Dexamethasone Administration in Diabetic Pregnant Women Undergoing Early-Term Cesarean-Sections: Effects on Neonatal Respiratory Morbidity and Hypoglycemia

Original Article

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ABSTRACT

Background: Babies born to mothers with diabetes mellitus have a higher chance of developing respiratory complications and hypoglycemia compared to those born to non-diabetic mothers. It is unclear if the use of antenatal corticosteroids after 37 weeks gestation alters these risks. The objective of this study was to examine the effect of administering Dexamethasone prior to elective early term cesarean delivery on neonatal respiratory morbidity and hypoglycemia in diabetic pregnant women.

Materials and Methods: This retrospective case control study analyzed the effect of antenatal Dexamethasone administration on pregnant women with diabetes who had undergone elective early term cesarean delivery. We focused on measuring the number of admissions to the neonatal intensive care unit (NICU) due to respiratory morbidity and hypoglycemia as our main outcomes.

Results: We found that Dexamethasone administration prior to elective early term cesarean delivery was associated with an increased incidence of neonatal hypoglycemia (12.3% vs 5.3%, *p value* = 0.036), but did not significantly impact neonatal respiratory morbidity (9.6% vs 11.2%, *p value* = 0.479), nor the overall admission to NICU (21.9% vs 16.5%, *p value* = 0.323).

Conclusion: Administering Dexamethasone to women with diabetes before elective term cesarean delivery may raise the likelihood of their newborns being admitted to neonatal intensive care unit because of hypoglycemia, without showing any substantial improvement in the neonatal respiratory morbidity.

Key Words: CS, dexamethasone, neonatal hypoglycemia, RDS, tachypnea.

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INTRODUCTION

Compared to vaginal birth, infants born via cesarean delivery are at a higher risk of respiratory distress syndrome (RDS), transient tachypnea of the newborn (TTN), and admission to the neonatal intensive care unit (NICU)[1]. In cases where a planned cesarean delivery is scheduled before 39 weeks of gestation, corticosteroids may be considered to diminish the risk of neonatal respiratory problems[2]. However, there is limited evidence on the benefits versus the potential harms of administering corticosteroids during late pregnancy. Antenatal corticosteroids may elevate the risk of neonatal hypoglycemia in term neonates[3,4]. A Cochrane systematic review has evaluated the effects of antenatal corticosteroids given before planned cesarean delivery at term, but it remains unclear whether these medications decrease the risk of RDS. Antenatal corticosteroids may reduce admission to the NICU for respiratory morbidity, but the evidence is currently insufficient to draw any definite conclusions[5].

Women with diabetes have been omitted from most randomized controlled trials of antenatal corticosteroids due to fears about their probable effects on glycemic control[6,7]. Although guidance from NICE recommends that diabetes should not be a contraindication to antenatal corticosteroids for fetal lung maturation[8], it is unclear whether early-term antenatal corticosteroid administration is beneficial for women with gestational or pre-gestational diabetes[9,10]. Indeed, pregnant women with diabetes who take corticosteroids may experience unpredictable maternal hyperglycemia and hypoglycemia in their newborns [11,12].

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The purpose of this study was to compare the rates of respiratory morbidity in pregnant women with diabetes who underwent elective early term cesarean delivery (ETCD) with and without maternal Dexamethasone administration. Additionally, the study evaluated the impact of Dexamethasone on neonatal hypoglycemia.

MATERIALS AND METHODS

During a period of 5 years, a retrospective case control study was carried out on 242 women who gave birth to a singleton baby. The study included all women who were admitted to the obstetric department of Suez Hospital in Egypt between January 1st, 2018 and December 31st, 2022, and data were collected from a hospital database. The study was approved by the Local Institutional Review Board and Ethics Committee (SUEZ Med-IRB/2023-No.4). The inclusion criteria for the study were pregnant women with diabetes who underwent scheduled cesarean section with a singleton pregnancy between 36 0/7 and 38 6/7 weeks of gestational age. The study excluded women who had emergency cesarean section, scheduled cesarean section before 37 weeks or after 38+6/7 weeks of gestation, scheduled cesarean section for twins, and those without diabetes.

The research collected baseline data on all included women, such as demographic information, obstetric and medical history, body mass index (BMI) at the first visit, HbA1C at the third trimester, indications for cesarean delivery, gestational age at delivery, neonatal gender, and birth weight. After analyzing the data, the women were divided into two study groups: group I (Dexamethasone group) incorporated diabetic pregnant women who received Dexamethasone before elective ETCD, while group II (control group) involved diabetic women who did not receive Dexamethasone. The study used the 2006 WHO criteria to diagnose gestational diabetes mellitus and Pre-gestational diabetes mellitus[13].

The primary outcome measures of the research were neonatal admission to NICU due to respiratory distress syndrome or transient tachypnea of the newborn and neonatal hypoglycemia. The secondary outcome measures included neonatal Apgar score, length of neonates stay in NICU, and need for surfactant therapy. The study diagnosed transient tachypnea of the newborn clinically if there was tachypnea developed immediately after birth or within two hours, with other predictable signs of respiratory distress, while respiratory distress syndrome was diagnosed when there was grunting, retractions, or other typical distress symptoms and usually lasted more than two days[14]. Finally, neonatal hypoglycemia was defined as per the American Academy of Pediatrics Committee on Fetus and Newborn which adopted a value of less than 47 mg/dL to define hypoglycemia in the first 48 hours of life[15].

Statistical Analysis

The study presented quantitative data with a parametric distribution as mean and standard deviations, and quantitative data with a non-parametric distribution as median and range. Qualitative variables were presented as number and percentages. The Chi-square test was used to compare the groups for qualitative data, while the Mann-Whitney U test or Student t-test was used for quantitative data, as appropriate. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated for the outcomes of interest. To adjust for various factors such as age, BMI, parity, gestational age at delivery, bronchial asthma, hypertensive disorders with pregnancy, diabetes mellitus, smoking habits, neonatal gender, and neonatal birth weight at delivery, multivariate logistic regression was used. The final models were tested with the Hosmer Lemeshow goodness-of-fit test. The Shapiro–Wilk test was used to evaluate the normality of distribution of the continuous variables. A p-value of less than 0.05 was considered significant. All analyses were performed using the Statistical Package for the Social Sciences, version 22.0 (SPSS Inc., Chicago, IL, USA), and GraphPad Prism, version 6 (GraphPad Software Inc., La Jolla, CA, USA).

RESULTS

After examining our hospital records, we found that 242 women with diabetes who had a scheduled cesarean section with a singleton pregnancy between 36 0/7 and 38 6/7 weeks of gestational age were included in our research study. We divided them into two groups: group I (Dexamethasone group) which consisted of 73 women and group II (control group) which included 169 women.

The demographic characteristics of both groups were compared, and there was no significant difference in maternal age, BMI, parity, gestational age, HbA1C, chronic maternal illness, and type of diabetes during pregnancy, nor the neonatal birth weight, or gender between the two groups (Table 1).

Furthermore, we found no statistically significant difference between the two groups regarding the total admissions of neonates to NICU, Apgar score at 1 minute and 5 minutes, and length of stay of neonates in the NICU. Additionally, we discovered that Dexamethasone administration prior to elective ETCD had no significant impact on the neonatal respiratory morbidity (9.6% vs 11.2%, *p value* = 0.479). However, we did find that antenatal Dexamethasone administration was associated with the incidence of neonatal hypoglycemia (12.3% vs 5.3%, *p value* = 0.036) (Table 2).

In our multivariate analysis, we found that diabetic pregnant women who were administered Dexamethasone prior to elective ETCD had higher odds for neonatal hypoglycemia (adjusted OR 2.835, 95% CI 1.023 - 7.856; *p value* = 0.045). However, we also found that Dexamethasone administration had no association with any of the remaining clinical outcome measures (Table 3).

Table 1: Demographic and clinical characteristics.

Variables	Dexamethasone (n= 73)	Control (n= 169)	*P value*
Age	29.7 ± 3.8	28.8 ± 4.7	0.131*
BMI	32.4 ± 3.3	32.5 ± 3.3	0.829*
Parity	3 (0-5)	3 (0-6)	0.749**
GA at delivery	37.9 ± 0.5	38 ± 0.4	0.110*
HbA1C	5.9 ± 0.3	5.7 ± 0.5	0.114*
Neonatal birth weight	3.1 ± 0.6	3.2 ± 0.5	0.181*
Smoking	1 (1.4)	2 (1.2)	0.904†
Bronchial Asthma	1 (1.4)	3 (1.8)	0.821†
Hypertension (any)	6 (8.2)	13 (7.7)	0.889†
Suspected FGR	2 (2.8)	4 (2.4)	0.864†
Neonatal gender			
Male	35 (48)	78 (46.2)	0.798†
Female	38 (52)	91 (43.8)	
Type of DM			
GDM	65 (89)	148 (87.6)	0.748†
Pre-gestational DM	8 (11)	21 (12.4)	
Indications for CD			
Previous CD	56 (76.7)	136 (80.5)	
Malpresentaion	7 (9.6)	13 (7.7)	0.870†
Placenta previa	1 (1.4)	2 (1.2)	
Fetal macrosomia	5 (6.8)	13 (7.7)	
Others	4 (5.5)	5 (2.9)	

BMI, body mass index; GA, gestational age; DM, diabetes mellitus; FGR, fetal growth restriction; CD, cesarean delivery.
Data are presented as mean ± standard deviation, median and range, or number (percent).
* Unpaired student t test was used; **Mann Whitney U test was used; †Chi-square test was used.
P value < 0.05 is significant.

Table 2: Clinical outcome measures of early term cesarean delivery in the study population.

Variables	Dexamethasone (n= 73)	Control (n= 169)	*P value*
Total admissions to NICU	16 (21.9)	28 (16.5)	0.323
Neonatal RDS/TTN	6 (9.6)	19 (11.2)	0.479
Neonatal hypoglycemia	10 (12.3)	9 (5.3)	0.036
Apgar score 1 minute	8 (6-9)	8 (6-9)	0.453
Apgar score 5 minutes	9 (8-10)	9 (8-10)	0.177
NICU length of stay	3 (1-8)	2 (1-7)	0.582
Prolonged NICU hospital staying (in days)			
0-5 days	70 (95.9)	164 (97)	0.646
More than 5 days	3 (4.1)	5 (3)	
Need for surfactant	0	0	
Neonatal death	0	0	

NICU, neonatal intensive care unit; RDS, respiratory distress syndrome; TTN, transient tachypnea of newborn.

Chi-square test was used. *P value* < 0.05 is significant.

Table 3: Association between Dexamethasone therapy and neonatal outcomes.

Variables	Unadjusted OR (CI)	P value	*Adjusted OR (CI)	*P value*
NICU admissions	1.414 (0.711-2.810)	0.323	1.195 (0.553-2.583)	0.651
RDS/TTN	0.707 (0.27-1.85)	0.480	0.451 (.133-1.524)	0.200
Hypoglycemia	2.822 (1.095-7.271)	0.032	2.835 (1.023-7.856)	0.045
Prolonged hospital staying	1.406 (0.327-6.044)	0.647	1.241 (0.263-5.849)	0.785

OR, odds ratio; CI, confidence Interval; NICU, neonatal intensive care unit; RDS, respiratory distress syndrome; TTN, transient tachypnea of newborn.

* Odds ratio were adjusted for age, BMI, parity, GA at delivery, bronchial asthma, hypertensive disorders with pregnancy, diabetes mellitus, smoking habits, neonatal gender, and neonatal birth weight at delivery.

P-value< 0.05 is significant.

DISCUSSION

In this study, we analyzed the incidence of respiratory problems and hypoglycemia in newborns of diabetic women who underwent elective early term cesarean delivery. Our data indicate that the administration of Dexamethasone before elective ETCD was found to be linked to a higher incidence of neonatal hypoglycemia, with 12.3% of newborns being affected compared to 5.3% in those who did not receive Dexamethasone. However, the study did not find any significant impact of Dexamethasone on neonatal respiratory morbidity, with 9.6% of newborns experiencing breathing difficulties in the Dexamethasone group compared to 11.2% in the group that did not receive the medication.

According to major international guidelines, the routine use of antenatal corticosteroids prior to cesarean section in late gestation is not recommended as the risks are believed to outweigh the benefits[16-18]. This recommendation is also extended to women with gestational diabetes (GDM) due to a lack of studies that specifically investigate the use of antenatal corticosteroids in this population. Previous systematic reviews have shown that very few studies investigating the benefits of antenatal corticosteroids included participants with diabetes, and for those that did, the prevalence was less than 18%[19,20]. Similarly, our data did not show a significant improvement in neonatal respiratory morbidity with the use of dexamethasone prior to cesarean section. However, a study by Paul and colleagues found a reduction in respiratory admissions to the NICU after the use of antenatal corticosteroids after 37 weeks gestation in women with GDM who delivered via cesarean section[21]. It should be noted that their study had a small sample size of only 60 patients (30 with corticosteroid therapy and 30 as a control), which may explain the difference in findings.

In agreement with our findings, Gupta and coworkers discovered that antenatal corticosteroid administration prior to cesarean section resulted in a significant increase in neonatal admission to the NICU due to hypoglycemia, but with no increase in RDS or TTN[3]. Likewise, di Pasquo and colleagues conducted a retrospective multicenter cohort study in two tertiary university units involving 99 neonates who received antenatal corticosteroid. They confirmed that a significant number of fetuses exposed to antenatal corticosteroid for RDS prevention experienced hypoglycemia during the first 48 hours of neonatal life[4].

There are a number of suggested mechanisms for neonatal hypoglycemia that occurs after corticosteroid administration. The most widely accepted explanation is that corticosteroid-induced hyperglycemia in mothers leads to hyperinsulinemia in the fetus and newborn, which can cause hypoglycemia due to the excessive growth of fetal pancreatic beta cells[22]. Another possible mechanism is corticosteroid-mediated fetal adrenal suppression, which has been shown to cause prolonged dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis in animal studies[23,24].

This study has several strengths, including comprehensive data and a thorough examination of maternal and neonatal characteristics, including various known risk factors associated with neonatal respiratory morbidity and hypoglycemia. However, it is important to note that the study also has some limitations, such as its retrospective design and the fact that it was conducted in a single medical center.

CONCLUSION

In conclusion, administering Dexamethasone to diabetic women before an elective early-term cesarean delivery may raise the chances of neonatal admission to NICU due to hypoglycemia, without showing any significant improvement in respiratory morbidity. Our findings suggest that there should be a proper counseling between diabetic women who are planning to have a cesarean delivery between 37+0 and 38+6 weeks, with their doctor about the advantages and risks of taking corticosteroids. A randomized controlled trial with more participants would be needed to determine the balance between respiratory benefits and potential side effects, particularly hypoglycemia, in diabetic women receiving antenatal corticosteroids before CS.

DATA AVAILABILITY

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

CONFLICT OF INTERESTS

There are no ccflicts interest.

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