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Impact of Antenatal Corticosteroid Administration Timing on Neonatal Respiratory Outcomes in Preterm Births

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Abstract **Background:** Respiratory complications remain a leading cause of morbidity and mortality in preterm neonates. Antenatal corticosteroids (ACS) are known to accelerate fetal lung maturation but the timing of administration in relation to delivery may significantly influence outcomes. **Objective:** This study aimed to evaluate the impact of ACS timing on neonatal respiratory outcomes in preterm births. **Methods:** A prospective observational study was conducted on 321 pregnant women who delivered between 24+0 and 34+6 weeks of gestation at [Insert Hospital Name]. Participants were categorized based on the interval between ACS administration and delivery: Group A (1-7 days), Group B (<24 hours) and Group C (>7 days). Neonatal outcomes including Respiratory Distress Syndrome (RDS), need for respiratory support, oxygen therapy duration, NICU stay and early neonatal mortality were recorded. Data were analyzed using SPSS [insert version], with $p<0.05$ considered statistically significant. **Results:** The incidence of RDS was significantly lower in Group A (27.8%) compared to Group B (51.0%) and Group C (48.7%) ($p<0.001$). Mechanical ventilation was required in 11.1% of Group A neonates, versus 27.1% in Group B and 21.4% in Group C ($p = 0.003$). CPAP need followed a similar trend (25.9, 41.7 and 42.7%, respectively; $p = 0.01$). The mean duration of oxygen therapy and NICU stay was also lowest in Group A (2.8±1.3 and 6.7±2.5 days, respectively; both $p<0.001$). Early neonatal mortality was lowest in Group A (3.7%) compared to Group B (8.3%) and Group C (7.7%), though not statistically significant ($p = 0.09$). **Conclusion:** It is concluded that administering antenatal corticosteroids within 1 to 7 days of preterm delivery is associated with significantly improved neonatal respiratory outcomes. Optimal timing reduces the risk of RDS, decreases the need for respiratory support and shortens NICU stays. These findings reinforce the need for timely intervention and coordination in obstetric care to maximize the therapeutic benefits of corticosteroids in preterm births.

Key Words Antenatal Corticosteroids, Respiratory Distress Syndrome (RDS), Neonatal Outcomes, Fetal Lung Maturation, NICU Stay, Neonatal Mortality

INTRODUCTION

Preterm birth, defined as delivery before 37 completed weeks of gestation, continues to pose a major public health challenge, contributing to nearly 1 million neonatal deaths annually, primarily due to respiratory complications. Respiratory Distress Syndrome (RDS), caused by surfactant deficiency in immature lungs, remains the most common and severe respiratory issue faced by preterm neonates,

especially those born before 34 weeks of gestation. Other respiratory morbidities, including transient tachypnea of the newborn (TTN) and bronchopulmonary dysplasia (BPD), further contribute to short- and long-term morbidity. In this context, antenatal corticosteroids (ACS) have been a cornerstone intervention, with a well-documented role in promoting fetal lung maturity and reducing the incidence and severity of neonatal respiratory morbidity.

ACS, particularly betamethasone and dexamethasone, stimulate the production of surfactant and enhance the structural and biochemical maturation of the fetal lungs. Landmark trials such as Liggins and Howie [1] demonstrated a significant reduction in neonatal mortality and RDS with a single course of corticosteroids. These findings led to the widespread adoption of ACS in obstetric practice and subsequent meta-analyses have further validated its benefits across different gestational ages and populations. The World Health Organization (WHO), the American College of Obstetricians and Gynecologists (ACOG) and other leading bodies recommend a single course of ACS between 24 and 34 weeks of gestation for women at imminent risk of preterm delivery.

However, a critical factor influencing the efficacy of ACS is the timing of its administration relative to the actual time of delivery. The biological effect of ACS in promoting surfactant production and lung maturation peaks around 24 to 48 hours after the first dose and gradually wanes after 7 days. Thus, infants born within this optimal window are more likely to benefit compared to those delivered either too soon or after a prolonged interval. In practice, many preterm deliveries occur outside this ideal window due to either spontaneous onset of labor, clinical uncertainty or delays in presentation to healthcare facilities [2-4].

Several observational studies and retrospective analyses have explored the relationship between the timing of ACS and neonatal outcomes. A growing body of evidence suggests that neonates delivered within 1 to 7 days of ACS administration have significantly lower rates of RDS, need for mechanical ventilation and neonatal intensive care unit (NICU) admission compared to those delivered outside this period. In contrast, the benefits of ACS become less pronounced when delivery occurs within 24 hours of the first dose or more than 7 days after the completed course. Furthermore, repeated courses or rescue doses of corticosteroids, although potentially beneficial in extending respiratory protection, remain controversial due to associated risks such as impaired fetal growth, altered neurodevelopment and Hypothalamic-Pituitary-Adrenal (HPA) axis suppression [5-7].

Despite the importance of ACS timing, there is still limited prospective data, particularly in low-resource settings, where access to timely and appropriate perinatal care is often compromised. The unpredictability of preterm labor further complicates the administration of corticosteroids within the optimal window [8,9]. As such, understanding the relationship between ACS timing and neonatal respiratory outcomes has direct clinical implications for obstetric decision-making, including the use of tocolytics, timing of delivery in indicated preterm births and the potential role of repeat dosing [10-14].

Objective

This study aims to investigate the impact of antenatal corticosteroid administration timing on the respiratory outcomes of neonates born preterm. By categorizing the interval between ACS administration and delivery, we aim to quantify the differential outcomes in terms of RDS incidence, respiratory support requirements, NICU stay duration and neonatal mortality.

METHODS

This was a prospective observational cohort study designed to evaluate the impact of timing of antenatal corticosteroid (ACS) administration on respiratory outcomes in preterm neonates.

Sample Size and Sampling Technique

A total of 321 pregnant women at risk of preterm delivery between 24 and 34 weeks of gestation were enrolled. Non-probability consecutive sampling was employed to recruit eligible participants presenting to the obstetrics department during the study period.

Inclusion Criteria

- Women with singleton or twin pregnancies between 24+0 and 34+6 weeks of gestation
- Received at least one dose of antenatal corticosteroids (betamethasone or dexamethasone)
- Delivered preterm during the study period
- Provided informed written consent for participation

Exclusion Criteria

- Major congenital anomalies in the neonate
- Stillbirths or intrauterine fetal demise
- Incomplete antenatal corticosteroid documentation
- Women who received corticosteroids for maternal medical indications (e.g., autoimmune diseases)

Grouping Based on Timing of ACS Administration

Participants were stratified into three groups based on the time interval between the first dose of ACS and the time of delivery:

- Group A (Optimal Window): Delivery within 1 to 7 days of ACS administration
- Group B (Suboptimal-Early): Delivery within <24 hours of ACS administration
- Group C (Suboptimal-Late): Delivery more than 7 days after ACS administration

Data Collection Procedure

Maternal demographic information, obstetric history, gestational age at delivery, type and timing of ACS administered and labor details were recorded using a structured proforma. Neonatal respiratory outcomes were obtained from the Neonatal Intensive Care Unit (NICU) records, including the occurrence of Respiratory Distress Syndrome (RDS), need for mechanical ventilation, CPAP requirement, duration of oxygen therapy and NICU stay. The primary outcome of interest was the incidence of Respiratory Distress Syndrome (RDS) in preterm neonates. Secondary outcomes included the need for mechanical ventilation or CPAP, total duration of oxygen therapy, length of NICU admission and neonatal mortality within the first week of life. These outcomes were chosen to comprehensively assess respiratory compromise and the clinical benefits of optimal ACS timing.

Statistical Analysis

All collected data were entered and analyzed using SPSS software version 26. Continuous variables such as gestational age and birth weight were expressed as Mean±standard deviation, while categorical variables like RDS incidence and ventilator use were reported as frequencies and percentages. The Chi-square test was employed for categorical comparisons and ANOVA test was used for continuous data across the three groups. To control for potential confounders such as gestational age, birth weight and mode of delivery, multivariate logistic regression analysis was also conducted. A p-value of less than 0.05 was considered statistically significant throughout the analysis.

Ethical Considerations

Ethical approval for the study was obtained from the Institutional Review Board (IRB) of ---. All participants were briefed about the purpose, risks and benefits of the study and informed written consent was obtained prior to data collection. Anonymity and confidentiality of patient data were strictly maintained and the study adhered to the ethical standards of the Declaration of Helsinki.

RESULTS

Data were collected from 321 participants. Out of the 321 women included in the study, 108 (33.6%) were categorized in Group A (optimal ACS-to-delivery interval of 1-7 days), 96 (29.9%) in Group B (delivered within <24 hours of ACS) and 117 (36.4%) in Group C (delivered >7 days after ACS administration). The mean maternal age was 29.4±5.3 years, with no statistically significant difference across the three groups (p = 0.62). The mean gestational age at delivery was slightly higher in Group A (32.1±1.4 weeks) compared to Group B (31.7±1.6 weeks) and Group C (31.5±1.5 weeks), though the difference was not statistically significant (p = 0.08). Birth weight was significantly higher in Group A (1890±330 g) compared to Group B (1750±310 g) and Group C (1780±340 g) (p = 0.04) (Table 1).

A total of 136 neonates (42.4%) developed RDS. The incidence of RDS was significantly lower in Group A (30/108; 27.8%) compared to Group B (49/96; 51.0%) and Group C (57/117; 48.7%) (p<0.001). This suggests that neonates delivered within the optimal window of ACS administration had the most respiratory benefit (Table 2).

Mechanical ventilation was required in 19.4% of cases (62 neonates). Group A had the lowest requirement (11.1%), followed by Group C (21.4%) and Group B (27.1%), with the difference being statistically significant (p = 0.003). Similarly, CPAP was needed in 118 neonates (36.8%), with a lower frequency in Group A (25.9%) compared to Group B (41.7%) and Group C (42.7%) (p = 0.01) (Table 3).

The mean duration of oxygen therapy was significantly lower in Group A (2.8±1.3 days) than in Group B (4.1±1.9 days) and Group C (3.9±1.8 days) (p < 0.001). Likewise, the length of NICU stay was shortest in Group A (6.7±2.5 days), followed by Group C (8.4±3.2 days) and Group B (9.1±3.5 days) (p<0.001) (Table 4).

The overall neonatal mortality rate within the first 7 days was 6.5% (21 neonates). Group A had the lowest mortality (3.7%), while Group B (8.3%) and Group C (7.7%) had higher rates. Although the trend suggested a benefit in Group A, the difference did not reach statistical significance (p = 0.09) (Table 5).

Table 1: Baseline Characteristics

Characteristic	Group A (1-7 days)	Group B (<24 hrs)	Group C (>7 days)	p-value
Number of Patients	108	96	117	-
Mean Maternal Age (years)	29.5±5.4	29.2±5.1	29.6±5.5	0.62
Mean GA at Delivery (weeks)	32.1±1.4	31.7±1.6	31.5±1.5	0.08
Mean Birth Weight (g)	1890±330	1750±310	1780±340	0.04

Table 2: Incidence of RDS

Group	RDS Cases (n)	Total in Group (n)	RDS Frequency (%)
Group A (1-7 days)	30	108	27.8
Group B (<24 hrs)	49	96	51.0
Group C (>7 days)	57	117	48.7

Table 3: Respiratory Support Need

Group	Mechanical Ventilation (n, %)	CPAP (n, %)	p-value (Ventilation)	p-value (CPAP)
Group A (1-7 days)	12 (11.1%)	28 (25.9%)	0.003	0.01
Group B (<24 hrs)	26 (27.1%)	40 (41.7%)	-	-
Group C (>7 days)	25 (21.4%)	50 (42.7%)	-	-

Table 4: Oxygen Therapy & NICU Stay

Group	O2 Therapy Duration (days)	NICU Stay (days)	p-value (O2)	p-value (NICU)
Group A (1-7 days)	2.8±1.3	6.7±2.5	<0.001	<0.001
Group B (<24 hrs)	4.1±1.9	9.1±3.5	-	-
Group C (>7 days)	3.9±1.8	8.4±3.2	-	-

Table 5: Neonatal Mortality

Group	Neonatal Deaths (n)	Total in Group (n)	Mortality Rate (%)	p-value
Group A (1-7 days)	4	108	3.7	0.09
Group B (<24 hrs)	8	96	8.3	-
Group C (>7 days)	9	117	7.7	-

DISCUSSION

This study evaluated the influence of timing between antenatal corticosteroid (ACS) administration and delivery on the respiratory outcomes of preterm neonates. Our findings reaffirm the critical importance of administering ACS within the optimal therapeutic window defined as 1 to 7 days prior to preterm birth. Neonates born during this period (Group A) demonstrated significantly lower rates of respiratory distress syndrome (RDS), reduced need for mechanical ventilation and CPAP, shorter durations of oxygen therapy and NICU stay and a trend toward lower early neonatal mortality, compared to those in suboptimally timed groups. The incidence of RDS in Group A was 27.8%, markedly lower than 51.0% in Group B (<24 hours) and 48.7% in Group C (>7 days), indicating the maximal pulmonary benefit of ACS occurs when delivery occurs within the 1-7 day window post-administration. This aligns with previously published evidence, including the NICHD consensus and Cochrane meta-analyses, which have repeatedly highlighted that the fetal lung maturation effect of corticosteroids peaks between 24 hours and 7 days after initiation of therapy [2,3].

Our study further demonstrates a lower requirement for respiratory support in Group A. The mechanical ventilation rate was just 11.1% compared to 27.1 and 21.4% in Groups B and C, respectively. Similarly, the need for CPAP was significantly less in the optimally timed group. These differences suggest that while corticosteroids may still offer partial benefit when delivered outside the optimal window, their full protective potential is strongly timing-dependent. Notably, our data show that administration too early or too late relative to delivery reduces the drug's efficacy, potentially due to insufficient time for lung maturation or the waning of corticosteroid effect after one week. Interestingly, neonatal mortality within 7 days of life, though not statistically significant, was also lowest in Group A (3.7%), further supporting the hypothesis that optimal ACS timing may confer a survival advantage. However, due to the small number of deaths, the study may have been underpowered to detect a statistically significant difference in mortality [15,16].

The shorter NICU stay and reduced oxygen requirement in the optimally timed group have important implications for healthcare resource utilization. These findings suggest that better synchronization of ACS administration with anticipated preterm delivery may not only improve clinical outcomes but also reduce the economic burden on neonatal care units. Several limitations of this study should be acknowledged. As an observational study, it is subject to potential confounding factors, despite our efforts to adjust for key variables such as gestational age and birth weight [17]. The unpredictability of spontaneous preterm labor remains a practical barrier to ensuring optimal ACS timing. Additionally, the findings are based on data from a single tertiary care center, which may limit generalizability, especially to low-resource settings. Nevertheless, the study's strengths include a relatively large sample size, prospective data collection and clear stratification of timing windows. The results emphasize the urgent need for clinical strategies such as timely referral, judicious use of tocolytics and enhanced antenatal surveillance to ensure ACS is administered within the effective window. Future research may focus on biomarkers or risk scoring systems that better predict imminent preterm labor, improving the precision of ACS use [18-20].

CONCLUSIONS

It is concluded that the timing of antenatal corticosteroid administration plays a decisive role in determining neonatal respiratory outcomes among preterm births. The study demonstrated that administering corticosteroids within the optimal window of 1 to 7 days before delivery significantly reduces the incidence of respiratory distress syndrome (RDS), the need for respiratory support, duration of oxygen therapy and length of NICU stay. Neonates born outside this window either within 24 hours of administration or after 7 days showed notably poorer outcomes, highlighting the time-sensitive nature of corticosteroid efficacy. While the intervention remains effective in improving fetal lung maturity, its maximal clinical benefit is highly dependent on precise timing. These findings underscore the importance of early risk identification, timely obstetric intervention and close coordination between maternal-fetal medicine and neonatology teams to ensure corticosteroid administration is optimally timed.

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