American Surgeon™. 2024 Sep;90(9):2165-9.

24. Martin JS, Botta CJ, Bowman S, Giliberti D. Pragmatic expansion of a neonatal antibiotic stewardship program in a community health care system. Pediatrics. 2024 Jan 1;153(1):e2022056356.
25. Mkony MF, VanNiekerk A, Shabani J, Engelbrecht H, Rhoda NR. Strengthening Antibiotics Stewardship at Mowbray Maternity Hospital–Neonatal Unit.
26. Carella F, Aliberti S, Stainer A, Voza A, Blasi F. Long-Term Outcomes in Severe Community-Acquired Pneumonia. InSeminars in Respiratory and Critical Care Medicine 2024 Feb 23. Thieme Medical Publishers, Inc.
27. Regin Y, Gie A, Eerdekens A, Toelen J, Debeer A. Ventilation and respiratory outcome in extremely preterm infants: trends in the new millennium. European Journal of Pediatrics. 2022 May;181 (5):1899-907.