

Comparison of neonatal respiratory morbidity in neonates delivered at term by elective caesarean section with and without antenatal Corticosteroid

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Author's Contribution

¹ Conception of study

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Abstract

Introduction: Performing elective caesarean section prior to 39 completed weeks, it can lead to breathing problems in neonates as compare to those, who are born through caesarean section without antenatal Corticosteroid. WHO recommends the administration of intramuscular corticosteroids either dexamethasone or betamethasone (total 24mg in divided doses) in the antenatal period, when there is a risk of preterm birth. The advantages and disadvantages of a similar regimen given after 37 weeks of pregnancy prior to elective caesarean section (LSCS) to prevent respiratory morbidity in a newborn is yet a topic of discussion.

In Pakistan still, many clinicians are doing caesarean section at 37 or 38 weeks without antenatal Corticosteroids. The rationale is to emphasize the use of steroids before caesarean at 39 weeks.

Objective: To compare neonatal respiratory distress in neonates delivered between 37 --38+6 weeks of gestation by elective caesarean section with and without antenatal Corticosteroid.

Study design: Randomized controlled trial.

Setting: Department of Gynae & Obstetrics, unit 2, Shalamar Hospital, Lahore.

Duration: Six months from 12th September 2018 to 12th March 2019.

Materials and Methods: The study included women who were, planned for elective LSCS at 37-38+6 weeks, divided into two groups .The sample size was 140 (70 in each group), recruited by non-probability consecutive sampling. Inclusion criteria were singleton pregnancy, at 37 to 38+6 weeks for elective LSCS due to indications like primi breech, previous caesarian scar/ scars, and maternal wish. All eligible participants were allocated to one of the following groups. Group (A) received an injection of dexamethasone 48 to 72 hours before elective LSCS. Group (B), did not receive an injection of dexamethasone. The outcome to be measured in this study were the Apgar score at 1& 5 minutes, the incidence of transient tachypnea of the neonate (TTN) and respiratory distress syndrome (RDS) in newborns, and the need for mechanical ventilation among neonates from two different groups. The data was collected and analyzed by SPSS version 20. Descriptive statistic were applied to calculate the mean and SD for age, gestation age & BMI. Student T-test was used to compare the continuous outcome measures. Neonatal respiratory morbidity was compared in two groups by using the chi-square test at the level of significance of 0.05.

Results: Mean age in Group-A was 28.12± 5.6 and in Group-B was 28.97± 6.3 years. There was no statistically significant difference in these groups in terms of Body mass index, gestational age at the time of delivery, age of mother, birth weight, Apgar score at 1 and 5 min, and indications for cesarean section. Neonatal respiratory morbidity was higher in Group-B as compared to Group-A (30% vs.12.9%) p-value-0.013.

Conclusion: Antenatal dexamethasone administration significantly reduces the respiratory morbidity among neonates delivered at 37 to 38+6 by elective cesarean section. But further studies are required to assess the beneficial role of dexamethasone in the reduction of neonatal respiratory morbidity with a large sample size.

Keywords: Neonatal respiratory morbidity, transient tachypnea of newborn, elective caesarean section, antenatal corticosteroids.

Introduction

Cesarean section is one of the most commonly performed procedures in obstetrics which is performed whenever there is a risk to the life of the mother or fetus during vaginal delivery.¹ However, there is an alarming rise in the caesarean section rate in the last 20 years and it's a matter of great concern to health experts globally. This rapid spurt in the rate of abdominal delivery in recent years deserves paramount concern.² Cesarean section rate should not be higher than 10%-15%³ according to World Health Organization (WHO) recommendation. The rising trend toward elective caesarean section is due to various indications like increasing maternal age at first pregnancy⁴, primigravida with breech presentation, maternal request and downswing in a trial of previous one caesarean section, etc. Safety of the procedure has been increased due to the availability of spinal anesthesia, antibiotic prophylaxis, and better control of hemorrhage with uterotonics leading to decreased risk of caesareans-related complications like hemorrhage, infection, and thromboembolic events. The result is that obstetricians as well as a patient have evolved a reduced threshold for selecting elective caesarean section as an easy mode of delivery. Although increased safety of the procedure has reduced maternal risks, the adverse effects on the baby due to elective caesarean delivery before the onset of labour is yet a matter of paramount concern and needs to be addressed. Change in trend has been seen currently in women especially primigravida's with high heads and post-dated pregnancies, requesting for elective caesarean section to avoid prolonged hours of induction of labor, and uncertain labor outcome⁵ which has emerged as another indication of C-section i.e. C-section on maternal wish. Trial of labor after caesarean delivery has also decreased significantly in many countries, due to fright of the risk of scar rupture of previous cesarean leading to increased maternal and perinatal mortality as compared to a planned caesarean section.^{6,7,8} Both the obstetrician, as well as pregnant women, feel more comfortable with the planned caesarean section as compared to taking risks associated with vaginal birth after C-section. The largest randomized controlled trial, The Term Breech Trial, compared the effect of the mode of breech deliveries on neonatal outcomes. Its results were published in the year 2000, showing a significant decrease in neonatal mortality & morbidity in elective caesarean compared to vaginal breech delivery. Publication of national guidelines after this trial

changed management practices regarding the mode of breech delivery.^{9,10} Cesarean rate increased by 28% within 3 months after the publication of the Term Breech Trial in the Netherlands. Similarly, an increasing rate of caesarean deliveries has been documented in Pakistan. The studies conducted in various regions of Pakistan have shown trends toward rising rates of abdominal deliveries.^{11,12} One of the known complications of elective C-Section conducted between 37-38⁶ weeks of gestation is neonatal respiratory morbidity which includes a range of conditions, varying from its milder form, transient tachypnea (TTN) of the neonate to its severe form i.e. respiratory distress syndrome (RDS). TTN is a self-resolving state caused by a delay in the absorption of fluid from the lung's alveoli after delivery. It usually presents with an increased respiratory rate of > 60 breaths per minute, grunting, and mild signs of respiratory distress usually lasting up to 48 to 72 hours. On the other hand, RDS is a severe form of respiratory distress, due to a deficiency of surfactant which is the main contributor to elastic properties of pulmonary tissue, leading to a collapse of lung alveoli. During fetal life, lung epithelium secretes a fluid in alveoli. Along with the passage of time as gestational age advances the production of this fluid decreases and gradually lung epithelium becomes more absorptive in nature rather than secretory due to the increase in the number and function of sodium channels. The factors responsible for this change in sodium channels are not well known, but it is well documented that with increasing gestational age and stress of labor, glucocorticoids are released leading to the maturation of type II pneumocytes, which produce surfactants. It results in a significant reduction of fluid volume in alveoli close to term and before delivery, with additional removal of fluid during labor. Elective caesarean bypasses this physiological process assisted by nature, thereby increasing the likelihood of neonatal respiratory morbidity.¹¹ This underlying physiology provides strong justification and philosophy for the administration of corticosteroids in the antenatal period to women who are planned to be delivered by elective caesarean section.¹² Exogenous corticosteroids are readily transported across the placenta to the fetus. The exact mechanisms of their action are not fully known. However, it is believed that antenatal corticosteroids when given intramuscularly improve respiratory outcomes in several ways i.e. by thinning of the alveolar septae, enhancing differentiation of type II pneumocytes, decreasing surface tension within alveoli, increasing

pulmonary circulation by endothelial nitric oxide synthase, improving pulmonary adaptation at birth due to increased number of epithelial sodium channels, which clears fluid from the alveolar lumen to the interstitium and preventing V/Q mismatch. Thereby reducing overall neonatal respiratory morbidity because the retained fluid in the alveoli leads to ineffective gas exchange through the respiratory membrane leading to respiratory distress, and tachypnea by stimulating the respiratory center in the medulla oblongata in the brain stem. An increase in respiratory rate continues until the fluid is absorbed generally takes 48 to 72 hours after delivery.

RCOG (Royal College of Obstetrics & Gynecology) recommends that the most appropriate time to perform elective LSCS is around 39 weeks of gestation.^{13,14} If an elective caesarean is desired to perform before 39 weeks of gestation, dexamethasone injections 48 to 72 hours before Caesarean Section should be given to decrease the risk of NRM.^{13,14} There are a limited number of studies conducted in Pakistan regarding this issue and yet most elective cesarean sections are being performed before 39 weeks without antenatal corticosteroids which increases the risk of respiratory morbidity in neonates. We carried out this study in our setup to compare neonatal respiratory morbidity in neonates delivered by elective cesarean between 37-38⁺⁶ weeks after administering dexamethasone as compared to neonates of those mothers who did not receive prophylactic dexamethasone before elective cesarean.

Materials and Methods

This study was conducted at a tertiary care level hospital in Lahore. It included those women who were delivered by elective lower segment caesarean section at 37-38⁺⁶ weeks.

The sample size was 140 (70 in each group) recruited by non-probability consecutive sampling technique. Inclusion criteria were pregnant women with a singleton pregnancy, gestational age ≥ 37 weeks with an indication for elective LSCS like previous caesarian scar/scars, primi breech, and maternal wish. Only those women included in the study who were sure of their last menstrual date, their previous menstrual cycle was regular and they had their early dating scan for confirmation of dates by measuring crown-rump length. Informed written consent was obtained for participation. We excluded women with obstetric complications including preeclampsia, diabetes

mellitus, ante-partum hemorrhage, fetal anomaly, twin pregnancy, and intrauterine growth restriction. All eligible participants were allocated to one of the following groups. Group A, received an injection of 12 mg dexamethasone, Intramuscular two doses 12 hours apart, 48 to 72 hours before elective CS. Group B did not receive dexamethasone. All patients underwent caesarean section under spinal anesthesia by senior residents/consultants. All deliveries were attended by senior pediatric residents; details of the resuscitation were recorded. Apgar scores at 1 and 5 minutes were recorded. Neonatal respiratory morbidity was compared between the two groups. All neonates were assessed for signs of transient tachypnea of newborn, which is a period of rapid breathing 40- 60 times/min, and RDS which is diagnosed based on the presence of at least 2 of the following criteria: tachypnea, central cyanosis in room air, expiratory grunting, subcostal, intercostals recessions, and nasal flaring. All neonates admitted to NICU had chest X-rays to exclusion of other associated pathologies and to confirm /rule out a diagnosis of RDS. The primary outcomes of this study were to see the incidence of TTN and RDS. The secondary outcomes included admission to NICU and the need for mechanical ventilation within 24 hours after birth. Data was entered and analyzed by SPSS version 20. Descriptive statistics were applied to calculate the mean and SD for age, gestation age, and BMI. Frequencies and percentages were calculated for outcome variables like parity, gravidity, and neonatal respiratory morbidity in both groups. The demographic data were compared between groups. Student T-test was used to compare the continuous outcome measures. Neonate respiratory morbidity in both groups was compared by using the chi-square test at the level of significance of 0.05.

Results

The total number of patients in the study was equally divided into two groups. The mean age of women in Group-A was 28.12 ± 5.62 and in Group B was 28.97 ± 6.36 years. There was no statistically significant difference in both groups in terms of parity, Body mass index, indications for C-section, and gestational age at the time of planned delivery. Birth weights of babies in both groups A & B were 2.47 ± 0.23 vs 2.48 ± 0.18 kilogram respectively. Neonatal respiratory morbidity was significantly higher in Group B as compared to Group A, 30% vs 12.9%.

Table 1: The demographic characteristics of the study participants

Variables	Group A (n=70)	Group B (n=70)	P-value
Age (years)+SD	28.12+5.62	29.97+6.36	>0.05.
Parity			>0.05.
• Primigravida (72)	31(44.3%)	41(58.6%)	
• Multigravida (68)	39(55.7%)	29(41.4%)	
BMI (Kg/m ²)+SD			
Normal	23(32.9%)	24(34.3%)	
Overweight	23(32.9%)	28(40%)	>0.05.
Obese	24(34.3%)	21(30%)	
Gestational age at the time of delivery (weeks),+SD	37.38+0.49	37.57+0.49	>0.05.
Indication of CS n (%)			
1. Caesarean sections, on maternal request.	15(21.4%)	13(18.5%)	
2. Breech presentation.	10(14.2%)	09(12.8%)	>0.05.
3. Previous scar/ scars	45(64.2%)	48(68.5%)	

Group-A: Study Group (Dexamethasone), Group-B: Controls Group (Without Dexamethasone)

Table 2: Comparison of Neonatal Respiratory Morbidity in Two Groups

Variables	Group(A)	Group(B)	P-value
Birth weight. mean+SD(range)	2.47+0.23	2.48+0.18	>0.05.
Apgar score, mean+SD			
At 1-minute	8.97 ± (0.21)	8.99 ± (0.14)	>0.05.
At 5-minute	9.99 ± (0.10)	10.00 ± (0.06)	
Neonatal respiratory morbidity, n (%)	9(12.9%)	21(30%)	
	RDS (0)	(Mild RDS) (2)	0.013
	TTN (9)	TTN (28)	
Need for mechanical ventilation	0%	0%	-----

Group-A: Study Group (Dexamethasone), Group-B: Controls Group

Table 3 Neonatal Respiratory Morbidity in relation to Gestational age

Gestational age	Respiratory Morbidity	Group-A (n=70)	Group-B (n=70)	P-value
38-38 ⁺⁶	Yes	5(11.6%)	8(26.7%)	0.021
	No	38(88.4%)	22(73.3%)	
37-37 ⁺⁶	Yes	4(14.8%)	13(32.5%)	0.011
	No	23(85.2%)	27(67.5%)	

Group-A: Study Group (Dexamethasone), Group-B: Controls Group

Discussion

The risk of neonatal respiratory morbidity including transient tachypnea of newborns, hyaline membrane disease, and persistent fetal circulation syndrome is higher for elective cesarean delivery compared with vaginal delivery earlier than 39 to 40 weeks of gestation.^{15,16,17} Several studies have been conducted to evaluate the correlation of gestation age at the time of birth with neonatal respiratory morbidity and all these strongly support an inverse relationship between

them, among infants born by elective caesarean birth.^{18,19}

Southfield et al reported in their research that planned caesarean section before 40 weeks gestation increases neonatal admissions due to breathing problems.² Respiratory morbidity was 1.7 times higher in those neonates who were delivered between 37 and 37⁺⁶ weeks of gestation as compared to those who had a delivery at 38-38⁺⁶ weeks; When the same group was compared with those newborns who were delivered at 39-39⁺⁶ weeks²⁶ risk of respiratory morbidity increased up to 2.4 times higher. Therefore, many guidelines

recommend that planned caesarean section should not be routinely carried out before 39 weeks of gestation.^{21,22}

Our study was designed to compare neonatal respiratory morbidity in patients delivered between 37 to 38⁺⁶ by planned caesarean section with or without injection of dexamethasone given intramuscularly to mothers 48 to 72 hours before delivery. Results of this study showed that neonatal respiratory morbidity was significantly higher in women who were not given dexamethasone i.e. Group-A (12.9%) vs Group-B (30%), p-value=0.013.

The results of our study are consistent with the findings of Mohammed N. Saleem who reported in his study that the incidence of neonatal respiratory morbidity was quite higher in the women, who had elective C-sections without prophylactic dexamethasone administration compared to the study group who received dexamethasone 48 to 72 hours before planned delivery through abdominal route (4.7% versus 0.8%, respectively; p=0.001).²³ A Cochrane systemic review in 2009, on the prophylactic administration of corticosteroids before elective C-Section at term deduced that although it reduced the number of neonatal admissions in NICU significantly but as far as incidence of respiratory distress syndrome and transient tachypnea of the newborn is concerned there was no statically significant difference in two groups who were delivered with or without prophylactic dexamethasone. (RR=0.15). The study concluded that more studies should be conducted before the routine recommendation of antenatal corticosteroid therapy for elective c-sections.²⁴ However, results of a meta-analysis have been published in 2018 in which the same researcher strongly supported the use of prophylactic antenatal corticosteroid to decrease the risk of respiratory distress syndrome significantly in patients who are delivered by elective C-section at term between 37 to 39 weeks.²⁴

Stutchfeld and coworkers performed a randomized trial which convinced that two doses of dexamethasone given within 48 to 72 hours before planned caesarean significantly decreases the risk of respiratory distress by converting the alveolar lining epithelium of lungs to be absorptive in nature rather than secretory in function.²⁵ Peter Stutchfield, Rhiannon Whitaker on behalf of, the large, Antenatal Steroids for Term Elective Caesarean Section Research (ASTECS) in 2005, a non blinded randomized trial has proven that incidence of respiratory distress at 37-39 weeks of gestation is remarkably decreased with

two doses of antenatal steroids, TTN decreases from 4% to 2.1% and RDS from 1% to 0.2%. This trial also showed that infants who received this therapy had lower rates of NICU admission and were less likely to require resuscitation/ventilation at birth. Results of our study also favored this trial as newborns delivered at 38 to 38⁺⁶ weeks of gestation had better neonatal respiratory outcomes as compared to those who delivered between 37 to 37⁺⁶ weeks of gestation, with 26.7% vs 32.5% neonatal respiratory morbidity respectively. Another non-blinded randomized trial by Ahmed et al measured the effectiveness of two doses of dexamethasone administered before elective delivery by C-section to a group of pregnant women at 37 weeks or beyond.²⁶ TTN was reduced in the dexamethasone group compared to the non-intervention group (7% vs. 19.6%).²⁷

Although there was no neonatal mortality in our control group, however, increased number of neonatal admissions caused increased anxiety to the parents and increased costs due to prolonged hospital stays and compromised mother & neonate bonding. Regarding the harmful effects of corticosteroids, studies have suggested that more than one course of antenatal steroids has harmful effects in terms of low birth weight and reduced neonatal head circumference size.²⁸ However there are a number of studies that have proven that a single course of antenatal corticosteroids is not related to an increased risk of maternal or fetal infection and has no adverse neurological effects.²⁹⁻³² Besides the mode of delivery, gestational age at the time of delivery also affects the risk of Neonatal respiratory problems as well as compromises mother-infant bonding due to staying in the neonatal nursery. In 2013, The American College of Obstetricians and Gynecologists (ACOG) suggested that early-term should be defined as delivery occurring between 37 to 39 weeks gestation. They noted that neonatal outcomes, in particular respiratory morbidity, were different depending on the time of delivery hence the need to redefine the traditional definition of term deliveries occurring between 37 and 41 weeks gestation.³³ However deferring planned caesarean section to 39 weeks or beyond has its own demerits because of the risk of labour to start or rupture of membranes prior to the date of planned caesarean section with increased risk of umbilical cord prolapse in footling/flexed breech, thus requiring caesarean section in an emergency with significantly increased risk of intrapartum complications like dense adhesions due to previous surgeries, hemorrhage, bladder injury, gut injury all leading to increased

maternal morbidity and increase workload for duty staff and blood transfusion services due to increasing in numbers of emergency LSCS. This increased maternal hazard associated with emergency needs to be weighed against the expected improved neonatal outcomes of performing elective LSCS near term. To balance the risk it is recommended that in women without additional risks, a planned caesarean section should be performed around 39 weeks of pregnancy. In those scenarios where delivery is anticipated before 39 weeks of pregnancy, the administration of corticosteroids has advantages in reducing neonatal respiratory morbidity. Dexamethasone has an advantage over betamethasone in terms of lower cost and wider availability.

However repeated courses of antenatal corticosteroids are yet not recommended until further studies prove increased benefit versus the potential risk of hazard to the mother and fetus.⁹

Conclusion

Results of this study showed that antenatal dexamethasone administration significantly reduces respiratory morbidity among neonates delivered at 37 to 38⁺⁶ by elective cesarean section. Obstetricians should weigh and balance the risks of elective cesarean delivery before 39 weeks gestation in terms of increased neonatal morbidity against the risks of caesarean section performed in an emergency. Ideally, elective caesarean should be performed around 39 completed weeks of gestation, but when early required to perform, an injection of dexamethasone should be administered 12 mg intramuscular 12 hours apart two doses 48 to 72 hours before elective delivery to decrease respiratory morbidity in newborns. But further studies are required to assess the beneficial role of dexamethasone in the reduction of neonatal respiratory morbidity with a large sample size

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