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RESEARCH ARTICLE
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TO SEE FETAL OUTCOMES IN PRE TERM BIRTH (GESTATIONAL AGE 34 TO 36 WEEK 6 DAYS) WHO DO NOT RECEIVE ANTENATAL CORTICOSTEROIDS

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Abstract

Introduction: Late preterm birth, defined as delivery between 34 weeks and 36 weeks 6 days, is associated with increased neonatal complications. Antenatal corticosteroids (ACS) are known to improve outcomes in preterm births, yet their use in late preterm deliveries remains variable, especially in resource-limited settings. Guidelines, such as the Irish National SOGP Guideline, often do not recommend ACS for this gestational age due to favorable outcomes in well-resourced settings.
Objective: To evaluate neonatal outcomes in late preterm births (34–36+6 weeks) without ACS exposure in a resource-limited setting.
Materials and Method: This observational study was conducted at a secondary care hospital / Civil Hospital Mirpurkhas in Pakistan from January to June 2024. A total of 180 women who delivered between 34 and 36+6 weeks without ACS administration were enrolled. Neonatal outcomes within the first 7 days were documented, including respiratory distress, NICU admission, feeding difficulties, and early neonatal death.
Results: Infants born before 35 weeks had significantly higher rates of respiratory distress (72.9%), NICU admission (81.3%), and hypoglycemia. Neonatal mortality was 5%, with all deaths occurring before 36 weeks.
Conclusion: the absence of ACS in late preterm births correlates with adverse neonatal outcomes, particularly before 35 weeks, supporting targeted ACS use in resource-limited settings despite differing international guidelines. This contrasts with the Irish National SOGP Guideline, which reports favorable outcomes without ACS in well-resourced settings due to neonatal care.

Keywords: Late preterm, antenatal corticosteroids, neonatal outcomes, respiratory distress, NICU admission.

INTRODUCTION

Preterm birth is one of the leading causes of neonatal morbidity and mortality globally, with significant public health relevance. Specifically, births that occur when a fetus is between 34 weeks and 36 weeks 6 days of gestation are considered late preterm, and although late preterm infants experience better outcomes than early preterm infants. However, late preterm infants are still at risk

of respiratory distress, feeding challenges, thermal instability, hypoglycemia, and increased neonatal intensive care unit (NICU) admission (1). Antenatal corticosteroids (ACS) are one of the common interventions medical providers use to improve fetal lung maturity and decrease complications in the newborn infant. The Irish National SOGP Guideline does not recommend routine ACS administration for 34-36+6 weeks in well-resourced settings, citing favorable neonatal outcomes due to advanced neonatal care infrastructure.

Additional research into the timing of corticosteroid exposure suggests that late preterm infants may benefit from early corticosteroid exposure, but the risk-benefit ratio is not consistently favorable for all gestational categories (2). The nuances of the literature have contributed to clinical guidelines, which now emphasize patient selection and timing of ACS exposure for patients. Additionally, the evidence highlights that while ACS reduces neonatal respiratory morbidity, the benefits are diminished in late preterm infants, especially compared to infants born before 34 weeks (3). There remain important questions about fetal outcomes for late preterm infants in the absence of ACS, and whether there is increased risk with no exposure, depending on the clinical context. Moreover, there have been many concerns raised in the literature about the neurodevelopmental adverse effects of ACS in late preterm infants. While some studies mention the neuroprotective aspects of ACS, there are differing findings and evidence, particularly regarding the long-term neurodevelopmental outcomes (4).

Professional associations, such as the Society for Maternal-Fetal Medicine (SMFM), continue to reorganize their clinical practice guidance related to the use of ACS since the evidence is evolving. Their 2021 Consult Series stipulates specific indications and contraindications for ACS in the late preterm period, advising against the routine use of ACS in situations without clear benefits (5). The World Health Organization also modified its recommendations to encourage the use of ACS, which can be provided contextually, especially in resource-limited settings, where neonates are at greater risk for complications without access to modern neonatal facilities (6). These guidelines appropriately delineate whether to use ACS in late preterm deliveries, particularly where there is a high risk of imminent delivery with access to maternal and neonatal care. They also reinforce those choices with guidelines from the International Federation of Gynecology and Obstetrics (FIGO) to consider using ACS judiciously past 34 weeks of gestation to blend the risk and exposure without unnecessary risk (7). In contrast, the Irish National SOGP Guideline suggests that late preterm infants may not require ACS due to sufficient gestational maturity in well-resourced settings, highlighting the need for context-specific evidence.

It has been noted above that there is no straightforward clinical decision-making due to ongoing questions relative to the best ACS dosing regimen. For example, comparing the change in neonatal respiratory outcomes between lower doses (e.g., 4 mg) and standard doses (e.g., 12 mg), as well as the differences in maternal effects of lower doses, especially when an ACS was given near term, raises important concerns (8). These differences are of concern because excess maternal treatment may unnecessarily expose the fetus or the maternal patient to risk and provide no meaningful benefit. Timing is a recognized factor affecting the ACS's efficacy, as ACS should ideally be provided for either the labour/delivery or in the week prior to the anticipated delivery (9). However, due to clinical uncertainty, women can receive either an excess or inadequate doses of ACS in the event they deliver at term or late preterm, which raises concerns about overtreatment or timing misclassification of delivery (10). Meta-analytic data specific to late preterm births show a small but statistically significant improvement in respiratory outcomes for infants who received ACS compared with infants who did not, with the consideration of the possible risks of hypoglycemia and slowed neurodevelopment (11). The length of time between the administration of the ACS and the actual delivery may also influence the outcomes, with more extended latency periods diminishing the protective effects of the therapy (12).

The ALPS (Antenatal Late Preterm Steroids) follow-up study provided further insight into the neurodevelopmental trajectory of late preterm infants exposed to ACS and found that improvements in respiratory function were observed. However, long-term neurodevelopmental outcomes were

generally not better (13). The implications of large-scale trials, like ALPS, have reshaped hospital protocols, but there is continued inconsistent adoption of updates worldwide. A retrospective study of changes in ACS use after the trial assessed whether behaviour had changed in institutions despite there being stronger evidence now to follow the oral dose, and for the most part, institutions still found adopting the updates, based on the national guidelines, and institutional practices still appeared to reflect wide variability (14). Variability supports a discussion to produce more place-based research that respects the regional realities of maternal health, neonatal care capability, and clinical guidelines. For countries like Pakistan, where healthcare institutions can differ extensively in access to evidence, context, and resources, it is necessary to generate local evidence to inform practice.

European guidelines have similarly emphasized the need to customize corticosteroid usage with specific gestational age ranges and cautioned against a "one size fits all" method. They call for greater clinical judgment when considering ACS administration in late preterm pregnancies, aiming to limit unnecessary exposure and ensure that potential benefits outweigh possible adverse risks (15). With the global debate ongoing and the current evidence being limited (especially from low- and middle-income countries), it is important to investigate fetal outcomes in late preterm infants who do not receive antenatal corticosteroids. This study will address this gap by evaluating outcomes in this demographic and contributing to evidence-based management of late preterm births at local clinical levels.

Objective: To evaluate fetal outcomes in preterm births between 34 weeks and 36 weeks 6 days of gestation who did not receive antenatal corticosteroids, in order to inform clinical decision-making.

MATERIALS AND METHODS

Design: Prospective Observational Study.

Study setting: The study was conducted at the Department of Obstetrics and Gynecology, Observational study conducted in Secondary care hospital District Headquarter Mirpurkhas.

Duration: The study was conducted over a six-month duration, from January 2024 to June 2024.

Inclusion Criteria:

All women with singleton pregnancies who gave birth from 34 weeks 0 days to 36 weeks 6 days of gestation and received no dose of antenatal corticosteroids were eligible. Early ultrasound dating or a reliable last menstrual period (LMP) was required to determine gestational age. Only live births were included. All neonates were followed up for early fetal outcomes, including respiratory distress, NICU admission, hypoglycemia, feeding issues, and neonatal death.

Exclusion Criteria

Women with multiple gestational pregnancies, known fetal congenital anomalies, intrauterine fetal demise, gestational diabetes, pre-gestational diabetes, meningitis, severe preeclampsia, antepartum hemorrhage, those who received antenatal corticosteroids (even a single dose), and those with incomplete medical records were excluded.

Methods

Eligible subjects were identified when admitted to the labor and delivery unit. Once informed consent was obtained, maternal obstetric histories were taken, which included maternal age, parity, gestational age, mode of delivery, and antenatal complications. Only infants who met the inclusion criterion and had confirmed no antenatal steroids were included in this study. Infant outcomes were notated right following delivery and during the early neonatal period. Important infant outcomes, assessed within the first 7 days of life, included infant birth weight, Apgar scores at 1 minute and 5 minutes, signs of respiratory distress, need for NICU admission, hypoglycemic episodes, feeding difficulties, and early neonatal death. Data were collected using a standardized proforma to ensure consistency and accuracy, then entered and analyzed in SPSS version 25. The proforma included maternal and neonatal variables such as gestational age, mode of delivery, and neonatal outcomes within the first 7 days. Using frequencies and percentages, categorical descriptive statistics were performed on

maternal and infant data. The outcome measures were compared by polarity of gestational age (32–33+6, 34–36+6), to investigate any trends in morbidity and mortality with gestational maturity in infants who did not receive antenatal steroids.

RESULTS

A total of 180 women met the inclusion criteria and delivered between 34 weeks 0 days and 36 weeks 6 days of gestation without receiving antenatal corticosteroids. The mean maternal age was 28.4 ± 5.2 years, and the majority of participants were multigravida (63.3%). Among the neonates, 95 (52.8%) were male and 85 (47.2%) were female. The distribution of deliveries by gestational age is presented in Table 1.

Table 1: Distribution of Participants by Gestational Age (n = 180)

Gestational Age (weeks)	Number of Deliveries	Percentage (%)
34 – 33+6	48	26.7
34 – 35+6	67	37.2
36 – 36+6	65	36.1

Among the neonates, the mean birth weight was 2.34 ± 0.41 kg. Low birth weight (<2.5 kg) was observed in 122 (67.8%) neonates, most commonly among those born before 34 weeks. Apgar scores at 1 and 5 minutes were lower in earlier gestations but generally indicated good adaptation, particularly in the 36- 36+6 weeks group, aligning with the Irish National SOGP Guideline's observation of favourable outcomes in late preterm infants without ACS in well-resourced settings. In this resource-limited setting, however, 83 neonates (46.1%) developed respiratory distress, with the highest incidence in the 34-34+6 weeks group (n=35, 72.9%). NICU admission was required in 98 neonates (54.4%), primarily due to respiratory issues, feeding intolerance, or hypoglycemia.

Table 2: Neonatal Outcomes by Gestational Age Group

Outcome	34–33+6 weeks (n=48)	34–35+6 weeks (n=67)	36–36+6 weeks (n=65)
Respiratory Distress	35 (72.9%)	31 (46.3%)	17 (26.2%)
NICU Admission	39 (81.3%)	34 (50.7%)	25 (38.5%)
Hypoglycemia	16 (33.3%)	12 (17.9%)	7 (10.8%)
Feeding Difficulties	18 (37.5%)	13 (19.4%)	9 (13.8%)

Neonatal mortality within 7 days occurred in 9 cases (5%), with 6 deaths in the 34-34+6 weeks group and 3 in the 35-35+6 weeks group. No casualties were reported in the 36- 36+6 weeks group, supporting the Irish National SOGP Guideline's assertion that outcomes are generally favourable in late preterm infants, particularly closer to term, even without ACS. Mortality was associated with severe respiratory distress and prematurity-related complications, likely exacerbated by limited neonatal care resources.

Table 3: Early Neonatal Mortality and Associated Complications

Gestational Age Group	Neonatal Deaths	Major Complications Present
34–33+6 weeks	6	RDS, hypoglycemia, sepsis
34–35+6 weeks	3	RDS, feeding difficulties
36–36+6 weeks	0	–

The data indicate an inverse relationship between gestational age and adverse outcomes, with neonates at 36-36+6 weeks demonstrating significantly better outcomes, including lower rates of respiratory distress (26.2%), NICU admission (38.5%), and no mortality. These findings align with the Irish

National SOGP Guideline, which suggests that sufficient gestational maturity at this stage supports favourable outcomes without ACS in settings with robust neonatal care. However, in this resource-limited setting, the absence of ACS was associated with higher morbidity, particularly before 35 weeks, suggesting that context-specific factors, such as access to advanced neonatal care, significantly influence outcomes.

DISCUSSION

Preterm birth remains a significant contributor to neonatal morbidity and mortality, even in cases classified as late preterm, i.e., between 34 weeks and 36 weeks and 6 days of gestation. The Irish National SOGP Guideline suggests that late preterm infants in well-resourced settings have favorable outcomes without ACS due to advanced neonatal care infrastructure, which mitigates complications such as respiratory distress and hypoglycemia. The high rates of respiratory distress (46.1%), NICU admissions (54.4%), hypoglycemia, and early neonatal mortality (5%), particularly before 35 weeks, highlight the vulnerability of late preterm infants without ACS. These findings contrast with the Irish National SOGP Guideline, which does not recommend routine ACS for 34–36+6 weeks, citing favorable outcomes in high-resource settings with advanced neonatal care infrastructure. The most common complications observed in this study were respiratory distress, hypoglycemia, NICU admissions, and early neonatal death. Respiratory distress syndrome (RDS) was noted in nearly half of the neonates overall, with the highest frequency among those born between 34–33+6 weeks, consistent with existing literature. Consistent with findings at Observational study conducted in Secondary care hospital District Headquarter Mirpurkhas, the absence of antenatal corticosteroids in late preterm births was associated with unfavorable neonatal outcomes, particularly respiratory distress and NICU admissions, highlighting the need for targeted ACS protocols in similar settings.

Ninan et al. (1) in their meta-analysis concluded that antenatal corticosteroid use in preterm births significantly reduces the incidence of RDS, emphasizing its importance in fetal lung maturation. In our study, the absence of ACS correlated with a higher burden of respiratory complications, which aligns with findings from other observational studies and randomized controlled trials (2). Late preterm neonates often present a clinical dilemma. While their outcomes are generally better than those born before 34 weeks, they still face complications not typically encountered in term infants. The modest but significant benefits of ACS for late preterm births have been highlighted in systematic reviews, including those by Üstün et al. (3) and Aviram et al. (4), who noted improvements in neonatal respiratory function and reduced NICU admissions following ACS administration. Our findings, by contrast, show the impact of withholding ACS, particularly in the 34–35 weeks group, where the majority of adverse outcomes were concentrated. The absence of ACS in our cohort likely exacerbated respiratory complications, supporting the potential benefit of targeted ACS use. Unlike the Irish/SOGP guidelines, which suggest sufficient gestational maturity mitigates risks without ACS, our findings indicate significant morbidity in resource-limited settings. The SMFM, WHO, and FIGO guidelines advocate selective ACS use when delivery is imminent and neonatal care is limited, aligning with our results.

The SMFM guidelines revised in 2021 (5) support the targeted use of ACS in late preterm pregnancies only when there is a high likelihood of delivery within seven days, and the maternal-fetal condition warrants it. This precaution is aimed at balancing the potential benefits against risks such as neonatal hypoglycemia and unnecessary exposure. The WHO guidelines similarly advocate for ACS use when neonatal and obstetric care is adequate and the risk of delivery is imminent (6). In our study, the absence of ACS likely reflects either missed opportunities or intentional avoidance in borderline gestations. However, given the significant respiratory and metabolic complications observed, especially among infants born before 35 weeks, the results underscore a need for careful reconsideration of local ACS protocols.

Moreover, the findings resonate with FIGO's recommendations (7), which discourage blanket ACS administration for all late preterm cases. Rather, the emphasis is on individualized decision-making. Neonates born in the later segment of the preterm period, particularly after 36 weeks, showed

markedly fewer complications in this study, supporting the notion that the benefit of ACS diminishes as gestational age approaches term. The current results are consistent with prior studies demonstrating minimal benefit—and even potential harm—from ACS in infants born at or near term (8, 9). Concerns regarding overuse of corticosteroids, particularly in cases that ultimately deliver at term, have been well documented. McKinzie et al. (10) reported differences in neonatal outcomes in term infants exposed to ACS, suggesting that indiscriminate use may not be harmless.

Deshmukh and Patole (11) further noted in their meta-analysis that while ACS reduced respiratory morbidity in late preterm infants, it increased the risk of neonatal hypoglycemia. This complication was evident in our cohort as well, particularly among infants born before 35 weeks, again highlighting the fine balance required in administering ACS. Additionally, the timing of corticosteroid administration relative to delivery significantly affects outcomes. Gulersen et al. (12) observed that prolonged latency between ACS administration and delivery diminishes its benefits. This reinforces the challenge of accurately predicting delivery timing and underscores the potential downside of treating patients who ultimately deliver later than anticipated. Since none of the infants in our study received ACS, the implications of this timing mismatch were avoided, but the severity of adverse outcomes in the absence of ACS remains clear. The ALPS follow-up study by Gyamfi-Bannerman et al. (13) added a long-term dimension to this debate by evaluating neurodevelopmental outcomes.

However, initial respiratory benefits were reported, the long-term cognitive and behavioral advantages were not significant. This suggests that while ACS can reduce immediate complications, it may not translate into long-term developmental gains, at least in the late preterm population. The inconsistency in long-term outcomes further complicates the decision-making process and suggests that blanket ACS usage may not always be warranted. Moreover, Kearsey et al. (14) evaluated how clinical practice changed after the ALPS trial, noting variations in the uptake of recommendations, which reflects ongoing uncertainty in clinical settings. The variability in ACS administration observed globally points to the need for local studies—such as ours—to generate context-specific evidence that considers resource availability, maternal health status, and delivery circumstances (15).

Lastly, the findings of this study indicate that the absence of antenatal corticosteroids in late preterm births, particularly in those delivered before 35 weeks, is associated with significantly higher rates of neonatal morbidity and mortality. These results support the judicious use of ACS in select cases within the late preterm period, in alignment with international guidelines. However, the decision to administer corticosteroids must be based on a careful assessment of risks, gestational age, and available neonatal care. Local protocols should consider the growing body of evidence advocating for individualized, evidence-based approaches to optimize outcomes for both mothers and neonates.

CONCLUSION

This study highlights the significant impact of antenatal corticosteroid (ACS) non-administration on fetal outcomes in late preterm births (34 to 36+6 weeks). Neonates born without ACS exposure, particularly before 35 weeks, exhibited higher rates of respiratory distress, hypoglycemia, feeding difficulties, NICU admissions, and early neonatal mortality. These findings underscore the critical role of ACS in enhancing fetal lung maturity and improving short-term neonatal outcomes, especially in the earlier spectrum of late preterm gestation. These findings contrast with the Irish National SOGP Guideline, which reports favorable outcomes without ACS in high-resource settings, likely due to differences in neonatal care access. As gestational age increases, complications decrease, but risks remain notable without ACS. In line with SMFM, WHO, and FIGO recommendations, targeted ACS use should be considered in resource-limited settings, with careful assessment of risks like hypoglycemia. Therefore, adopting context-specific, evidence-based ACS protocols in secondary care settings across Pakistan is essential to optimize perinatal outcomes, reduce complications, and improve neonatal survival in late preterm deliveries.

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