

# Respiratory Distress Syndrome in Neonates Delivered at Term-gestation by Elective Cesarean Section at Tertiary Care Hospital in Oman

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# ABSTRACT

Objectives: We sought to assess the relationship between respiratory distress syndrome (RDS) in neonates delivered by elective cesarean section at term gestation with and without corticosteroids cover. We also aimed to determine other neonatal complications such as sepsis, hypoglycemia, and hyperbilirubinemia. Methods: We conducted a retrospective descriptive study from January 2010 to December 2015 on all Omani women who delivered by elective cesarean section at Sultan Qaboos University Hospital between 37+0 and 38+6 weeks gestation. *Results:* Among 650 patients included in the study, 20.8% (n = 135) received corticosteroids antenatally and 79.2% did not. RDS was found in 16 out of 650 neonates, making the prevalence of RDS 2.5%. Higher gravidity and parity and a mean gestational age of less than 37.6 weeks, were associated with a significant risk of RDS. Administration of antenatal corticosteroids did not change the respiratory morbidity in the newborns (p = 0.340). A mean birth weight of 2.9 kg was associated with a significant risk of RDS (p = 0.043). All 16 newborns required neonatal intensive care unit admission and ventilator support. The most common ventilatory support used was continuous positive airway pressure (56.2%). The most common secondary complication in neonates diagnosed with RDS was transient tachypnea of the newborn (53.8%). Conclusions: The prevalence of RDS was low. Giving antenatal corticosteroids for patients with planned elective cesarean at term did not seem to have a beneficial effect on neonatal respiratory morbidity. Further studies with larger sample size including multiple centers is recommended.

espiratory distress syndrome (RDS) caused by surfactant deficiency is described not only in preterm infants but also in term infants born by cesarean section. The rates of cesarean section have been increasing worldwide due to various reasons. Although cesarean section can be a lifesaving procedure, adverse events occur in both mothers and neonates. Respiratory morbidity, hypoglycemia, sepsis, and neonatal intensive care unit (NICU) admissions are the most common neonatal complications observed. Admission of the newborn to the NICU has various impacts on the family and caregivers. Previous studies have demonstrated the

beneficial effect of steroids in reducing respiratory morbidities in neonates by increasing the production of surfactant by pneumocytes.<sup>4</sup>

A retrospective cohort study conducted at a secondary level hospital in Karachi reviewed 196 pregnant women who delivered by elective cesarean section at 37 to 38+6 weeks gestation.<sup>5</sup> The women were equally divided into those who received prophylactic dexamethasone (group A) and those who did not receive dexamethasone (group B). In group A, only one (1%) baby developed transient tachypnea of the newborn compared to 10 (10%) babies in group B (p = 0.005). Eleven (11%) newborns were admitted to nursery in group B

compared to one (1%) in group A (p = 0.005). None of the newborns were referred to any tertiary care hospital for intensive care. The study concluded that prophylactic dexamethasone is beneficial in reducing neonatal respiratory morbidity, but recommended further prospective studies with larger sample size.<sup>5</sup>

A multicenter randomized trial involving 10 maternity units with 998 women participants randomized 503 women to a corticosteroid treatment group. The women received two intramuscular doses of 12 mg betamethasone, 48 hours before delivery.6 The trial evaluated admission rates to special care baby unit with respiratory distress and their corresponding severity. In this trial, 35 babies were admitted to a special baby unit with respiratory distress; 24 from the control group and 11 from the treatment group (p = 0.02). The incidence of admission with respiratory distress was 0.051 in the control group and 0.024 in the treatment group (relative risk, 0.46; 95% confidence interval: 0.23-0.93). The trial concluded that antenatal betamethasone and delaying delivery until 39 weeks both reduced admissions to special care baby unit with respiratory distress after elective cesarean section at term.

For a planned cesarean before 38+6 weeks gestation, administration of corticosteroids is recommended by some of the international guidelines, including the Royal College of Obstetricians and Gynecologists (RCOG).<sup>7</sup> Because of higher respiratory morbidity associated with lower gestational age, the American Council of Obstetricians and Gynecologists (ACOG)<sup>8</sup> and National Institute for Health and Care Excellence (NICE)<sup>9</sup> have recommended all planned cesarean sections not to be carried out (if possible) before 39 weeks gestation.

The primary objective of this study was to evaluate the rate of RDS and to assess the relationship between RDS in neonates delivered by elective cesarean at term with and without corticosteroids cover. The secondary objective was to determine other neonatal complications such as sepsis, hypoglycemia, and hyperbilirubinemia.

### **METHODS**

We conducted a retrospective, descriptive study between January 2010 and December 2015 on all Omani women who delivered by elective cesarean section at Sultan Qaboos University Hospital between 37+0 and 38+6 weeks gestation. Ethical approval was obtained from the Medical & Research Ethics Committee at the College of Medicine and Health Sciences, Sultan Qaboos University, Muscat, Oman (Reference: MREC#1033).

A total of 650 Omani women were included in the study. We excluded non-Omani patients, those with anomalous fetuses, preterm delivery (< 37 weeks gestation), delivery after 39 weeks gestation, those who received steroids before 28 weeks gestation, multiple gestations, and growth-restricted fetuses from the study. The data was collected from the delivery ward, NICU records, and the Hospital Information System.

Maternal demographic data collected included age, gravidity, parity, medical comorbidities, antenatal corticosteroids, antenatal growth scan and amniotic fluid volume, gestational age at the time of cesarean section, and type of anesthesia administered during the cesarean. All neonatal information and complications were recorded, including birth weight, gender, Apgar score, cord pH at delivery, admission to NICU, diagnosis of RDS, other complications, medical intervention, and ventilatory support.

We used descriptive statistics to characterize the study sample in tabular and graphical formats. Continuous variables were presented as means and standard deviations, while categorical variables as frequencies and percentages. We used Pearson's chi-squared to establish associations between independent and dependent categorical variables. A p-value of  $\leq 0.050$  was considered statistically significant. Data was analyzed using SPSS Statistics (IBM Corp. Released 2015. IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

# RESULTS

Among the study cohort, 135 (20.8%) pregnant women received steroids. RDS was found in 16 (2.5%) newborns born from both groups. Maternal characteristics were analyzed stratified by RDS. The mean gestational age, gravidity, and parity for women who gave birth to the 16 newborns with RDS were 37.6 weeks, 5.8 and 3.6, respectively. Women who gave birth to the 634 newborns without RDS, had a mean gestational age, gravidity and parity of 37.8 weeks, 4.3, and 2.6, respectively. Mothers in the RDS group were associated with increasing gravidity

**Table 1:** Baseline characteristics of women giving birth to neonates stratified by respiratory distress syndrome (RDS) (N = 650).

Characteristic	RDS		<i>p</i> -value
	Yes (n = 16)	No $(n = 634)$	
Age	$34.6 \pm 5.2$	$33.0 \pm 4.8$	0.174
Gravidity	$5.8 \pm 1.9$	$4.3 \pm 2.4$	0.017
Parity	$3.6 \pm 1.8$	$2.6 \pm 1.9$	0.042
Gestational age at delivery	$37.6 \pm 0.4$	$37.8 \pm 0.5$	0.034

Data are given as mean±standard deviation.

and parity, and lower gestational age at birth with significant p-values of 0.017, 0.042, and 0.034, respectively. We did not find a significant association between maternal age and RDS in the newborn (34.6 vs. 33.0 years; p = 0.174) [Table 1].

Maternal comorbidities were analyzed and presented in Table 2. Among the women who delivered babies with RDS, 10 (62.5%) had medical comorbidities, nine (56.3%) had diabetes or gestational diabetes, three had a hematological condition (18.8%), and a neurological disorder was found in one (6.3%) mother. Among the women who delivered babies without RDS, 369 (58.2%) had medical comorbidities, 52 (8.2%) had hypertension or gestational hypertension, 245 (38.6%) had diabetes or gestational diabetes, 71 (11.2%) had a hematological condition, 16 (2.5%) had connective tissue disorders, 5 (0.8%) had psychiatric problems, 21 (3.3%) had respiratory disease, 13 (2.1%) had a neurological disorder, and 22 (3.5%) had endocrine disorders other than diabetes. The above results show

that preexisting diabetes and gestational diabetes were the most common maternal medical conditions in our sample.

There were no significant differences in the development of RDS between those mothers that received corticosteroids and those that did not receive corticosteroids (3.7% vs. 2.1%; p = 0.340).

Table 3 illustrates the different characteristics of the neonates delivered during our study period. Among the 16 newborns who developed RDS, the mean birth weight was  $2.9\pm0.3$  kg. Two newborns (12.5%) required resuscitation at the delivery. Continuous positive airway pressure (CPAP) was the most common ventilatory support used (56.2%), and transient tachypnea of the newborn was the most common secondary complication (53.8%). The neonatal characteristics of the babies who did not develop RDS (n = 634) included a mean birth weight of  $3.1\pm0.4$  kg, and two (0.3%) newborns required resuscitation at the delivery scene. Regarding ventilatory support among babies without RDS, 615

**Table 2:** Maternal medical comorbidities stratified by respiratory distress syndrome (RDS).

Comorbidity	RDS		<i>p</i> -value
	Yes, (n = 16) n (%)	No, (n = 634) n (%)	
Maternal comorbidity	10 (62.5)	369 (58.2)	0.802
HTN/gestational HTN	0 (0.0)	52 (8.2)	0.630
DM/GDM	9 (56.3)	245 (38.6)	0.195
Hematological	3 (18.8)	71 (11.2)	0.412
CTD	0 (0.0)	16 (2.5)	1.000
Psychiatry	0 (0.0)	5 (0.8)	1.000
Respiratory	0 (0.0)	21 (3.3)	1.000
Neurological	1 (6.3)	13 (2.1)	0.297
Endocrine	0 (0.0)	22 (3.5)	1.000
Cardiac diseases	0 (0.0)	9 (1.4)	1.000
Infectious diseases	0 (0.0)	53 (8.4)	0.633

HTN: hypertension; DM: diabetes mellitus; GDM: gestational diabetes mellitus; CTD: connective tissue disorders.



**Table 3:** Neonatal characteristics and outcomes stratified by respiratory distress (RDS).

Outcome characteristic	RDS		<i>p</i> -value
	Yes, (n = 16) n (%)	No, (n = 634) n (%)	
Birth weight, mean ± SD	$2.9 \pm 0.3$	$3.1 \pm 0.4$	0.043
Apgar in 1 min, mean ± SD	$6.8 \pm 2.0$	$8.5 \pm 1.1$	< 0.001
Apgar in 5 min, mean ± SD	$8.5 \pm 1.4$	$9.8 \pm 0.5$	< 0.001
Cord pH, mean ± SD	$7.3 \pm 0.0$	$7.3 \pm 0.0$	0.932
Duration of stay in NICU, mean ± SD	$4.8 \pm 3.4$	$3.1 \pm 3.5$	0.113
Gender			
Boy	11 (68.8)	337 (53.2)	0.759
Girl	5 (31.3)	297 (46.8)	
Resuscitation at delivery	2 (12.5)	2 (0.3)	0.003
Ventilator support			
None	0 (0.0)	615 (97.0)	< 0.001
Nasal cannula	3 (18.8)	8 (1.3)	
CPAP	9 (56.2)	6 (0.9)	
Intubation	4 (25.0)	5 (0.5)	
Surfactant use	0 (0.0)	1 (0.2)	0.045
Antibiotic use	1 (6.3)	4 (0.6)	0.007
Other complications			< 0.001
Apnea	0 (0.0)	9 (22.5)	
Hypoglycemia	3 (23.1)	13 (32.5)	
Sepsis	0 (0.0)	1 (2.5)	
Hyperbilirubinemia	3 (23.1)	4 (10.0)	
Transient tachypnea	7 (53.8)	13 (32.5)	

 $SD: standard\ deviation; NICU: neonatal\ intensive\ care\ unit;\ CPAP: continuous\ positive\ airway\ pressure.$ 

(97.0%) required no means of ventilatory support. One newborn (0.2%) had secondary apnea and suspected RDS, so empirical surfactant was given. Four (0.6%) required antibiotics for suspected sepsis, but cultures were negative. All newborns with RDS required admission to the NICU and ventilatory support (p < 0.001).

#### DISCUSSION

The rates of elective cesarean section have been increasing worldwide due to various factors, including fetal and maternal causes. 5,10,11 Cesarean section can be associated with several maternal and neonatal complications, which are highlighted in previous studies 12-16 making health care providers more aware of them and, most importantly, assist them in counseling patients. RDS in newborns following elective cesarean section because of surfactant deficiency is a well-reported neonatal complication and many interventions have been

introduced to reduce such risk.<sup>11–13</sup> Corticosteroid administration is one of these interventions that has a recognized effect in lowering the occurrence of respiratory distress as it enhances surfactant production and provides better lung air exchange in the newborns.<sup>17,18</sup>

The rate of RDS in our study was 2.5%, and this is in keeping with the rate reported in other studies. 5,12,14 A total of 3.7% of RDS newborns in our study received antenatal corticosteroids. Giving corticosteroids for preterm birth has been studied extensively with clear evidence of decreasing respiratory morbidity and other neonatal complications. However, giving it for late preterm or term babies is controversial due to unknown short- and long-term safety and limited beneficial effects. Hence, one study did not recommend routine administration of antenatal corticosteroids to women planned for cesarean section at term and before 39 weeks gestation. 19 On the contrary, it is recommended to plan elective cesarean section at 39

weeks wherein the risk of RDS could be reduced.<sup>8,9</sup> A recent Cochrane review of four trials found some beneficial effect of the use of steroids. Still, it concluded that more high-quality studies with larger sample sizes that are adequately powered to detect the effect of prophylactic antenatal corticosteroids on outcomes of respiratory morbidity are needed, given the potential for bias in the above studies. In addition, further trials on the long-term outcomes of these infants are needed to identify any potential harms and complications of antenatal corticosteroid administration at term.<sup>20</sup> Our results did not show the beneficial effect of antenatal corticosteroid administration in improving respiratory morbidities (p = 0.340). However, this could be due to the small sample size.

Our study showed that all newborns diagnosed with RDS required admission to NICU and ventilatory support, mainly CPAP (56.2%), which can an impact on families and healthcare services. Those who received corticosteroids had a shorter duration of stay; however, this was not significant. Similar to our findings, there were no significant differences noted in other neonatal complications between newborns with and without RDS.21,22 A recent study published in 2019 by Mirzamoradi and his group concluded that administering a course of betamethasone after 37 weeks of gestation in women undergoing early-term cesarean section did not have a significant effect on respiratory morbidities in neonates. However, it decreased the frequency of admission to NICU, especially admission due to respiratory distress, which could indicate that respiratory morbidities were less severe in the betamethasone group compared to the control group.<sup>23</sup>

Delivery time plays an important role in reducing respiratory morbidities in newborns. <sup>10</sup> Our results showed that the mean gestational age at the time of delivery of 37+6 weeks or less was associated with RDS compared to higher gestational age, which supports the international guidelines on planned elective cesarean sections at a gestational age of not less than 39 weeks. <sup>7-9</sup> However, in certain situations such as high-risk pregnancies, an elective cesarean section might have to be done earlier. Surprisingly, our results found that increasing maternal gravidity and parity were associated with increased risk of RDS in the newborn. However, further studies are needed to confirm such associations.

The study has some limitations, including its nature, as it was retrospective and included only 650 Omani women from a single tertiary center in Oman. Limited data is available regarding the rate of RDS in Omani women who delivered at other government and private institutions. Collaborations between all health sectors in the country are required to obtain accurate data regarding the benefits of corticosteroids use at term that might help in improving maternal, fetal, and neonatal care and reduce the burden on maternity/neonatal ICU. Concerns regarding missing data and information regarding maternal risk factors and detailed neonatal outcomes, including documentation of RDS could have affected the results. Subgroup analysis between diabetic and non-diabetic women would have been better but, due to small sample numbers, this was not carried out.

# CONCLUSION

We found a low rate of RDS in our study period. Giving antenatal corticosteroids for women planned for elective cesarean section at a gestational age of 37+0 to 38+6 weeks did not seem to have a beneficial effect with respect to neonatal respiratory morbidity. Further studies with a larger sample size, including other centers in Oman, are warranted to confirm our findings.

#### Disclosure

The authors declared no conflicts of interest. No funding was received for this study.

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