

## Fetal Lung Maturity Testing and Neonatal Respiratory Complications in Women with Type 1 Diabetes mellitus Electively Delivered before 39 Weeks Gestation

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### Abstract

**Objective:** To compare the rate of neonatal respiratory complications among newborns of women with type 1 Diabetes mellitus (DM) delivered before 39 weeks gestation following documentation of Fetal Lung Maturity (FLM) to the neonatal outcome of similar women delivered after 39 weeks.

**Material and Methods:** We retrospectively studied the neonatal outcome of women with type 1 DM delivered electively by cesarean section before 39 weeks gestation after documentation of fetal lung maturity. We compared the outcome of these neonates to neonates born to women with type 1 DM delivered by elective cesarean section after 39 weeks gestation without fetal lung maturity analysis.

**Results:** Between January 1, 2004 and December 31, 2008, 95 women with type 1 DM underwent fetal lung maturity testing before 39 weeks gestation. Seventy-eight (82.1%) tests suggested lung maturity and the women were delivered at 37±1 weeks. Five neonates (5.3%) required respiratory assistance and seven others (7.4%) required admission to the neonatal intensive care unit due to respiratory related symptoms. The overall respiratory complication rate was 12.6%. Six neonates experienced delay in discharge from the hospital. There were four newborns with respiratory complications (4.3%) in the control group of 94 similar women delivered after 39 weeks gestation (P=0.0001).

**Conclusion:** Even when fetal lung maturity had been documented, neonates of women with type 1 DM electively delivered before 39 weeks gestation are at an increased risk of respiratory complications compared with neonates of similar women delivered after 39 weeks.

### Introduction

The American College of Obstetricians and Gynecologists (ACOG) recommends documentation of fetal lung maturity when a delivery is performed before 39 weeks gestation [1]. Despite adherence to the ACOG guidelines preventable morbidity continues to occur in women delivered before 39 weeks gestation. Although the false positive rate of fetal lung maturity tests is very low, it may account for some of the cases where despite tests that had suggested mature lungs neonates develop respiratory complications after delivery. The risk for such complications is higher in newborns delivered by cesarean section [2] and in those delivered to mothers with diabetes [3]. It is therefore important to evaluate the occurrence of neonatal respiratory complications among babies born before 39 weeks after fetal lung maturity had been documented, especially among women with type 1 DM.

The purpose of this study was to evaluate the rate of neonatal respiratory complications among neonates delivered to women with type 1 DM who underwent elective cesarean deliveries before 39 weeks gestation after documentation of fetal lung maturity, compared to neonates born to similar women after 39 weeks. We elected to study only neonates delivered by cesarean sections because these newborns were at a higher risk of developing respiratory complications than newborns delivered vaginally [2]. In addition, we wanted to minimize the possibility that variables associated with vaginal delivery (e.g. length and mode of induction, risk of chorioamnionitis, instrumental delivery etc.) may contribute to the respiratory complications we studied.

### Materials and Methods

The study population included a cohort of neonates delivered by elective cesarean section to women with type 1 DM before 39 weeks

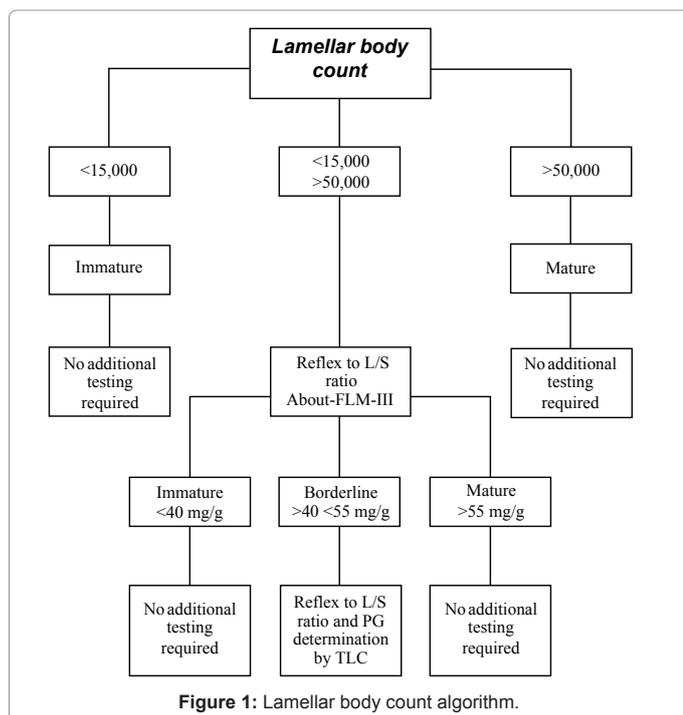
gestation after documentation of fetal lung maturity by amniotic fluid analysis. All deliveries took place at Miami Valley Hospital in Dayton, Ohio between January 1, 2004 and December 31, 2008. Indications for fetal lung maturity testing included: scheduled repeat cesarean section due to previous classical uterine incision or history of uterine incision extension, suspected fetal macrosomia (defined as equal or above 4,500g), or inadequate glycemic control (fasting blood sugar values  $\geq 95$  mg/dl or blood sugar values that were repeatedly  $\geq 140$  mg/dl or  $\geq 120$  mg/dl one or two hours after meals, respectively) with suspected fetal macrosomia and polyhydramnios. The algorithm used to assess fetal lung maturity is described in Figure 1 [4]. The cutoffs used to define lung maturity were not altered for maternal diabetes (lamellar body count cutoff of 50,000; for Fetal Lung Maturity test (FLM III): 55, and Lecithin/Sphingomyelin ratio: 2.0) [5,6]. Neonatal outcome parameters included Apgar scores at 5 minutes, umbilical cord blood gases, birth weight, need for respiratory assistance at birth, admission to the Neonatal Intensive Care Unit (NICU) due to respiratory complications (e.g. episodes of apnea, requirement of oxygen, ventilation or CPAP),

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and delay in hospital discharge due to Respiratory Related Symptoms (RRS) defined as hospital stay longer than 96 hours after the c-section.

The control group consisted of neonates delivered by elective caesarean section at the same hospital during the same period after 39 weeks gestation without fetal lung maturity studies to women with type 1 DM. The women were similar by age, race, gravidity and parity, duration of maternal diabetes, and insulin requirement. Similar neonatal outcome parameters were assessed in the control group.

Statistical analysis was performed using Graphpad Software (Graphpad Software, Inc., San Diego, California); we used two tailed t-tests for continuous data and/or chi-square analysis for proportions. A *p* value of less than 0.05 was considered significant. The study was approved by the Institutional Review Board.

## Results

The study population included 95 women with type 1 DM who underwent amniocentesis for fetal lung maturity studies at 37±1 weeks gestation. Seventy eight lung maturity tests (82.1%) suggested maturity and these women underwent elective cesareans. Seventeen tests (17.9%) suggested immaturity; these women were retested one week later, at an average gestational age of 38±2 weeks; all tests suggested maturity and the women were delivered.

All deliveries were by cesarean sections. The indications for surgery were: 45 repeat cesarean sections (47.4%), 12 breech presentations (12.6%), 12 women had poor glycemic control (12.6%), 10 with estimated fetal weight over 4,500 g (10.5%), seven had 4<sup>th</sup> degree perineal tear during previous delivery (7.4%), seven were done at patients request (7.4%) and two had low cervical leiomyomas (2.1%). The indications for cesarean delivery in the control group were comparable to the study group.

Seven of the 78 neonates (9%) whose lung maturity studies were mature at the time of the first amniocentesis required admission to the Neonatal Intensive Care Unit (NICU) due to respiratory complications.

Five additional neonates from this group (6.4%) required respiratory assistance at birth. The overall neonatal respiratory complication rate in the group of women delivered after the first amniocentesis was 15.4%, and the rate for the entire study group of 95 women was 12.6%. The hospital discharge of six of the study group's neonates was delayed due to RRS. The number of respiratory complications in the control group was four of 94 (4.3%) (*P*=0.0001) (Table 1).

## Discussion

In 1996 ACOG's published the recommendation to confirm fetal maturity before elective delivery prior to 39 weeks gestation [1]. The validity of this recommendation was demonstrated in recent studies. Stutchfield et al. [7] reported in 2005 that delaying cesarean deliveries until 39 weeks gestation reduced the rate of admissions to neonatal special care units due to respiratory distress [7]. However, even when the ACOG's recommendation is followed and fetal lung maturity is documented prior to delivery, a small number of newborns delivered by elective deliveries before 39 weeks gestation develop respiratory complications. The risk of such complications is increased among babies delivered early by planned cesarean section since cesarean delivery is associated with an increased risk of neonatal respiratory complications compared with vaginal delivery. Recently Kamath et al. [2] conducted a retrospective study on neonatal outcomes after elective cesarean delivery and reported significantly higher rates of respiratory morbidity, NICU admissions, and longer hospital stay compared to vaginal birth after cesareans.

The positive predictive value of fetal lung maturity tests is over 95%, [1] however, some test results can be falsely positive. Women with diabetes, especially when poorly controlled, may have delayed fetal lung maturation, an increased risk of false fetal lung maturity test results, or both [1]. In 2002, Moore postulated that fetal pulmonary maturation, as evidenced by the onset of phosphatidylglycerol production in the amniotic fluid, is delayed in pregnancy complicated by maternal diabetes by 1 to 1.5 weeks [3]. The possibility of false positive test results may be even higher in pregnancies complicated by pre-pregnancy diabetes. The risk of a false positive test may be minimized by avoiding fetal lung maturity all together: in a recent study, Kjos et al. [8] studied the rate of Respiratory Distress Syndrome (RDS) among newborns of diabetic mothers and concluded that routine FLM testing did not change the prevalence of RDS when pregnancies were reliably dated, and suggested that such testing be abandoned. They also reported that cesarean delivery was associated with an increased rate of RDS [8].

It is possible that the method we used for assessing fetal lung maturity in these women was responsible for the relatively high number of newborns with respiratory complications. The algorithm we used for testing fetal lung maturity was previously described in an earlier study [4]. It was based on a consensus protocol published by Neehof and his associates in 2001 [5]. We previously reported that employing this algorithm for analyzing amniotic fluid samples resulted in a significant monetary saving [9]. Recently Janicki et al. [6] questioned the 50,000 lamellar body count thresholds and demonstrated the need for hematology analyzer specific thresholds.

COMPLICATIONS	Study group	controls
Number	95	94
NICU admissions	7 (7.4%)	2 (2.1%)
Respiratory assistance	5 (5.3%)	2 (2.1%)
Overall respiratory complication	12 (12.6%)	4 (4.3%)
Delayed hospital discharge	6 (6.3%)	1 (1.1%)

**Table 1:** Neonatal Complications.

This was a retrospective cohort study conducted at a single tertiary care center; nevertheless, it raises concern regarding elective cesarean deliveries performed prior to 39 weeks gestation, especially in women with type 1 DM. Similar findings were recently reported by Kamath et al. [2] who conducted a retrospective study of neonatal outcomes among non-diabetic mothers who underwent elective cesarean delivery. They observed significantly higher rates of respiratory morbidity, NICU admissions and longer length of hospital stay compared with newborns delivered vaginally [2]. It should be noted that we did not study other potential neonatal complications that may also develop in immature neonates.

Providing appropriate medical care limits physical and emotional hardship to newborns and their families and contributes to patient's satisfaction. The financial savings associated with avoidance of costs associated with prolonged care and delayed hospital discharge is an additional benefit.

## Conclusion

Preventing adverse neonatal outcomes is one of the higher priorities of obstetric care. Our findings emphasize the importance minimizing the number of elective cesarean deliveries prior to 39 weeks gestation, especially in women with pre-pregnancy diabetes mellitus.

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