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Neonatal morbidity after documented fetal lung maturity in late preterm and early term infants

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Abstract

OBJECTIVE—Fetal lung maturity often is used as the sole criterion that late preterm infants are ready for postnatal life. We therefore tested the hypothesis that fetal lung maturity testing does not predict the absence of morbidity in late preterm infants.

STUDY DESIGN—We performed a retrospective cohort study to examine 152 infants who were born in the late preterm (34 0/7 to 36 6/7 weeks) and early term (37 0/7 to 38 6/7 weeks) periods after mature fetal lung indices and compared them with 262 infants who were born at 39 weeks' gestation and who were matched by mode of delivery.

RESULTS—Despite documented fetal lung maturity, infants who were born at <39 weeks had significantly higher rates of neonatal morbidities compared with infants who were born at 39 weeks' gestation. After adjustment for significant covariates, we found that infants who were born at <39 weeks' gestation had an increased risk of composite adverse outcome (odds ratio, 3.66; 95% confidence interval, 1.48–9.09; $P < .01$).

CONCLUSION—Fetal lung maturity testing is insufficient to determine an infant's readiness for postnatal life.

Keywords

amniocentesis; fetal lung maturity; late preterm infant; neonatal outcome

The American College of Obstetricians and Gynecologists (ACOG) currently recommends the delay of elective delivery until 39 weeks' gestation and that fetal lung maturity test should be performed to avoid iatrogenic prematurity if the scheduled delivery is planned at <39 weeks' gestation.¹ Although ACOG notes that fetal lung maturity at <39 weeks' gestation is not an indication for delivery,¹ fetal lung maturity testing by amniocentesis for the purpose of delivery planning remains a common obstetric practice.^{2,3} In our institution, we calculated a rate of amniocentesis for fetal lung maturity of 15.5 per 1000 live births from the years 2005–2010 for such decision-making purposes.

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Although some recent data exist for infants at 37–39 weeks' gestation,⁴ no study has focused specifically on neonatal morbidity in late preterm (34 0/7 to 36 6/7 weeks) and early term (37 0/7 to 38 6/7 weeks) infants after documented mature lung indices in the mother's amniotic fluid; these are the 2 groups in which fetal lung maturity is most commonly performed. Because documented fetal lung maturity sometimes is used to justify elective delivery at <39 weeks' gestation and is equated with readiness for postnatal life, thereby qualifying an infant as "term," we believed it important to focus on the spectrum of neonatal morbidity that was seen in this patient population. Although the morbidity that was seen in infants between 34 and 39 weeks' gestation has been thought to be inconsequential and transient, more recent studies indicate that these infants are a particularly vulnerable population who comprise the greatest proportion of premature infants and may have graver long-term outcomes than previously suspected.^{5–7}

As such, the aim of our study was to examine the rate of neonatal morbidity in infants who were born from 34 0/7 to 38 6/7 weeks' gestation after amniocentesis with documented fetal lung maturity, compared with a reference group of infants who were born from 39 0/7 to 40 6/7 weeks' gestation. Because of continued physiologic and autonomic immaturity, we hypothesized that, despite documented fetal lung maturity, infants who are born at <39 weeks' gestation would have significant neonatal morbidity.

Materials and Methods

We performed a retrospective cohort study, using a list of all mothers who had an amniocentesis for fetal lung maturity between January 1, 2005 and February 28, 2010, and subsequently delivered at Good Samaritan Hospital in Cincinnati, Ohio, the hospital with the largest delivery volume in the state. The study group included births to women between 34 0/7 and 38 6/7 weeks' gestation after amniocentesis with documented fetal lung maturity. The reference group included births that occurred from gestational ages 39 0/7 to 40 6/7 weeks; the data were selected at random by the hospital's medical records office for the years of our study period and were matched by rate of cesarean delivery, because this mode of delivery has been associated independently with neonatal morbidity.^{2,3} Pregnancies were dated according to the best obstetric estimate; dating from the last menstrual period and first antenatal ultrasound scans are used. The institutional review board approved the study.

Fetal lung maturity was affirmed when the mother's amniotic fluid had 1 of the following indices that indicated maturity: assay with TDx-FLM II 55 mg surfactant/g albumin in the nondiabetic patient (70 mg surfactant/g albumin in the diabetic patient), presence of phosphatidylglycerol, or lamellar body count (LBC) at >29,000 per μL . Although the threshold levels for TDx-FLM II and phosphatidylglycerol assays are well-established as labeled here,¹ the threshold level for LBC was determined according to the laboratory standards of the study institution. The fetal lung maturity panel at the study institution included all 3 tests; however, for a short time during the study period, the phosphatidylglycerol assay was not available. Apart from this period, all amniotic fluid samples were tested for fetal lung maturity with each of the 3 tests: TDx-FLM II assay, LBC, and phosphatidylglycerol assay.

Study exclusions were pregnancies that were complicated by congenital anomalies, chromosomal abnormalities, or multifetal gestation. Mothers who delivered outside the study institution were also excluded. The Figure shows the screening process that yielded the eventual study population of 152 infants who were born from 34 to 38 6/7 weeks' gestation, after amniocentesis that documented lung maturity; the reference group of 262 infants was born between 39 to 40 6/7 weeks' gestation.

The charts of all the women and their infants who met inclusion criteria were reviewed for the variables of interest. One study investigator abstracted data from all charts; a second investigator did a quality assurance review of 10% of the charts and found discrepancies in <5% of all data variables that were collected. The primary study outcome was a composite measurement of neonatal morbidity that included admission to neonatal intensive care, hypoglycemia that required intravenous infusion, treatment with antibiotics for presumed sepsis, gavage feeding, or treatment for hyperbilirubinemia with phototherapy. These neonatal outcomes were chosen to form the composite adverse outcome because they are common morbidities that are seen in the late preterm and early-term population^{4,8,9} and require a higher level of monitoring or follow-up evaluation than a healthy, uncomplicated newborn infant. Secondary outcomes included each of these individual morbidities, in addition to resuscitation required in the delivery room, hypoglycemia (documented glucose level, <45 mg/dL), sepsis evaluation (screening complete blood count and/or blood culture), need for central venous access, and length of stay. Respiratory outcome was evaluated through data that were collected about the need for ongoing respiratory support or oxygen and surfactant administration. At the study institution, mechanical ventilation and surfactant are considered when an infant has clinical signs of respiratory distress, with an elevated pCO₂ or FiO₂ of >40%. Admission to neonatal intensive care is required for infants at <34 weeks' gestation; therefore, the infants in our study group would have otherwise been sent to the well-baby nursery if no other complications were present. Maternal demographic characteristics that were analyzed as possible confounders were mother's age, history of premature delivery, history of cesarean delivery, and presence of labor before delivery. Pregnancy complications included hypertensive disease (chronic, gestational, or preeclampsia), diabetes mellitus (preexisting or gestational), prolonged rupture of membranes, oligohydramnios, preterm labor, or antenatal hospitalization.

Based on published reports, an estimated rate of composite adverse neonatal outcome of approximately 23% could be expected in the study group, which was calculated from a rate of 30% in births at 34 0/7 to 36 6/7 weeks' gestation⁸ and 15.7% in births at 36 0/7 to 38 6/7 weeks' gestation.⁴ Assuming a 5% rate of composite adverse neonatal outcome in the comparison group of births at 39 0/7 to 40 6/7 weeks' gestation,⁸ a sample size of 68 subjects in each group would be required to detect the aforementioned difference in composite adverse neonatal outcome with 80% power and an alpha of 0.05. During the study period, we identified 152 patients who met inclusion criteria for the study group. We then randomly selected 119 subjects for the reference group. Because of significant differences in the rate of cesarean delivery between the 2 groups (67% in the study group and 28% in the comparison group), we increased the sample size of the reference group to match the rate of cesarean deliveries (67%) to the study group. These additional reference group subjects were also selected at random from births during the study period, which yielded a final sample size of 262 for the reference group, with births at 39 0/7 to 40 6/7 weeks' gestation.

The data were analyzed with SAS software (version 9.2; SAS Institute, Inc, Cary, NC). Differences between categorical and continuous variables were tested with the χ^2 (or Fisher's exact test, where necessary) and Kruskal-Wallis test, respectively. Multivariate logistic regression was used to estimate the odds of composite adverse neonatal outcome for infants who were born after amniocentesis with documented lung maturity and were adjusted for covariates with significant differences that were seen in univariate analyses. Backward selection yielded a final model of statistically influential and biologically plausible covariates. Covariates that were included in the final model were hypertensive disease, diabetes mellitus, birthweight of infant, use of antenatal steroids, history of cesarean delivery, and presence of labor before delivery. Comparisons with associated probability

values $< .05$ and 95% confidence intervals (CIs) that were not inclusive of the null value of 1 were considered statistically significant differences.

Results

Of the 735 charts that were screened of women who had amniocenteses for fetal lung maturity testing during the study period (Figure), 152 women and infants met inclusion criteria and had documented fetal lung maturity by at least 1 of the 3 fetal lung maturity tests measured on the panel (TDx-FLM II, phosphatidylglycerol, or LBC). Fetal lung maturity was positive by TDx-FLM II (61.2%), by phosphatidylglycerol (45.7%), and by LBC (74.3%) of the time. Of the women with positive fetal lung maturity, 40% had only 1 mature fetal lung test; 39% had 2 mature indices, and 20% had 3 mature indices.

Women who delivered at < 39 weeks' gestation after an amniocentesis with mature fetal lung indices had a higher incidence of a previous premature infant and previous cesarean delivery, hypertensive disease and diabetes mellitus, preterm labor, and intrauterine growth restriction (Table 1). More women in the reference group (delivery at ≥ 39 weeks' gestation) had the presence of labor before delivery. Of the women who did undergo labor, 78.9% of the women in the study group were induced, as compared with 45.1% of the women in the reference group ($P < .01$). Of note, 10.1% of the women (15 patients) in the study group also received antenatal steroids.

Taking into consideration the important effect of gestational age on neonatal outcomes, we stratified our study group, all of whom were born after mature amniocentesis, into those born late preterm (34 0/7 to 36 6/7 weeks' gestation) and early term (37 0/7 to 38 6/7 weeks' gestation), according to the classification by Engle and Kominarek¹⁰ (Table 2). The rate of composite adverse neonatal outcome was significantly higher in both the late preterm and early-term infants who were born after mature amniocentesis, compared with the reference group. Rates of composite adverse outcome, hypoglycemia, treatment with intravenous fluids, gavage feeding, phototherapy, sepsis evaluation, neonatal intensive care admission, and oxygen supplementation were significantly different when compared among the 3 groups. We also compared the late preterm group and early-term group separately with the reference group who were born at ≥ 39 weeks' gestation. Despite the assertion that infants who are born at ≥ 37 weeks' gestation have little morbidity, we found significant increases in the incidence of composite adverse neonatal outcome, hypoglycemia, phototherapy, and need for oxygen supplementation in early-term infants compared with the reference group.

We repeated analyses and compared the 2 groups for neonatal outcomes by changing the criteria by which fetal lung maturity was determined, using 1 fetal lung maturity test at a time (Table 3). When each test was used individually and when TDx-FLM II assay was used in combination with phosphatidylglycerol assay (after omission of LBC), significant differences in composite score, hypoglycemia, gavage feeding, sepsis evaluation, and neonatal intensive care admission remained.

Because differences in the rates of maternal medical comorbidities, steroid administration, and previous cesarean delivery between the study and reference groups could influence neonatal outcome, we examined the effect of potential confounding by these factors in 2 ways. First, we removed women with medical comorbidities from the cohort and repeated our analysis comparing the association between adverse neonatal outcomes between the mature amniocentesis study group and the ≥ 39 -week gestation reference group in women who were most likely to be low risk (remaining, 76 in the study group and 214 in the reference group). Mothers with the complications of hypertensive disorders, premature rupture of membranes, diabetes mellitus, growth restriction, and oligohydramnios were

those considered to have medical comorbidities. These maternal or fetal conditions are recognized by ACOG to be possible indications for delivery at <39 weeks' gestation¹¹ and that these mothers may have infants who are predisposed to greater morbidity. In a similar fashion, to assess the potential influence of antenatal steroid administration on the relationship between mature amniocentesis and neonatal outcome, we removed the 15 mothers from the cohort who received steroids during their pregnancy and repeated the analysis. Finally, we performed a third subanalysis of only the mothers who had a history of cesarean delivery. In the study group, fetal lung maturity testing was ordered before their repeat cesarean delivery (remaining, 68 in the study group and 70 in the reference group). In these 3 separate subanalyses, despite removal of high-risk groups, we continued to find significant differences ($P < .05$) in the incidence of the composite adverse neonatal outcome between the study and reference groups.

Second, we used multivariate regression analyses to account for potential confounding. Using multivariate modeling, we assessed the association between adverse neonatal outcome and mature amniocentesis while adjusting the risk estimate for these same influential factors as noted earlier: medical comorbidities, onset of labor before delivery, antenatal steroids, and cesarean delivery. With this approach, the risk of composite adverse neonatal outcome in women who delivered at <39 weeks' gestation after an amniocentesis with mature fetal lung indices was 3.66-fold increased (95% CI, 1.48–9.09; $P < .01$), compared with deliveries at ≥39 weeks' gestation, even after adjustment for important confounding factors that included hypertensive disease, diabetes mellitus, birthweight of infant, use of antenatal steroids, history of cesarean delivery, and presence of labor before delivery. When we analyzed the subgroup of infants ($n = 71$) after removal of mothers with medical comorbidities that included diabetes mellitus, hypertension, oligohydramnios, intrauterine growth restriction or premature rupture of membranes, or administration of antenatal corticosteroids, we continued to find 3.22-fold higher risk (95% CI, 1.14–9.07; $P = .03$) of adverse outcome in infants who were delivered at <39 weeks' gestation after mature amniocentesis and after adjustment for onset of labor before delivery and history of cesarean delivery.

Furthermore, after stratifying the study group by gestational age, we found that the risk of adverse neonatal outcome was increased for both late preterm births (odds ratio, 3.56; 95% CI, 1.15–11.03; $P = .03$), and early-term births (odds ratio, 3.73; 95% CI, 1.38–10.06; $P < .01$), compared with those pregnancies that delivered at ≥39 weeks' gestation, after adjustment for the same important confounding factors. Additionally, despite accounting for the same confounding factors, infants who were born at <39 weeks' gestation, despite mature fetal lung indices, also had significantly higher risk of hypoglycemia, need for phototherapy, and oxygen supplementation (Table 4).

Comments

Our study demonstrates that, despite documented fetal lung maturity, infants who are born at <39 weeks' gestation continue to have significant neonatal morbidity, which adds support to other studies that show that documented fetal lung maturity itself is insufficient to determine an infant's readiness for postnatal life.^{4,12–14} We recognize that our study and reference groups are inherently different: patients in whom fetal lung maturity is ordered may be at a slightly higher risk for neonatal morbidity because of maternal or fetal risk factors. Still, even after using several different methods to account for these confounding risks, we continued to find significant differences in both composite adverse neonatal outcome and individual neonatal morbidities between the study and reference groups. In our multivariate modeling, we included risk factors that were significantly different in univariate analyses (diabetes mellitus, hypertensive disease, presence of labor before delivery, history of

cesarean delivery, use of antenatal steroids) yet still found increased risk of adverse neonatal outcome in those infants born at <39 weeks' gestation after mature fetal lung indices, even after adjustment for these possible influential confounders. Because the definition of our study group correlated gestational age and mature fetal lung indices, we believe that gestational immaturity is most responsible for these adverse outcomes.

Although fetal lung maturity testing was designed to detect respiratory distress syndrome (RDS), which is one of the most common complications of premature delivery, it is far from perfect. Indeed, most fetal lung maturity tests indirectly are a measure of pulmonary surfactant, which is known to be deficient in RDS. Because of the high negative predictive value of these fetal lung maturity tests, lung maturity testing predicts the absence of RDS.¹ Indeed, in our study, the rate of oxygen need in infants who were born at <39 weeks' gestation after documented lung maturity was not significantly different than those infants who were born at >39 weeks' gestation, although our study was not powered to find differences in respiratory morbidity. In general, however, approximately 50% of infants with immature fetal lung testing results do not have RDS,¹⁵ and the risk of RDS can be as high as 8% in 34-week infants with mature fetal lung indices.¹⁶ In one study of late preterm infants, 34–37 weeks' gestation, who were born to hospitalized women with mild preeclampsia after positive fetal lung maturity testing, 10% of the infants had RDS.¹⁷ Clearly, the continued occurrence of RDS, despite documented fetal lung maturity, indicates that substantial opportunity still exists for improved fetal lung maturity testing.

Neonatal morbidity in births after documented fetal lung maturity has been examined in several previous studies. Several studies included infants who were born at <34 weeks' gestation,^{12–14} which may overestimate morbidity rates in the study group, because those infants who were born at <34 weeks' gestation routinely are admitted to neonatal intensive care based on gestational age criterion alone. Indeed, these studies show a high rate of neonatal morbidity in those infants who are born prematurely but have been methodologically limited by the lack of a reference group without lung maturity testing for comparison.^{13,14} One study that was similar in design to ours limited comparisons among only infants who were born from 36 to <39 weeks' gestation after fetal lung maturity testing and only among those infants who were tested with the lecithin-sphingomyelin ratio or the presence of phosphatidylglycerol.⁴ In this study, we sought to expand the generalizability of our findings by assessing outcomes of neonates who were born after mature indices from a variety of the most commonly used amniotic fluid lung maturity tests (TDx-FLM II assay, LBC, and phosphatidylglycerol assay) and to quantify the risk of neonatal morbidity that was stratified by the wide range of gestational ages at which lung maturity testing is most commonly used in obstetric practice, 34–39 weeks' gestation. Nevertheless, all 3 of the fetal lung maturity tests that were examined here have limitations in the prediction of a fetus's readiness for postnatal life, as shown in this study by the high incidence of morbidity that was seen in the infants who were born at <39 weeks' gestation.

We recognize that LBC is an inexpensive, but simple, test of fetal lung maturity and is also the test with the most variability. Several studies have documented low- and high-risk ranges of RDS that do not agree.^{18–21} Although multiple studies state that each institution should validate its own standards according to the methods used,^{20,22} we recognized that the inclusion of LBC as a test for fetal lung maturity, with our hospital laboratory cutoff of >29,000 per μL , might be interpreted as a weakness of the study. Thus, we stratified our analysis in the basis of the specific lung maturity test that was used. When comparing differences between the study and reference group and considering only study subjects with mature TDx-FLM II or phosphatidylglycerol tests, we continued to find significant differences in neonatal morbidity and composite adverse neonatal outcome. Therefore, we

conclude that the results of our study are valid, regardless of those who may have been deemed mature by LBC testing alone.

It is important to consider the risks to the mother and fetus of delaying delivery until 39 weeks' gestation if the pregnancy is complicated by a condition that may worsen over time by continuing the pregnancy. Obstetricians commonly weigh the risk of early delivery against the benefit of avoiding increasing risk over time by pregnancy prolongation in a variety of pregnancy complications. A weakness of our study is that we are unable to determine fully the individual clinical risk assessment that took place in each scenario. We did attempt to take into consideration risk estimates in those neonates who were born after mature fetal lung indices who were most likely delivered electively. To do this, we removed mothers with medical conditions that may necessitate early delivery from the study group, repeated our analysis, and still found significant differences in neonatal morbidity compared with those infants who were born at >39 weeks' gestation. Although we do not have sufficient data to appreciate fully the exact circumstances in which each of these fetal lung maturity tests were performed, the obstetric care providers ordered them for clinical scenarios in which they had time to ponder and act on the results, which implies that the timing of delivery was elective.

Certain pregnancy conditions do require premature delivery; when delivery is indicated, awaiting results from fetal lung maturity testing should be irrelevant, because one would not have the luxury to wait for fetal lung maturity in the first place. Robinson and Grobman²³ affirm this assertion with their study regarding the timing of delivery for women with placenta previa and accreta, who are typically delivered early to avoid increasing risks of maternal and neonatal morbidity with advancing gestation. They found that the timing of delivery under a variety of circumstances was ideal at 34 weeks' gestation and that, at any gestational age, amniocentesis for fetal lung maturity did not result in better outcomes.²³ Similarly, Stotland et al²⁴ performed a computerized decision analysis to assess different delivery strategies for women with a history of classic cesarean delivery; early delivery at 36 weeks' gestation without amniocentesis provided better maternal outcomes rather than delaying delivery until amniocentesis indicated fetal lung maturity. In both scenarios, early delivery was warranted because the risks to the mother outweighed the risk of premature delivery, and the mother was treated accordingly.

In the event, however, in which pregnancy or maternal factors do not indicate clearly premature delivery, our study supports the notion that it is gestational maturity itself that has the strongest correlation to a lack of neonatal morbidity. Although fetal lung maturity may help to predict the absence of RDS, it does not absolve the infant from complications because of immaturity of other organ systems. If delivery is indicated on the basis of the maternal or fetal condition at <39 weeks' gestation, after careful consideration of the risks to mother and fetus, fetal lung maturity testing should be irrelevant. Therefore, we continue to espouse strict adherence to the ACOG recommendation that infants should not be delivered electively at <39 weeks' gestation, whether or not fetal lung maturity is demonstrated.

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FIGURE. Flow diagram of the study population

Kamath. Neonatal outcomes after documented fetal lung maturity. *Am J Obstet Gynecol* 2011.

TABLE 1

Comparison of maternal factors

Maternal characteristic	Mature amniocentesis at 34.0–38.6 wk of gestation (n = 152)	Reference group at 39.0 wk of gestation (n = 262)	P value
Maternal age, y ^a	29.2 ± 6.3	27.8 ± 6.3	.04
History of premature infant, n (%)	57 (37.5)	20 (7.6)	< .01
History of cesarean delivery, n (%)	68 (44.7)	70 (26.8)	< .01
Cesarean delivery, n (%)	103 (67.8)	171 (65.3)	.60
Hypertensive disease, n (%)	33 (21.7)	16 (6.1)	< .01
Diabetes mellitus, n (%)	40 (26.3)	21 (8.0)	< .01
Premature rupture of membranes, n (%)	2 (1.3)	0	.13
Preterm labor, n (%)	22 (14.5)	2 (0.8)	< .01
Intrauterine growth restriction, n (%)	9 (5.9)	2 (0.8)	< .01
Oligohydramnios, n (%)	14 (9.2)	13 (5.0)	.09
Antenatal steroids, n (%)	15 (10.1)	0	< .01
Presence of labor before delivery, n (%)	71 (46.7)	184 (70.2)	< .01

^aData are given as mean ± SD.

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TABLE 2

Comparison of neonatal factors by late preterm, early term, and term

Neonatal outcome	Late preterm mature amniocentesis at 34.0–36.6 wk gestation, n (%) ^a	Early-term mature amniocentesis at 37.0–38.6 wk gestation, n (%) ^b	Term at 39.0–40.6 wk gestation, n (%) ^c	P value ^d
Composite adverse neonatal outcome ^e	16 (21.1) ^f	10 (13.2) ^f	11 (4.2)	< .01
Hypoglycemia	18 (23.7) ^f	13 (17.1) ^f	15 (5.7)	< .01
Intravenous fluids for hypoglycemia	2 (2.6)	2 (2.6)	0	.03
Gavage feeds	8 (10.5) ^f	0	0	< .01
Phototherapy	4 (5.3) ^f	7 (9.2) ^f	3 (1.2)	< .01
Sepsis evaluation	13 (17.1) ^f	4 (5.3)	9 (3.5)	< .01
Treatment with antibiotics	2 (2.6)	2 (2.6)	2 (0.8)	.31
Central venous line	1 (1.3)	1 (1.3)	0	.18
Neonatal intensive care admission	14 (18.4) ^f	4 (5.3)	8 (3.1)	< .01
Oxygen supplementation	1 (1.3)	3 (4.0) ^f	1 (0.4)	.04

^a n = 76 women;^b n = 76 women;^c n = 262 women;^d Denotes χ^2 statistic for comparison among 3 groups for each neonatal outcome;^e Consists of neonatal intensive care admission, phototherapy, antibiotic treatment, intravenous fluids for hypoglycemia, or gavage feeding;^f Denotes significant difference ($P < .05$) between the group in the column heading when compared individually to the reference group at 39 weeks' gestation.

Kamath. Neonatal outcomes after documented fetal lung maturity. Am J Obstet Gynecol 2011.

TABLE 3

Adverse neonatal outcomes by fetal lung maturity test

Neonatal outcome	Lung maturity			
	Determined by TDx-FLM II assay and phosphatidylglycerol only: lamellar body count removed (n = 114)	Determined by TDx-FLM II assay only (n = 93)	Determined by phosphatidylglycerol only (n = 58)	Determined by lamellar body count only (n = 113)
Gestational age at positive fetal lung maturity results, wk ^a	36.6 ± 1.2	36.6 ± 1.2	36.9 ± 1.1	36.6 ± 1.2
Composite adverse neonatal outcome, n (%) ^b	20 (17.5) <i>P</i> < .01 ^c	18 (19.4) <i>P</i> < .01 ^c	10 (17.2) <i>P</i> < .01 ^c	19 (16.8) <i>P</i> < .01 ^c
Delivery room interventions: oxygen or more, n (%)	25 (21.9) <i>P</i> = .08	20 (21.5) <i>P</i> = .05	13 (22.4) <i>P</i> = .22	31 (27.4) <i>P</i> < .01 ^c
Hypoglycemia, n (%)	23 (21.1) <i>P</i> < .01 ^c	21 (22.6) <i>P</i> < .01 ^c	10 (17.2) <i>P</i> < .01 ^c	19 (16.8) <i>P</i> < .01 ^c
Intravenous fluids for hypoglycemia, n (%)	3 (2.6) <i>P</i> = .03 ^c	3 (3.2) <i>P</i> = .02 ^c	1 (1.7) <i>P</i> = .18	3 (2.7) <i>P</i> = .03 ^c
Gavage feeds, n (%)	5 (4.4) <i>P</i> < .01 ^c	4 (4.3) <i>P</i> < .01 ^c	2 (3.5) <i>P</i> = .03 ^c	7 (6.2) <i>P</i> < .01 ^c
Phototherapy, n (%)	8 (7.0) <i>P</i> < .01 ^c	7 (7.5) <i>P</i> < .01 ^c	3 (5.2) <i>P</i> = .08	8 (7.1) <i>P</i> < .01 ^c
Sepsis evaluation, n (%)	11 (9.7) <i>P</i> = .01 ^c	10 (10.8) <i>P</i> < .01 ^c	7 (12.1) <i>P</i> = .01 ^c	14 (12.4) <i>P</i> < .01 ^c
Treatment with antibiotics, n (%)	3 (2.6) <i>P</i> = .15	3 (3.2) <i>P</i> = .12	2 (3.5) <i>P</i> = .15	3 (2.7) <i>P</i> = .16
Central venous line, n (%)	1 (0.9) <i>P</i> = .30	1 (1.1) <i>P</i> = .26	1 (1.7) <i>P</i> = .18	1 (0.9) <i>P</i> = .30
Neonatal intensive care admission, n (%)	14 (12.3) <i>P</i> < .01 ^c	13 (14.0) <i>P</i> < .01 ^c	7 (12.1) <i>P</i> < .01 ^c	13 (11.5) <i>P</i> < .01 ^c
Oxygen supplementation, n (%)	3 (2.6) <i>P</i> = .08	3 (3.2) <i>P</i> = .06	2 (3.5) <i>P</i> = .09	3 (2.7) <i>P</i> = .08

Comparison is between study group (34 0/7 weeks' gestation born after positive fetal lung maturity, as determined by different fetal lung maturity tests, and the reference group (39 0/7 to 40 6/7 weeks' gestation).

^aData are given as mean ± SD;

^bConsists of neonatal intensive care admission, phototherapy, antibiotic treatment, intravenous fluids for hypoglycemia, or gavage feeding;

^cDenotes significant differences: *P* < .05.

Kamath. Neonatal outcomes after documented fetal lung maturity. Am J Obstet Gynecol 2011.

TABLE 4

Risk of neonatal morbidity in infants with positive fetal lung maturity

Neonatal outcome	Adjusted odds ratio (95% CI) ^a
Composite adverse neonatal outcome ^b	3.66 (1.48–9.09)
Delivery room interventions: oxygen or more	1.43 (0.77–2.66)
Hypoglycemia	3.95 (1.76–8.85)
Phototherapy	6.67 (1.52–29.18)
Sepsis evaluation	2.72 (0.95–7.81)
Treatment with antibiotics	4.23 (0.55–32.69)
Neonatal intensive care admission	2.68 (0.91–7.89)
Oxygen supplementation	19.14 (1.62–225.88)

The risk of neonatal morbidity in infants born at <39 weeks with documented fetal lung maturity, compared to the reference group born at 39 0/7 to 40 6/7 weeks' gestation is shown.

CI, confidence interval.

^a Adjusted for hypertensive disease, diabetes mellitus, birthweight of the infant, use of antenatal steroids, and presence of labor before delivery;

^b Consists of neonatal intensive care admission, phototherapy, antibiotic treatment, intravenous fluids for hypoglycemia, or gavage feeding.

Kamath. Neonatal outcomes after documented fetal lung maturity. *Am J Obstet Gynecol* 2011.