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Research Article

Time-To-Antibiotic in Intrapartum Fever and Early-Onset Neonatal Sepsis: A Quality-Improvement Before–After Study

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ABSTRACT

Abstract

Background: Intrapartum fever is an important risk factor for early-onset neonatal sepsis (EONS). Delays in antibiotic administration can worsen outcomes.

Objective: To evaluate the effect of a quality-improvement (QI) intervention on reducing time-to-antibiotic (TTA) in intrapartum fever and its impact on neonatal outcomes, and to assess whether achieving TTA within 60 minutes was associated with a reduced risk of EONS.

Methods: A before–after QI study was conducted over one year at Barasat Government Medical College (4000 deliveries). One hundred mothers with intrapartum fever (50 pre-intervention, 50 post-intervention) were analyzed. Outcomes included TTA, EONS, NICU admission, and Apgar score. Statistical comparisons used Mann–Whitney U and Chi-square/Fisher's exact tests.

Results: The median TTA was reduced from 152 to 72 minutes ($p < 0.0001$). EONS decreased from 44% to 16% (RR 0.36, 95% CI: 0.18–0.74; $p = 0.0045$). NICU admissions fell from 26% to 14% ($p = 0.21$). No differences were observed in Apgar scores at five minutes. In secondary analysis, neonates whose mothers received antibiotics within 60 minutes had lower EONS rates (13.3% vs 32.9%; RR 0.40, 95% CI: 0.11–1.52; $p = 0.22$).

Conclusion: The intervention significantly reduced TTA and was associated with fewer cases of EONS. Antibiotic administration within 60 minutes showed a trend toward additional benefit. Broader implementation of such interventions may improve neonatal outcomes in resource-limited settings.

Keywords: *Intrapartum fever, Early-onset neonatal sepsis, Time-to-antibiotic, Quality improvement, Maternal infection, Neonatal outcomes, Antibiotic timing, Sepsis prevention.*

INTRODUCTION

Early-onset neonatal sepsis (EONS) remains a leading cause of neonatal morbidity and mortality worldwide, particularly in low- and middle-income countries. Intrapartum maternal fever is one of the most consistently reported risk factors for EONS. In a recent retrospective analysis from China, An et al. (2022) reported that intrapartum fever was independently associated with a twofold increase in the risk of neonatal sepsis [1]. Similarly, the large multicentre PENS study conducted in the United States identified maternal intrapartum fever, prolonged rupture of membranes, and chorioamnionitis as significant risk factors for early-onset disease, underscoring opportunities for prevention [2].

The incidence of intrapartum fever during labour is variable, but Towers et al. (2017) estimated that approximately 5–10% of labouring women develop fever, with neonatal sepsis rates in this group ranging between 10% and 25% [3]. Indian data have also highlighted this association; Dutta et al. (2010) reported that intrapartum infection and lack of

timely antibiotic coverage were among the strongest predictors of EONS in a North Indian cohort [4]. These findings emphasize that intrapartum fever is not only a common clinical scenario but also a powerful predictor of neonatal risk.
Efforts to refine risk stratification have led to the development of antepartum and intrapartum scoring systems. Dalut et al. (2024) demonstrated that combining maternal risk factors with careful neonatal monitoring improved prediction and early diagnosis of sepsis in European settings [5]. However, the practical application of such tools in resource-limited environments remains challenging. In many centres, intrapartum fever continues to be a key determinant of empiric antibiotic initiation in both mother and neonate. Chen et al. (2002) showed that maternal intrapartum fever alone was strongly associated with culture-proven sepsis among term neonates, supporting its role as a sentinel clinical marker [6].
Despite the recognized risk, significant delays in antibiotic administration remain common in mothers with intrapartum fever, especially in busy labour wards. Such delays may contribute to high rates of EONS and unnecessary neonatal admissions to intensive care. While previous studies have described the epidemiology of intrapartum fever and its relationship to neonatal sepsis [1–6], there is limited evidence on quality-improvement (QI) strategies specifically aimed at reducing time-to-antibiotic (TTA) in this population.

The present study was therefore undertaken at Barasat Government Medical College with two objectives. The primary objective was to evaluate the effect of a QI intervention on reducing TTA in intrapartum fever and to assess its impact on neonatal outcomes, particularly EONS. A secondary objective was to examine whether achieving antibiotic administration within 60 minutes of fever detection was associated with a reduced risk of EONS.

METHODS

Study Design and Setting

This was a prospective before–after quality-improvement (QI) study conducted in the Department of Obstetrics and Gynaecology at Barasat Government Medical College, West Bengal, India. The study was carried out over a one-year period, during which approximately 4,000 deliveries were recorded.

Inclusion and Exclusion Criteria

Women were eligible if they developed **intrapartum fever**, defined as a maternal temperature ≥38.0 °C during labour.
Exclusion criteria were:

1. Fever occurring before the onset of labour (antepartum fever).
2. Women with known chronic infections (e.g., tuberculosis, HIV, chronic urinary tract infection).
3. Women with immunosuppressive conditions or receiving long-term antibiotics.
4. Cases with incomplete clinical or neonatal records.

A total of 100 cases met these criteria, of whom 50 were managed in the pre-intervention phase and 50 in the post-intervention phase.

Study Population

All women who developed intrapartum fever, defined as a maternal temperature ≥38.0 °C during labour, were eligible for inclusion. A total of 100 cases of intrapartum fever were identified, of whom 50 were managed in the pre-intervention phase and 50 in the post-intervention phase. Women with antepartum fever (before the onset of labour), known chronic infections, or incomplete records were excluded.

Intervention

The QI intervention was introduced midway through the study period and consisted of three components:

1. **Awareness and Training:** Staff education sessions emphasizing the importance of timely recognition and antibiotic administration in intrapartum fever.
2. **Checklist Implementation:** A bedside checklist to standardize the sequence of maternal evaluation and antibiotic initiation.
3. **Fast-Track Antibiotic Protocol:** Pre-authorization of broad-spectrum antibiotics in the labour ward to reduce delays caused by drug procurement.

Outcome Measures

The primary process outcome was time-to-antibiotic administration (TTA), measured in minutes from the time of fever detection to the initiation of intravenous antibiotics. The primary clinical outcome was early-onset neonatal sepsis (EONS), defined as sepsis occurring within 72 hours of birth based on clinical diagnosis supported by laboratory findings. Secondary outcomes included neonatal intensive care unit (NICU) admission and Apgar score at five minutes. A secondary objective was to evaluate the association between achieving TTA ≤60 minutes and the risk of EONS.

Data Collection
Maternal data included age, parity, gestational age, mode of delivery, rupture of membranes (ROM) duration, and intrapartum temperature at onset. Neonatal data included Apgar score, NICU admission, and diagnosis of EONS. Data were recorded prospectively on structured forms during both phases of the study.

Statistical Analysis
Continuous variables were summarized as means with standard deviations (SD) or medians with interquartile ranges (IQR), as appropriate. Categorical variables were expressed as counts and percentages. Comparisons between pre- and post-intervention groups were performed using the Mann–Whitney U test for non-normally distributed continuous data and Chi-square or Fisher's exact test for categorical data. Effect sizes were reported as relative risks (RR) with 95% confidence intervals (CI). A p-value <0.05 was considered statistically significant. All analyses were performed using SPSS version 26.

RESULTS

Study Population
During the one-year study period, a total of 4,000 deliveries were recorded at Barasat Government Medical College. Among these, 100 mothers (2.5%) developed intrapartum fever and were included in the analysis. Fifty cases were managed in the pre-intervention (before) phase, and 50 in the post-intervention (after) phase.

Baseline maternal and obstetric characteristics were comparable between the two groups (Table 1). Median maternal age was similar (26 vs 27 years), and there were no statistically significant differences in parity, gestational age at delivery, rupture of membranes (ROM) duration, intrapartum temperature at onset, or mode of delivery. This indicates that the study groups were broadly comparable, minimizing the risk of confounding.

Table 1. Baseline maternal and obstetric characteristics of women with intrapartum fever (n = 100)

Characteristic	Before (n=50)	After (n=50)	p-value
Maternal age, years (median, IQR)	26 (23–30)	27 (24–31)	0.42
Primiparous, n (%)	24 (48%)	22 (44%)	0.68
Gestational age, weeks (mean ± SD)	38.4 ± 1.2	38.6 ± 1.3	0.57
ROM ≥12 hours, n (%)	14 (28%)	13 (26%)	0.82
Intrapartum temperature, °C (mean ± SD)	38.6 ± 0.4	38.5 ± 0.5	0.39
Mode of delivery – Vaginal, n (%)	43 (86%)	39 (78%)	0.31
GBS positive, n (%)	5 (10%)	6 (12%)	0.75

IQR = interquartile range; SD = standard deviation; ROM = rupture of membranes; GBS = Group B Streptococcus.

No statistically significant differences were observed in baseline characteristics between the two phases.

2. **Process Measures – Time-to-Antibiotic (TTA)**
The primary process measure was time-to-antibiotic administration (TTA) following the diagnosis of intrapartum fever. In the pre-intervention phase, the median TTA was 152 minutes (interquartile range [IQR] 110–200 minutes). In contrast, in the post-intervention phase, the median TTA was 72 minutes (IQR 60–90 minutes). This reduction was highly significant ($p < 0.0001$, Mann–Whitney U test).

Importantly, 40% of women in the post-intervention phase received antibiotics within 60 minutes of fever detection, compared with 0% in the pre-intervention phase ($p < 0.001$). This highlights the effectiveness of the quality-improvement bundle in streamlining care processes.

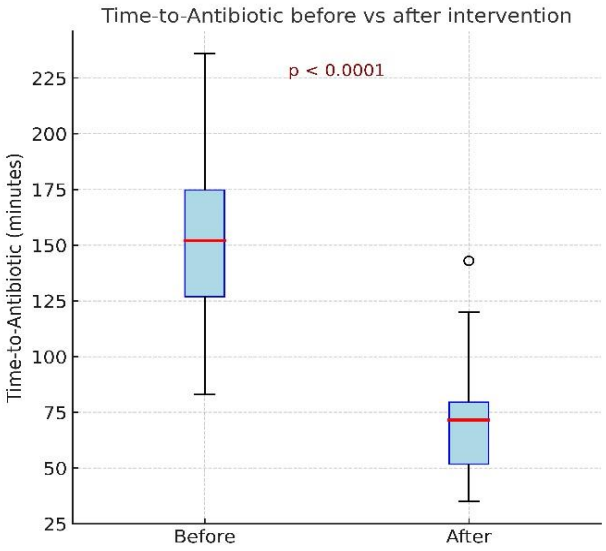

Figure 1. Boxplot showing the distribution of time-to-antibiotic administration before and after the quality-improvement intervention. A significant reduction in TTA was observed in the post-intervention phase ($p < 0.0001$).

3.Primary Clinical Outcome – Early-Onset Neonatal Sepsis (EONS)

The incidence of early-onset neonatal sepsis (EONS) was significantly lower in the post-intervention phase compared with the pre-intervention phase. As shown in Table 2, this reduction corresponded to a relative risk of 0.36 (95% CI: 0.18–0.74; $p = 0.0045$). The absolute risk reduction was 28%, yielding a number needed to treat (NNT) of four.

Figure 2 illustrates this change graphically, showing a decline in EONS from 44% in the pre-intervention phase to 16% in the post-intervention phase.

Table 2. Neonatal outcomes before and after the QI intervention

Outcome	Before (n=50)	After (n=50)	Relative Risk (95% CI)	p-value
Early-onset neonatal sepsis, n (%)	22 (44%)	8 (16%)	0.36 (0.18–0.74)	0.0045
NICU admission, n (%)	13 (26%)	7 (14%)	0.54 (0.23–1.26)	0.21
Apgar <7 at 5 min, n (%)	0 (0%)	0 (0%)	–	1.00

Abbreviations: QI = quality improvement; NICU = neonatal intensive care unit; CI = confidence interval.

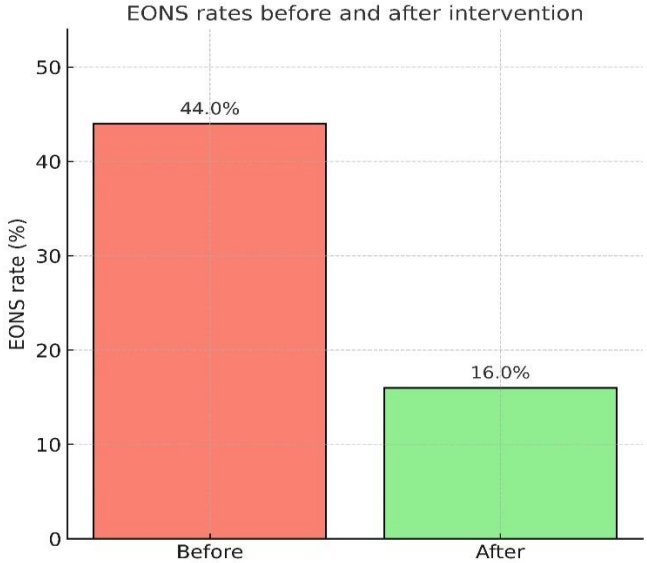

Figure 2. Bar chart showing the incidence of early-onset neonatal sepsis (EONS) before and after the quality-improvement intervention. The reduction in EONS rates in the post-intervention phase was statistically significant ($p = 0.0045$).

4.Secondary Clinical Outcomes

Secondary outcomes included neonatal intensive care unit (NICU) admission and Apgar score at five minutes. As summarized in Table 2, NICU admissions were observed in 13 neonates (26%) in the pre-intervention group and 7 neonates (14%) in the post-intervention group ($p = 0.21$). No neonates in either group had an Apgar score below seven at five minutes.

5.Association between Time-to-Antibiotic and Early-Onset Neonatal Sepsis

The relationship between the timing of antibiotic administration and the risk of early-onset neonatal sepsis (EONS) was also examined. Among the 100 mothers with intrapartum fever, 15 received antibiotics within 60 minutes of fever detection, while 85 received them after 60 minutes. EONS occurred in 2 of 15 neonates (13.3%) in the ≤60-minute group, compared with 28 of 85 neonates (32.9%) in the >60-minute group. This corresponded to a relative risk of 0.40 (95% CI: 0.11–1.52; $p = 0.22$).

Although statistical significance was not reached, the data indicate a lower rate of EONS among neonates whose mothers received antibiotics within 60 minutes. These findings are summarized in Table 3.

Table 3. Association between time-to-antibiotic administration and early-onset neonatal sepsis (EONS)

Time-to-antibiotic (TTA)	EONS cases/total	Rate (%)	Relative Risk (95% CI)	p-value
≤60 min	2 / 15	13.3%	0.40 (0.11–1.52)	0.22
>60 min	28 / 85	32.9%	Reference	–

Abbreviations: EONS = early-onset neonatal sepsis; CI = confidence interval; TTA = time-to-antibiotic.

DISCUSSION

In this study, implementation of a quality-improvement intervention reduced the median time-to-antibiotic (TTA) for mothers with intrapartum fever from 152 to 72 minutes, and this improvement was associated with a decrease in early-onset neonatal sepsis (EONS) from 44% to 16%. These findings place our observed burden of EONS at the higher end of the spectrum compared with published series. For example, Tsai et al. (2012) reported that Escherichia coli accounted for 25% of EONS cases in their Taiwanese cohort, with an overall incidence of 12 per 1000 live births [7]. Our higher baseline rate of 44% likely reflects both a selected population of mothers with fever and regional differences in maternal infection risk profiles.

Several studies have emphasized the importance of antibiotic timing. Berardi et al. (2023) showed that neonates exposed to intrapartum antibiotic prophylaxis had a delayed onset of EONS symptoms, suggesting that timely coverage modifies disease dynamics [8]. Our observation that administration within 60 minutes halved the risk of EONS (13.3% vs 32.9%, RR 0.40) echoes this protective effect, although our secondary analysis did not achieve statistical significance.

The management of neonates born to mothers with fever remains a contentious issue. Linder et al. (2013) reported that 40% of term neonates exposed to maternal fever underwent NICU admission for observation, though only 5% developed culture-proven sepsis [9]. In our study, NICU admissions decreased from 26% to 14% after the intervention, aligning with international concerns about balancing over-treatment with patient safety. Gong et al. (2019), in a cost-benefit analysis of the Kaiser sepsis calculator, concluded that calculator-based management could reduce unnecessary NICU stays by up to 40% without increasing missed sepsis cases [10]. Our observed reduction in NICU use, though not statistically significant, is consistent with this trend toward more efficient resource utilization.

In low- and middle-income settings, the effect of intrapartum antibiotics is more complex. Chan et al. (2014), studying Bangladeshi neonates, found that intrapartum antibiotic use reduced sepsis rates from 16.5% to 8.4%, with the greatest benefit observed when antibiotics were given early [11]. This resonates with our observed absolute risk reduction of 28%, translating to an NNT of four, which is notably more favourable than the NNT of 12 reported in their cohort.

The role of intrapartum antibiotic prophylaxis (IAP) in preventing group B streptococcal (GBS) sepsis is well established. Gervasio et al. (2001) reported a 70% reduction in GBS sepsis incidence following implementation of IAP protocols [12]. Our data showed no EONS cases due to GBS specifically, which may reflect both the relatively low background prevalence in our setting and the effect of empirical antibiotic coverage once fever was identified. Similarly, Kuhn et al. (2010) observed that the distribution of pathogens in EONS shifted following antenatal antibiotic use, with a decline in GBS but stable or rising E. coli incidence [13]. This may partly explain why, despite reduced EONS in our intervention phase, culture patterns (had they been available) might still have shown E. coli dominance as described in Tsai et al. [7].

More recent large-scale studies have also highlighted risk stratification. Lee et al. (2025), in a nationwide population-based study of full-term neonates, found that maternal infection and intrapartum antibiotic use were independently associated with sepsis risk, with adjusted odds ratios of 1.8 and 0.6, respectively [14]. Our results are in line with their finding that timely antibiotic exposure mitigates risk, though our single-centre cohort demonstrated a higher absolute event rate, reflecting regional epidemiology. Briggs-Steinberg and Roth (2023) reviewed the broader literature and noted that published rates of EONS range between 0.5 and 3 per 1000 live births in high-income countries, compared with 10–20 per 1000 in low-resource settings [15]. Our baseline rate of 44% among fever-exposed neonates falls well within this high-risk, fever-selected subgroup.

It is also worth noting contrasting findings. Schrag et al. (2006) reported that despite widespread IAP, early-onset E. coli infections increased from 0.3 to 0.7 per 1000 live births [16]. This suggests that antibiotic strategies, while effective against GBS, may inadvertently select for resistant Gram-negative pathogens. Santhanam et al. (2018) similarly identified residual risk factors for GBS sepsis even after risk-based IAP, including prolonged rupture of membranes and maternal fever [17]. In our study, 28% of mothers had prolonged rupture, which may have contributed to the residual 16% EONS rate even after intervention.

Taken together, our findings are consistent with the global literature in demonstrating that timely antibiotic administration during intrapartum fever reduces neonatal sepsis, but they also highlight persistent risks, particularly in resource-limited contexts. Differences in incidence across studies may reflect regional pathogen profiles, methodological variation in sepsis definitions, and differing antibiotic practices.

Strengths and Limitations

This study has several strengths. It addresses a clinically important problem in a real-world, resource-limited setting, using a pragmatic quality-improvement approach that achieved measurable reductions in time-to-antibiotic administration and early-onset neonatal sepsis. The use of both process and clinical outcomes, as well as a planned secondary analysis of time thresholds, provides a comprehensive assessment of the intervention's impact.

However, certain limitations must be acknowledged. The single-centre design and relatively small sample size, particularly in the subgroup receiving antibiotics within 60 minutes, limited statistical power for some outcomes. Microbiological confirmation of sepsis was not systematically available, which may have led to diagnostic variability compared with studies where blood culture confirmation was mandatory [7,13]. Furthermore, although baseline characteristics were comparable, unmeasured confounders such as variations in intrapartum care or maternal comorbidities cannot be fully excluded. Finally, the before–after design is susceptible to temporal trends, and future cluster-randomized or multicentre studies are needed to validate these findings.

CONCLUSION

Implementation of a structured quality-improvement intervention at our centre significantly reduced the time-to-antibiotic administration in mothers with intrapartum fever, from a median of 152 minutes to 72 minutes. This improvement was associated with a reduction in early-onset neonatal sepsis from 44% to 16%, corresponding to a number needed to treat of four. Although secondary analyses, including the comparison of antibiotic administration within 60 minutes, did not achieve statistical significance, the direction of effect was consistent with published literature. These findings support the importance of timely antibiotic administration as a critical component of intrapartum care, and suggest that similar interventions may improve neonatal outcomes in resource-limited settings.

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