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Lamellar Bodies Count In Amniotic Fluid From Vaginal Pool as A Predictor For Fetal Lung Maturity In Preterm Premature Rupture of Membranes

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ABSTRACT

Background: Lamellar body count (LBC) is a newer method which predict fetal lung maturity. The purpose of this study was to assess the efficacy of the amniotic fluid lamellar body counting from vaginal pool in predicting fetal lung maturity in women with preterm premature rupture of membranes. Methods: In a prospective study, Amniotic fluid samples was collected by a sterile speculum inserted in the posterior fornix of the vagina with gestational age between 28 and 36 completed weeks . LBC was estimated in uncentrifugated amniotic fluid samples using The Sysmex K – 800 hematological analyzer and its platelet channel. Results: ninety-two pregnant women were collected were between 28 to 37 completed weeks. The study showed a significant correlation between level of LBC and fetal lung maturity using 38.0 (x103/µL) as a cut-off point for LBC; as it is can be considered a good predictor for fetal lung maturity with sensitivity 92.9% and specificity 90.6% , positive predictive value of 81.3% and negative predictive value of 96.7%. Conclusions: Counting of lamellar bodies in amniotic fluid may be used to predict fetal lung maturity.

Keywords: Lamellar body counting (LBC), Preterm Premature Rupture of Membranes (PPROM), Respiratory Distress Syndrome (RDS), Fetal lung maturity

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INTRODUCTION

Preterm Premature Rupture of Membranes (PPROM) defines as spontaneous rupture of the amniotic membranes before 37 weeks gestation and before the time of labor. There are many risk factors for PPROM, Infection is the main one (15-25%), especially at earlier gestational ages. Previous history of PPROM, shortness of cervical length, second-trimester and third-trimester hemorrhage, decreased body mass index, bad socioeconomic status, smoking, and drugs intake are also major risk factors for PPROM [1].

Neonatal respiratory distress syndrome (RDS) is due to lung immaturity with a high mortality characterized by decreased concentrations of pulmonary surfactant. Gestational age of the fetus shows risk based on level of pulmonary surfactant [2]. Laboratory investigations of the fetal pulmonary maturity help obstetricians in evaluating the risk of respiratory distress syndrome (RDS) when premature delivery of an infant is done [3].

Lamellar body count (LBC) is a newer method which predict fetal lung maturity. Final storage of surfactant happens within lamellar bodies, which are released from type-II pneumocytes into the alveoli [4]. The purpose of this study was to assess the efficacy of the amniotic fluid lamellar body counting from vaginal pool in predicting fetal lung maturity in women with preterm premature rupture of membranes

METHODS

After approved by the research ethical committee of Faculty of Medicine, Zagazig University, A prospective study was held in the labor and delivery ward of the department of Obstetrics and Gynecology at El–Monera General Hospital. This study was conducted on 92 pregnant women with singleton normal pregnancies between 28 and 37 completed weeks of gestation, diagnosed to have PPROM. Written informed consent was obtained from all patients, the work was carried out for studies involving humans in accordance with the World Medical Association's Code of Ethics (Helsinki Declaration).

Inclusion criteria: Pregnant women with preterm premature rupture of membranes, singleton pregnancies, gestational age from 28-36 weeks, the fetus is alive with regular heart beats by ultrasound, delivery within 2 days after sample collection.

Gestational age was confirmed by known regular last menstrual period and confirmed by ultrasound measurement during the first trimester of pregnancy. Amniotic fluid samples were collected by a sterile speculum inserted in the posterior fornix of the vagina. Samples containing 2 mL of amniotic fluid were immediately transported to the clinical laboratory in a test tube and analyzed according to an established protocol. LBC was estimated in uncentrifugated amniotic fluid samples using The Sysmex K – 800 hematological analyzer and its platelet channel.

Management according to Prelabor Rupture of Membranes (PROM) protocol; The regimen of prophylactic antibiotics was given for seven days to pregnancies <34 weeks of gestation at the time of membrane rupture. Course of Corticosteroids was given to pregnancies between 23 and 34 weeks of gestation.

The presence of RDS was defined clinically when the newborn developed tachypnea and grunting, had a chest radiography showing a diffuse reticular pattern and air bronchogram, and required oxygen for 24 hours or more. Obstetricians, neonatologists and radiologists were blinded to the results of the LB count attained from the exam.

Statistical Analysis:

The collected data were computerized and statistically analyzed using SPSS program (Statistical Package for the Social Sciences) version 25.0. Qualitative data were represented as frequencies and relative percentages. Continuous data were presented as mean±SD if normally.

RESULTS

In the current study the lamellar body count (LBC) was used in prediction of fetal lung maturity. The study included 92 pregnant women with singleton normal pregnancies between 28 and 37 completed weeks of gestation; amniotic fluid sample was collected for each woman for performance of lamellar body count.

After delivery, neonates were assessed clinically for evidence of respiratory distress syndrome (RDS). Neonatal respiratory distress syndrome (RDS) was diagnosed in 28 neonates. These neonates with diagnosis of prenatal lung immaturity had significantly younger gestational age.

Table (1): Comparison according to respiratory distress regarding maternal and neonatal characteristics

Variables		RD (N=28)	No RD (N=64)	P
Age (years)		26.4±4.7	27.3±3.9	^0.328
BMI (kg/m^2)		26.3±2.2	26.1±2.0	^0.741
LB (x10^3/µL)		25.4±10.7	57.5±15.5	**^<0.001***
Parity	**Primi**	9 (32.1%)	23 (35.9%)	#0.725
	Multi	19 (67.9%)	41 (64.1%)	
Mode of delivery	**VD**	15 (53.6%)	44 (68.8%)	#0.162
	CS	13 (46.4%)	20 (31.3%)	
GA (weeks)		31.9±2.4	34.8±0.9	**^<0.001***
Birth weight (kg)		1.8±0.5	2.4±0.2	**^<0.001***

Table (1) showed that no significant difference according to respiratory distress regarding **maternal age, BMI, parity and mode of delivery.** Cases with respiratory distress significantly had lower **LB, GA and birth weight.**

Table (2): Comparison according to LB level regarding maternal and neonatal characteristics

Variables		LB ≤38.0 (N=32)	LB >38.0 (N=60)	P
Age (years)		26.8±4.6	27.1±3.9	^0.714
BMI (kg/m^2)		26.2±2.2	26.1±2.0	^0.880
Parity	**Primi**	9 (28.1%)	23 (38.3%)	# 0.326
	Multi	23 (71.9%)	37 (61.7%)	
Mode of delivery	**VD**	18 (56.3%)	41 (68.3%)	# 0.250
	CS	14 (43.8%)	19 (31.7%)	
GA (weeks)		31.9±2.4	34.8±0.9	**^<0.001***
Birth weight (kg)		1.9±0.5	2.4±0.2	**^<0.001***
APGAR1		5.5±1.6	7.6±0.6	**^<0.001***
APGAR5		6.4±1.6	8.5±0.6	**^<0.001***
Respiratory distress (RD)		26 (81.3%)	2 (3.3%)	**#<0.001***
Respiratory distress grade (N=26,2)	**I**	13 (48.1%)	2 (100.0%)	&0.483
	II-IV	14 (51.9%)	0 (0.0%)	

^Independent t-test. #Chi square test. &Fisher's Exact test. *Significant

Table (2) showed that cases with LB ≤38.0 significantly had lower **GA, birth weight and APGAR scores** and significantly had more frequent **respiratory distress**.

Table (3): Diagnostic characteristics of LB ≤38.0 (x10^3/µL) in predicting respiratory distress

Characteristics	Value	95% CI
Sensitivity	92.9%	76.5%–99.1%

Specificity	90.6%	80.7%–96.5%
Diagnostic accuracy (DA)	91.3%	83.6%–96.2%
Youden's index	83.5%	71.6%–95.4%
Positive Predictive value (PPV)	81.3%	63.6%–92.8%
Negative Predictive value (NPV)	96.7%	88.5%–99.6%
Positive likelihood ratio (LR+)	9.90	4.59–21.36
Negative likelihood ratio (LR-)	0.08	0.02–0.30
Diagnostic odd ratio (LR)	125.67	23.76–664.78
Kappa	0.803	0.673–0.932

CI: Confidence interval

Table (3) showed that **LB ≤38.0 (x10^3/µL)** had high diagnostic characteristics in predicting respiratory distress.

DISCUSSION

The current study revealed a highly significant increase in the lamellar body count with a mean of 57.5 ± 15.5 in cases giving birth to neonates without RDS compared to 25.4 ± 10.7 in cases giving birth to neonates with RDS. This result was similar to the findings of **Štimac et al.** [5] who stated that antenatal amniotic fluid LBC method was able to differentiate between the neonates without RDS and the neonates who are expected to develop moderate and/or severe forms of acute RDS. And hence, based on their results, more severe forms of RDS were accompanied by lower median LBC.

The present study revealed no statistically significant difference between LBC and age of the mother which is in contrary to the result. The present study revealed no statistically significance difference between LBC and parity of the mother which is in contrary to the result.

Results of the present study showed a significant negative correlation between respiratory distress syndrome and gestational age [34.8±0.9 weeks in neonates with no RDS compared to 31.9±2.4 weeks in neonates suffering from RDS. This finding goes in accordance with ***Nelson (2013)*** who stated a negative relationship between gestational age and incidence of respiratory distress syndrome.

On the contrary, this finding was in disagreement to the results revealed by ***Rimar et al.*** [6] who reported that the incidence of RDS in newborns born after week 32 of gestation did not significantly change. What did change are the causes. They attributed this to some leading causes of RDS (e.g. sepsis, the influence of which diminished due to better prenatal care).

The present study showed also a significant correlation between level of LBC and fetal lung maturity using **38.0 (x10^3/µL)** as a cut-off point for LBC; as it is can be considered a good predictor for fetal lung maturity with sensitivity 92.9% and specificity 90.6% , positive predictive value of 81.3% and negative predictive value of 96.7%

This finding was in difference with ***Zarean et al.***[7] who conducted a study with 128 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% [7].

Ruiz-Hernandez and colleagues conducted a prospective, blinded study to measure LBCs on 264 patients using amniotic fluid collected at the time of caesarean section or delivery. The rate of RDS in this population was 14.8%. A cutoff of >79,000/µL resulted in 100% sensitivity and 43% specificity. Although this cutoff of >79,000/µL is greater than the consensus protocol recommendation of 40,000/µL, it is supported by **Szallasi's** comparison of the Cell-Dyn 3500 with the Beckman Coulter Gen-S analyzer. When compared with the Beckman Coulter Gen-S on a Bland-Altman plot, the Cell-Dyn 3500 had a positive slope (0.76; 95% CI, 0.66 to 0.87; P<0.001) and LBC cutoff of 40,000/µL on the Gen-S analyzer corresponded to ~80,000/µL on the Cell-Dyn 3500 [8].

Wijnberger et al reported that a LBC 32000/µL guaranteed fetal lung maturity. They showed that the performance of the LBC in the prediction of RDS equal to the L/S ratio. In their Meta-analysis they concluded the LBC may be considered as the test of first choice in the assessment of fetal lung maturity [9]

KulKarni and Jayamma found that Among 50 cases, LBC was <30,000/µl in 15 cases between 30,000-35,000/µl in five cases and >35,000/µl in 30 cases. Those who developed RDS had LBC < 30,000/µl. Sensitivity and specificity of LBC to predict RDS with cut-off values of 30,000/µl was 100% and 97.2% respectively [10] ***(KulKarni and Jayamma, 2013).***

CONCLUSIONS

There was a significant correlation between level of Lamellar body counting (LBC) and fetal lung maturity. LBC could be considered a good predictor for fetal lung maturity**.**

Further studies are needed to compare between lamellar bodies count and other tests used to detect fetal lung maturity as lecithin/sphingomyelin ratio and phosphatidyl glycerol. Obvious mucus, blood and meconium has a clear effect on lamellar body counts. Amniotic Fluid volume may affect quantitative tests such as the lamellar body count.

REFERENCES

1. American College of Obstetricians and Gynecologists Practice Bulletin No. 139: Premature rupture of membranes. October 2013.

2. Alter D and Grenache D. Grenache. Fetal Lung Maturity Testing Clinical Chemistry. 2009; 131:286-299.
3. Lu J, Gronowski AM and Eby C. Lamellar Body Counts Performed on Automated Haematology Analyzers to Assess Fetal Lung Maturity. Lab Medicine 2008; 39(7): 419-423.
4. Boron WF, Boulpaep EL. Medical Physiology - A Cellular and Molecular Approach. 2005; 1319.
5. Štimac T, Petrović O, Krajina R, Prodan M, Bilić-Zulle L. Lamellar body count as a diagnostic test in predicting neonatal respiratory distress syndrome. Croatian Medical Journal. 2012; 53(3):234-238.
6. Rimar Z, Milas V, Medimurec M, Mesić I. Respiratory distress syndrome in newborns of gestational age of over 32 weeks. Coll Antropol. 2014 Jun;38(2):621-6.
7. Zarean E, Memarzadeh F, Fadaei B. Accuracy of Amniotic Fluid Lamellar Body Counting for Evaluating Fetal Lung Maturity.Med Arh. 2012; 66(2): 101-103.
8. Szallasi P, Gronowski A, Eby C. Lamellar body count in amniotic fluid: A comparative study of four different hematology analyzers. Clin Chem. 2003;49:994–997.
9. Wijnberger LD, Huisjes AJ, Voorbij HA, Franx A, Bruinse HW, Mol BW. The accuracy of lamellar body count and lecithin/sphingomyelin ratio in the prediction of neonatal respiratory distress syndrome: a meta-analysis. BJOG: An International Journal of Obstetrics & Gynaecology 2001;108:583-8.
10. KulKarni S and Jayamma Y. Amniotic Fluid Lamellar Body Count as a Predictor of Fetal Lung Maturity, Indian Journal of Clinical Practice, 2013; 23(12).