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ORIGINAL PAPER

Accuracy of Amniotic Fluid Lamellar Body Counting for Evaluating Fetal Lung Maturity

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Background: Respiratory distress syndrome (RDS) is one of the important causes of mortality in neonates. This study was designed to assess the role of the amniotic fluid lamellar body counting in predicting fetal lung maturity. **Method:** This study was conducted during 2010, April to 2011, February, at Isfahan University of Medical Sciences, Isfahan, Iran. One hundred and twenty eight amniotic fluid samples were obtained during normal delivery, or before rupturing the membrane in cesarean, and lamellar body was assessed by cellular counter. The respiratory statuses of neonates were determined at delivery and the optimal cut-off point was assessed by receiver operating characteristic (ROC) curve. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were evaluated in optimal cut-off point. **Results:** One hundred and twenty eight amniotic samples and 131 infants were evaluated. The means of maternal and gestational ages were 28.12 ± 3.84 years and 32.56 ± 2.72 weeks, respectively. The mean of lamellar body was 31266 ± 15831 µl in matured lung infants compared to 63081 ± 16966 µl in immature lung infants ($p < 0.001$). The optimal cut-off point was evaluated as 47500 µl in predicted pulmonary maturity with sensitivity of 85.1%, specificity of 91.2%, positive predictive value of 92.6% and negative predictive value of 82.5%. **Conclusion:** This study indicated that lamellar body counting test has a high positive predictive value with a good sensitivity, specificity and negative predictive value. Future studies for different cellular counters are warranted. **Key words: Respiratory distress syndrome, Lung maturity, Lamellar body, Sensitivity.**

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1. INTRODUCTION

Respiratory distress syndrome (RDS) is one of the most common reasons of mortality in neonates. American College of Obstetrics and Gynecology recommended determining the status of fetal lung maturity, in infants with less than 39 weeks of gestational age, to avoid RDS (1). So, evaluating of fetal lung maturity plays an important role in managing of RDS. There are some tests for evaluating the fetal lung maturity with some advantages and disadvantages. For example, the ratio of sphingomyelin to lecithin is a traditional test for assessing the fetal lung maturity (2); but taking the long time to do, being costly, lack of widely access, and none ability to use when meconium or blood stained the amniotic fluid, are its disadvantages.

Lamellar bodies are produced by type II pneumacytes in fetal alveolus and secreted to amniotic fluid during respiratory movement. These bodies are similar to platelet and can be assessed by cellular counter instruments easily (3); this diagnostic method, in contrast of previous tests, is faster, simpler and cheaper. Some studies have showed that counting lamellar bodies can be useful in estimation of lung maturity (4).

In regard to deficiency of neonatal intensive care units (NICU), medical orderly, and specialist and not widely measurement of sphingomyeline to lecithin ratio in Iran, this study was aimed to evaluate the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of amniotic lamellar body in predicting fetal lung maturity.

2. METHODS

This analytic study was conducted from 2010, April to 2011, February, at AL-Zahra Hospital, the main referral university hospital of Isfahan University of Medical Sciences, Isfahan, Iran. Women with 28-37 weeks of gestational age, who had been decided to terminate their pregnancy, were enrolled in the study.

Fetal anomalies, intra uterine fetal death (IUFD), blood in amniotic fluid, rapture of placenta, and patient dissatisfaction were the exclusion criteria. The study protocol was approved in the Ethics Committee of Isfahan University of Medical Sciences and the consent form was assigned by all participants. The study was registered at ClinicalTrials.gov (Identifier: NCT01463722).

After registering demographic data, based on computer randomized table, 128 women divided into two groups. The amniotic fluid samples were ob-

tained by amniocentesis (by Principal investigator) during normal delivery or before rupturing the membrane in cesarean. These samples were sent to the laboratory, as soon as possible; after centrifuging with 500 rounds per minute for 3 minutes, they were placed in the cell counter machine (STKR coulter, Beckman-Coulter™ Company, Fulton, MO).

All patients, who were under 34 weeks of gestational age, received corticosteroid therapy before their delivery due to standard schedule.

The respiratory status of each neonate was determined and recorded at delivery. The diagnosis of immaturity and RDS was based on the following criteria:

a) Physical examination findings such as: nasal flaring, retraction, grunting, and tachypnea.

b) Needing Oxygen support for more than 24 hours with three chest x-ray findings.

The optimal cut-off point was assessed with receiver operating characteristic (ROC) curve. The sensitivity, specificity, NPV and PPV were also evaluated.

The outcome assessors were blinded to the results and this study was single blinded.

The maximum sample size, based on the coefficient of confidence, with $\alpha = 0.05$, $P = 0.5$ and $d = 0.1$, was assessed as 98 persons. All statistical analyses were done with $SPSS_{16}$ software (version 16, SPSS Inc., Chicago, IL) and the $p < 0.05$ was determined as the statistical difference level. Independent-t was the used statistical test.

Variables		With lung maturity (n = 74)	Without lung maturity (n = 57)	P-value
Age (Year)		28.4 ± 3.98	27.7 ± 3.7	0.339*
Gestational age (Week)		34.28 ± 1.86	30.33 ± 1.92	< 0.001*
Parity		1.96 ± 0.96	1.86 ± 0.93	0.551*
Lamellar body (µl)		63081 ± 16966	31266 ± 15831	< 0.001*
Type of delivery	NVD	16 (21.6%)	14 (24.6%)	0.7**
	C/S	58 (78.4%)	43 (75.4%)	

Data were presented as Mean ± SD and number (%)
*Independent t-test
**Chi-square test
NVD: Normal vaginal delivery; C/S: Cesarean section

Table 1. Demographic data of the studied mothers

Cut-off point (µl)	Sensitivity	Specificity	Cut-off point (µl)	Sensitivity	Specificity
1199	1.000	1.000	49500	0.743	0.088
1600	1.000	0.982	50500	0.716	0.088
4500	1.000	0.965	51500	0.703	0.088
9000	1.000	0.947	53000	0.676	0.070
12000	0.986	0.947	54500	0.649	0.070
14000	0.986	0.930	56000	0.622	0.070
16000	0.986	0.895	57500	0.608	0.070
17500	0.986	0.842	58500	0.568	0.070
19000	0.986	0.807	59500	0.527	0.070
20500	0.986	0.754	62000	0.500	0.053
22500	0.986	0.702	64500	0.486	0.053
24500	0.986	0.684	66500	0.432	0.053
26000	0.986	0.614	68500	0.419	0.053
27500	0.986	0.596	69500	0.392	0.035
29000	0.986	0.526	70500	0.351	0.035
32000	0.986	0.421	72000	0.311	0.035
34500	0.986	0.386	73500	0.270	0.035
35500	0.986	0.316	74500	0.243	0.035
37000	0.986	0.298	76500	0.230	0.035
38500	0.986	0.228	78500	0.203	0.035
39500	0.946	0.211	79500	0.189	0.035
40500	0.919	0.175	81000	0.095	0.018
41500	0.905	0.175	83500	0.095	0.000
42500	0.905	0.158	87000	0.081	0.000
43500	0.905	0.123	90500	0.068	0.000
44500	0.892	0.123	95000	0.041	0.000
46000	0.865	0.088	99500	0.027	0.000
47500	0.851	0.088	101500	0.014	0.000
48500	0.797	0.088	102001	0.000	0.000

Table 2. The sensitivity and specificity of amniotic lamellar body in different concentrations

3. RESULTS

One hundred and twenty eight pregnant women with 131 infants were evaluated. The mean of maternal and gestational ages were 28.12 ± 3.84 years and 32.56 ± 2.72 weeks, respectively. Of 128 pregnancies, 126 women were singleton, one had twins, and one was triple. Fifty two mothers were gravida 1, 48 were gravida 2, 23 were gravida 3, 6 were gravida 4, and 2 were gravida 5.

The mothers' demographic data are shown in table 1. Seventy four newborns have matured lung and 57 were delivered with RDS. The mean of mother's age in immature and matured lung infant were 25.75 ± 3.66 and 28.40 ± 3.89 years, respectively. There was no significant relationship between lung immaturity with maternal age ($p = 0.339$).

The mean maternal gravity in fetal immature lung group was 1.58 ± 0.39 compared with 1.59 ± 0.59 in fetal maturity lung group. The lung maturity had no significant relationship with mother's gravity ($p = 0.551$). The gestational age of mothers with matured fetal lung (34.28 ± 1.86 weeks) was significantly higher than mothers with immature lung infant (30.33 ± 1.92 weeks) ($p < 0.001$).

The mean value of lamellar body was 31266 ± 15831 µl in immature lung infants compared with 63081 ± 16966 µl in matured lung infant ($p < 0.001$) with a strongly direct correlation between gestational age and lamellar body concentration ($r = 0.734$, $p = 0.001$) (Figure 1).

In ROC curve, the area under-curve the was about 0.923 ($r < 0.001$) which indicated that lamellar body counting test had a fair accuracy for diagnosis of fetal lung maturity (Figure 2).

According to ROC curve, the optimal cut-off point for lamellar body counting was 47500 µl with the sensitivity of 85.1%, specificity of 92.6%, NPV

of 82.5, and PPV of 92.6 (Table 2).

4. DISCUSSION

Our findings indicated that lamellar body counting test has a high confidence value in detecting fetal lung maturity. The sensitivity of 85.1% and specificity of 91.2% showed that this test is suitable for detecting fetal lung maturity.

Rapid and accurate diagnosis of fetal lung maturity in management of high risk pregnancies has an important role to avoid RDS. Lamellar body counting is one of rapid, accurate, and cheap tests which can be useful in detecting fetal lung maturity.

This study showed when lamellar body concentration is 47500 µl, as a cut-off point, the sensitivity, specificity, PPV, and NPV are 85.1%, 91.2%, 92.6%, and 82.5%, respectively. Ashwood et al. reported that lamellar body counting is a suitable test for predicting fetal lung maturity. They also found the optimal cut-off point of 55000 µl for making decision in fetal lung maturity (5). Dalence et al. reported 30000 µl as optimal cut-off point (6). The differences in the optima cut-off points may be due to the difference in the used centrifuge protocols and counter instruments.

Neerhof et al. (7) showed that centrifuge is not a necessary process for this test and suggested 50000 µl as an optimal cut-off point. They also reported that under the 15000 µl of lamellar body concentration, immaturity of fetal lung existed with 100% sensitivity. The difference between their study and our findings may be due to different methods of lamellar body measurement.

Wijnberger et al. (8) in a meta-analysis mentioned that 32000 µl of concentration is suitable for prediction fetal lung maturity. They indicated that capability of fetal lung maturity prediction with lamellar body counting is equal to sphingomyeline to lecithin ratio test. Therefore, they recommended lamellar body counting test as the first choice for fetal lung maturity assessing. Our findings supported this idea.

We found the NPV of 82.5 % and PPV of 92.6% for the lamellar body counting test. Khazardoost et al. in Tehran, Iran showed NPV of 97% and PPV of 48% and Beinlich et al. showed PPV of 50% and NPV of 90% for this test. These differences probably may be because of differences in sample size, inclusion criteria, or used instruments. The sensitivity in our findings was 85.1% which were similar to other studies (9,10).

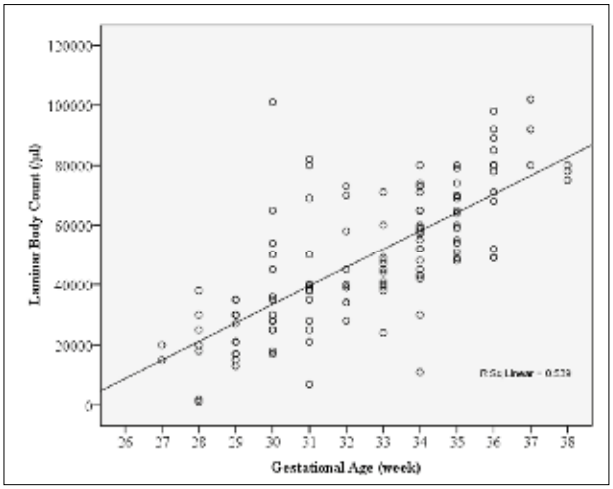

Figure 1. Correlation of gestational age with lamellar body count

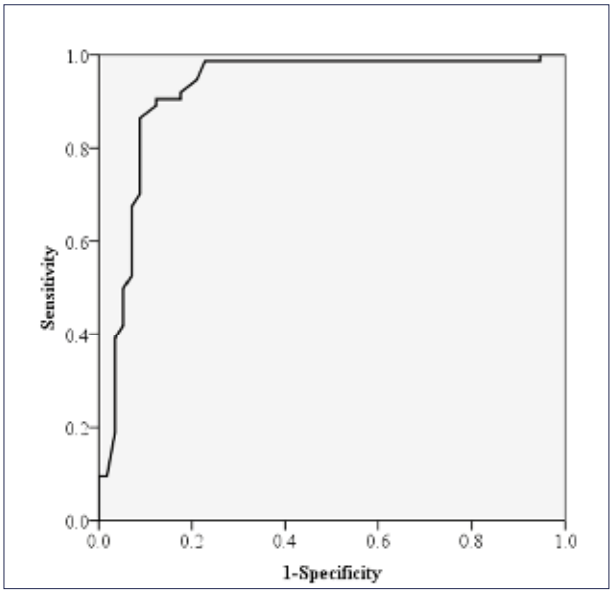

Figure 2. ROC curve for determining the optima cut off.

5. CONCLUSIONS

This study indicated that lamellar body counting test has a high PPV with a good sensitivity, specificity, and NPV. Future studies for different cellular counter are warranted.

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Conflict of interest: none declared.

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