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Impact Of Antenatal Corticosteroids On Neonatal Hypoglycemia And Hyperbilirubinemia In Preterms - A Prospective Cohort Study

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ABSTRACT

Background: Antenatal corticosteroids (ACS) are routinely administered to pregnant women at risk of preterm delivery to promote fetal lung maturation and reduce neonatal morbidity and mortality. However, emerging evidence suggests that ACS may influence neonatal outcomes such as hypoglycemia and hyperbilirubinemia, with inconsistent findings across studies.

Objectives: To evaluate the association of antenatal corticosteroid exposure with neonatal hypoglycemia and hyperbilirubinemia in preterm neonates.

Methods: This prospective cohort study was conducted over 1.5 years at R.L. Jalappa Hospital. A total of 120 preterm neonates (<37 weeks gestation) were enrolled—60 with maternal ACS exposure and 60 without. Neonates with maternal diabetes, sepsis, hypoxic ischemic encephalopathy, or Rh incompatibility were excluded. Blood glucose was monitored every 6 hours for 72 hours post-birth. Hyperbilirubinemia was assessed via transcutaneous or serum bilirubin every 12 hours. Data were analysed using SPSS v21.0, with $p < 0.05$ considered statistically significant.

Results: Hypoglycemia was significantly more common in the ACS group (55%) compared to the non-ACS group (5%) ($p < 0.001$), with an odds ratio of 23.22 (95% CI: 6.53–82.48). In contrast, the rate of hyperbilirubinemia was comparable between groups (41.7% in ACS vs. 53.3% in non-ACS, $p = 0.20$).

Conclusion: Antenatal corticosteroid exposure in preterm neonates is significantly associated with an increased risk of neonatal hypoglycemia but not hyperbilirubinemia. These findings highlight the importance of vigilant glucose monitoring in ACS-exposed preterm infants, particularly during the first 72 hours of life.

Keywords: *maternal, antenatal corticosteroids, Hypoglycemia, hyperbilirubinemia, preterm, neonate.*

1. INTRODUCTION

Preterm birth, affecting approximately 14.8 million infants annually, is a leading cause of neonatal mortality, accounting for nearly 35% of neonatal deaths worldwide.[1] To improve outcomes, antenatal corticosteroids (ACS) are widely administered to mothers at risk of preterm delivery, with proven benefits in reducing respiratory distress syndrome(RDS), intraventricular haemorrhage(IVH), necrotizing enterocolitis(NEC), and neonatal intensive care unit(NICU) admissions.[2,3]

However, ACS may also lead to adverse metabolic outcomes. Maternal hyperglycemia, a known effect of corticosteroids, can cause fetal hyperinsulinemia and predispose neonates to postnatal hypoglycemia through altered glucose homeostasis mechanisms.[4,5] Additionally, the effect of ACS on neonatal hyperbilirubinemia remains unclear. While some studies suggest

that ACS may inhibit bilirubin uptake and binding, others report a protective role by accelerating hepatic enzyme maturation, particularly UDP-glucuronosyltransferase.[6–8]

Neonatal hypoglycemia and hyperbilirubinemia are clinically significant, potentially leading to neurodevelopmental impairments and bilirubin-induced neurologic dysfunction (BIND), respectively.[9] Despite this, limited studies have addressed the association of ACS with these metabolic complications in preterm neonates. [4] This study aims to evaluate the impact of antenatal corticosteroid exposure on the burden of neonatal hypoglycemia and hyperbilirubinemia in preterm.

2. MATERIAL AND METHODS

This prospective cohort study was conducted over 1.5 years in the NICU of R.L. Jalappa Hospital, affiliated with Sri Devaraj Urs Medical College. Ethical clearance was obtained, and informed consent was secured from parents.

Preterm neonates (<37 weeks gestation) admitted to the hospital were enrolled and divided into two groups based on whether maternal antenatal corticosteroid (ACS) exposure was present. Mothers who received a standard course of dexamethasone (6 mg IM every 12 hours x 4 doses) or betamethasone (12 mg IM every 24 hours x 2 doses) prior to delivery were considered ACS-exposed. Neonates with maternal diabetes, chorioamnionitis, Rh incompatibility, major congenital anomalies, hypoxic-ischemic encephalopathy, or sepsis were excluded.

Maternal and neonatal data including gestational age, birth weight, mode of delivery, and ACS details, were recorded. Gestational age was determined based on last menstrual period or ultrasonography. Preterm were classified as moderate to late preterm, very preterm, and extreme preterm based on gestational age. Birth weight was categorised as small for gestational age (SGA), appropriate for gestational age(AGA), or large for gestational age (LGA).[9,10]

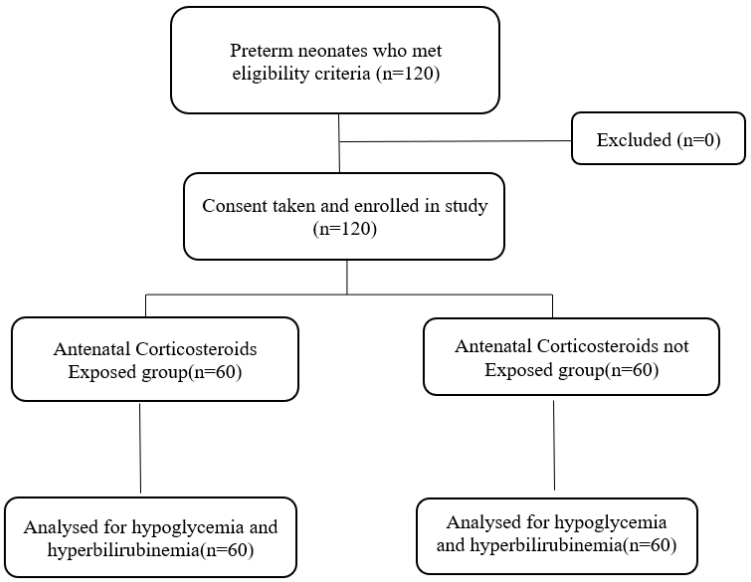
Neonatal hypoglycemia was defined as blood glucose <45 mg/dL, measured via heel-prick using Sinocare Safe AQ glucometer 1 hour after birth and every 6 hours for 72 hours.[11] Hyperbilirubinemia was defined as bilirubin levels within phototherapy range, assessed using transcutaneous or serum bilirubin every 12 hours for 72 hours, and managed as per NICE guidelines.[12]

Sample size was estimated based on the difference in incidence of hypoglycemia between corticosteroid-exposed group and the nonexposed control group as reported in the study by Nuran Ustun et al.[13] with an observed difference of 7.6%. Considering 15% incidence of hypoglycemia, with 95% confidence and 80% power, yielding 60 neonates per group. Data were analysed using SPSS v21.0. Normality was assessed using the Shapiro–Wilk test. Continuous variables were compared using Student's t-test, and categorical variables using the Chi-square test. Multivariate logistic regression was used to adjust for confounders. Adjusted odds ratios (aORs) with 95% confidence intervals (CIs) were reported, and $p < 0.05$ was considered statistically significant.

3. RESULTS

A total of 120 preterm neonates were enrolled, with 60 in the ACS-exposed group and 60 in the non-exposed group as shown in figure1.

Figure 1: Flow diagram for collection and analysis of data



Baseline characteristics, including gestational age, birth weight, and mode of delivery, were comparable between the two groups(Table 1).

Table 1. Baseline Characteristics of neonates ACS and Non-ACS Groups(n=60 each)

	Variable	ACS* Group(%) (n=60)	Non-ACS* Group(%) (n=60)	P value
Gestational age	Moderate-late preterm	39(65%)	42(70%)	0.048
	Very preterm	21(35%)	13(21.7%)	
	Extreme preterm	0(0%)	5(8.3%)	
Birth weight	Mean birth Weight ± SD@ (kg)	1.63 ± 0.42	1.67 ± 0.53	0.014
Weight for gestational age	AGA^	40(66.7%)	40(66.7%)	1.000
	SGA+	19(31.7%)	18(30.0%)	
	LGA#	1(1.6%)	2(3.3%)	
Mode of delivery	LSCS$ (%)	46(76.6%)	32(53.3%)	0.013
	Vaginal Delivery (%)	14(23.4%)	28(46.7%)	

*ACS-Antenatal corticosteroids, ^AGA- Appropriate for gestational age, +SGA-Small for gestational age, #LGA-Large for gestational age, $LSCS-Lower segment caesarean section, @SD-standard deviation

Table 2: Association between ACS and hypoglycaemia

	Hypoglycaemia		P value	Odds ratio
	Present	Absent		
With ^ACS(n=60)	33 (55.0%)	27 (45.0%)	<0.001*	23.22 (6.53 – 82.48)
Without ^ACS (n=60)	3 (5.0%)	57 (95.0%)		
Total(n=120)	36 (30.0%)	84 (70.0%)		

*p value <0.05; Hence statistically significant; ^ACS- Antenatal corticosteroids

Table 3: Association between ACS and hyperbilirubinemia

	Hyperbilirubinemia		P value	Odds ratio
	Present	Absent		
With *ACS (n=60)	25 (41.7%)	35 (58.3%)	.201	0.625 (0.304 – 1.286)
Without *ACS (n=60)	32 (53.3%)	28 (46.7%)		
Total(n=120)	57 (47.5)	63 (52.5)		

*ACS- Antenatal corticosteroids

It was observed that 55% of neonates in the ACS group had hypoglycaemia against 5% in the non-ACS group. Neonates in the ACS group had almost 23.22 times(95% CI: 6.53-82.48) odds of developing hypoglycemia compared to the non-ACS group, which was statistically significant with p<0.001(Table 2). It was observed that hyperbilirubinemia was present in 41.7% and 53.3% of the ACS and non-ACS groups, respectively, which was not statistically significant (p=.201)(Table 3).

4. DISCUSSION

This prospective cohort study evaluated the association of ACS exposure with neonatal hypoglycemia and hyperbilirubinemia among 120 preterm neonates. A significant association was found between ACS exposure and

hypoglycemia, while no significant link was identified with hyperbilirubinemia.

In this study, 55% of neonates in the ACS group developed hypoglycemia compared to 5% in the non-ACS group, with an adjusted odds ratio of 23.22. This aligns with findings by Üstün et al.[13] and Gyamfi-Bannerman et al.,[14] who also reported increased rates of neonatal hypoglycemia following corticosteroid exposure, especially in late preterm. The mechanism is thought to involve steroid-induced maternal hyperglycemia, leading to fetal hyperinsulinemia and postnatal glucose dysregulation.

Interestingly, hypoglycemia was prevalent among neonates who received two doses of ACS, suggesting a dose-dependent effect. However, no significant association was found between hypoglycemia and the type of corticosteroid (betamethasone vs. dexamethasone) or the timing of administration. These findings are consistent with studies by Zhou et al. [15] and di Pasquo et al.,[16] who noted that complete steroid courses and longer intervals post-ACS administration may increase hypoglycemia risk.

Conversely, the incidence of hyperbilirubinemia did not differ significantly between the ACS (41.7%) and non-ACS (53.3%) groups. This finding supports the conclusions of El-Hawary et al.[17] and Üstün et al.,[13] who also observed no statistically significant impact of ACS on neonatal bilirubin levels. While some studies have suggested that corticosteroids may enhance hepatic enzyme maturation and reduce bilirubin levels, others propose potential inhibitory effects on bilirubin uptake and binding. The lack of association in our study underscores the complexity of this relationship and suggests that ACS does not independently contribute to increased hyperbilirubinemia risk in preterm neonates.

Our study reinforces the need for targeted glucose monitoring in exposed neonates. Given the transient yet clinically relevant nature of steroid-induced hypoglycemia, early postnatal screening and management are essential.

The study limitations, being a single-centre study with a relatively small sample size, long-term outcomes such as neurodevelopmental follow-up were not assessed. Future multicentric studies with larger cohorts and extended follow-up are recommended to validate these findings and assess the long-term implications of ACS exposure.

5. CONCLUSION

This study demonstrated a significant association between antenatal corticosteroid (ACS) exposure and an increased risk of neonatal hypoglycemia in preterm infants, particularly following complete steroid courses. No significant association was found between ACS exposure and neonatal hyperbilirubinemia. These findings support the continued use of ACS in preterm birth management due to its well-established benefits but emphasize the need for vigilant glucose monitoring during the early postnatal period in ACS-exposed neonates. Routine bilirubin surveillance protocols remain appropriate, as ACS did not confer additional risk for hyperbilirubinemia in this population.

REFERENCES

[1] Chawanpaiboon S, Vogel JP, Moller AB, Lumbiganon P, Petzold M, Hogan D, et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. Lancet Glob Health 2019;7(1):e37–46.

[2] Gyamfi-Bannerman C, Thom EA, Blackwell SC, Tita ATN, Reddy UM, Saade GR, et al. Antenatal Betamethasone for Women at Risk for Late Preterm Delivery. New England Journal of Medicine 2016;374(14):1311–20.

[3] McGoldrick E, Stewart F, Parker R, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database of Systematic Reviews 2020;2021(2).

[4] Pettit KE, Tran SH, Lee E, Caughey AB. The association of antenatal corticosteroids with neonatal hypoglycemia and hyperbilirubinemia. The Journal of Maternal-Fetal & Neonatal Medicine 2014;27(7):683–6.

[5] Olefsky J, Nolan J. Insulin resistance and non-insulin-dependent diabetes mellitus: cellular and molecular mechanisms. Am J Clin Nutr 1995;61(4):980S-986S.

[6] Németh I, Szeleczki T, Boda D. Hyperbilirubinemia and urinary D-glucaric acid excretion in premature infants following antepartum dexamethasone treatment. J Perinat Med 1981;9(1):35–9.

[7] Moisiadis VG, Matthews SG. Glucocorticoids and fetal programming part 1: outcomes. Nat Rev Endocrinol 2014 Jul 27;10(7):391–402.

[8] Moisiadis VG, Matthews SG. Glucocorticoids and fetal programming part 2: mechanisms. Nat Rev Endocrinol 2014;10(7):403–11.

[9] Goldenberg RL, Culhane JF, Iams JD, Romero R. Epidemiology and causes of preterm birth. The Lancet 2008;371(9606):75–84.

[10] Hamer J, Jabeen M, Gurney L, Morris RK, Morton VH. A practical guide to understanding fetal growth and

newborn birthweight charts. Obstet Gynaecol Reprod Med 2024;34(9):244–51.

[11] Adamkin DH. Neonatal hypoglycemia. Semin Fetal Neonatal Med 2017 ;22(1):36–41.

[12] Amos RC, Jacob H, Leith W. Jaundice in newborn babies under 28 days: NICE guideline 2016 (CG98). Arch Dis Child Educ Pract Ed 2017;102(4):207–9.

[13] Üstün N, Hocaoğlu M, Turgut A, Arslanoğlu S, Ovalı F. Does antenatal corticosteroid therapy improve neonatal outcomes in late preterm birth? The Journal of Maternal-Fetal & Neonatal Medicine 2022 ;35(1):11–7.

[14] Gyamfi-Bannerman C, Jablonski KA, Blackwell SC, Tita ATN, Reddy UM, Jain L, et al. Evaluation of Hypoglycemia in Neonates of Women at Risk for Late Preterm Delivery: An Antenatal Late Preterm Steroids Trial Cohort Study. Am J Perinatol 2023;40(05):532–8.

[15] Zhou C, Zheng W, Zhang M, Tung TH, Wang L, Wang L. Effects of antenatal corticosteroids on neonatal blood glucose fluctuation in late-preterm infants. Front Pediatr 2022;10.

[16] di Pasquo E, Saccone G, Angeli L, Dall'Asta A, Borghi E, Fieni S, et al. Determinants of neonatal hypoglycemia after antenatal administration of corticosteroids (ACS) for lung maturation: Data from two referral centers and review of the literature. Early Hum Dev 2020;143:104984.

[17] El-Garhy MA GA. Antenatal Corticosteroid Exposure As a Risk Factor For Neonatal Hyperbilirubinemia. Fayoum University Medical Journal 2021;8(4):12–9.