Lamellar Bodies Count to Predict Fetal Lung Maturity in Pregnant Women with Preterm Premature Rupture of Membranes

Thesis

Submitted for partial fulfillment of
master degree in Obstetrics and Gynecology

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Contents

List of Abbreviations

ACOG	:	American College of Obstetricians and Gynecologists
AF	:	Amniotic fluid
AFI	:	Amniotic fluid index
AFS	:	Antenatal fetal surveillance
BMI	:	Body mass index
BPP	:	Biophysical profile
DPPC	:	Dipalmitoy1 phosphatidylcholine
ER	:	Endoplasmic reticulum
FLM	:	Fetal lung maturity
FSI	:	Foam stability index
G A	:	Gestational age
HFUPR	:	Hourly fetal urine production rate
IUGR	:	Intrauterine growth restriction
L/S	:	Lecithen / Sphingomylin
LBC	:	Lamellar body count
NICHHD	:	National Institute of Child Health and Human Development
NICU	:	Neonatal intensive care unit
NST	:	Non-stress test
PG	:	Phosphatidy1-glycerol
PPROM	:	Preterm premature rupture of membranes
RDS	:	Respiratory Distress Syndrome
ROC	:	Receiver operating characteristics
ROM	:	Rupture of membranes
SP	:	Surfactant protein
TDx-FLM II	:	Thermal demand transmitter test for fetal lung maturity
V/Q	:	Ventilation/perfusion

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Protocol of thesis

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Introduction

Respiratory distress syndrome (RDS) is the most common cause of respiratory failure in neonates, and it is a major cause of mortality in the newborn period. Respiratory distress syndrome is caused by the insufficient production of pulmonary surfactant by immature fetal lungs, and the risk of developing RDS decreases with advancing gestational age ***(Lu et al., 2008).***

When babies are very premature, respiratory distress syndrome is a result of a combination of both alveolar epithelial cells immaturity (the lining cells have not yet thinned out) and a deficiency in surfactants. Later in pregnancy (near term), severe respiratory distress syndrome can sometimes also occur but at this point, it is usually the result of insufficient surfactants alone but the end result can be just as devastating ***(Fantz et al., 2002).***

Preterm premature rupture of membranes is the rupture of membranes during pregnancy before 37 weeks of gestation. It occurs in 3 percent of pregnancies ***(Tanya et al., 2006).***

The approach to the diagnosis of membrane rupture is clinical, with over 90% of cases being confirmed based on the presence of a suspicious history and ultrasonographic finding followed by documentation of fluid passing from the cervix or the presence of a nitrazine/ ferning positive vaginal pool of fluid, but the nitrazine and ferning tests can be falsely positive ***(Kim et al., 2005)***.

Preterm premature rupture of membranes (P-PROM) is responsible for about a third of preterm deliveries. Beside preterm delivery, P-PROM increases neonatal and maternal complications by increasing the risk of infection, cord accident and placental abruption. According to the American College of Obstetricians and Gynecologists (ACOG), with P-PROM at

32-33 completed weeks of gestation, labor induction may be considered if fetal lung maturity is documented ***(Salim et al., 2009).***

Assessment of fetal lung maturity in amniotic fluid plays an important role in the management strategies to prevent respiratory distress syndrome (RDS), particularly in women at risk for preterm delivery before term. Fetal lung maturity status can be assessed with different methods, including lecithin/sphingomyelin (L/S) ratio, phosphatidylglycerol (PG), and lamellar body count among others ***(Ghidini et al., 2005).***

Amniocentesis is the accepted mode of attaining amniotic fluid to perform tests for fetal lung maturity. However, it is an invasive procedure with risks that include placental abruption, fetal maternal hemorrhage, infection and early onset of delivery. The procedure is often technically challenging and potentially more complex when oligohydramnios is present as is often the case with preterm premature rupture of membranes ***(Salim et al., 2009).***

Amniotic fluid can be obtained transabdominally, but in patients with ruptured membranes, collection of amniotic fluid is easily possible from the vagina. The effects of potential vaginal contamination on the outcome of the LBC and L/S ratio have been studied before, but has not been related to the performance of the tests in predicting RDS ***(Lia et al., 2010).***

Lamellar body is a surfactant containing lamellated structure that is secreted by the type II pneumocyte ***(Khazardoost et al., 2005).***

Lamellar bodies (LB) originate from the fetal alveoli and are released into AF by fetal breathing movements. They contain “packed” surfactant, mainly consisting of phospholipids. Due to their size (0.2-2 mm) which corresponds

to the one of platelets (1-3 mm), they can easily be quantified by electronic cell counters ***(Beinlich et al.,1999).***

The advantage of lamellar bodies count over other physical tests (click test, stable microbubble test (SMT)) is that it is not operator dependent ***(Batista et al., 2010).***

Lamellar bodies count was selected also, because the test can be performed with equipment found in most clinical analysis laboratories. Furthermore, such counting had been reported as reliably predicts fetal lung maturity, simple, rapid and inexpensive ***(Salim et al.,2009).***

Aim of the work

The aim of this study is to evaluate the role of lamellar bodies count in the prediction of neonatal respiratory distress syndrome in women with preterm premature rupture of membranes.

Patients and Methods

Study design:
A prospective cohort study.

Setting:
Ain Shams University Maternity Hospital after the approval of research ethics committee.

Population:
Ninety three pregnant women with preterm premature rupture of membranes between 28 to 36 weeks of gestation will be recruited from obstetric outpatient antenatal clinic. A written informed consent will be obtained from each participant in the study.

Sample size estimation:-
A sample of 93 patients was found to be adequate for the study. The sample was calculated using ***(Epi- Info 2002)*** putting in consideration a sensitivity of 92 % and a specificity of 72 % as was found by a previous study guided by:-

- Confidence level = 95 %.
- Power of the test (beta error) = 80 %.
- Alpha error = 5 %.

Inclusion criteria:
1- Gestational age between 28 to 36 weeks confirmed by either documented ultrasound during first trimester of pregnancy or by known regular last menstrual period and documented ultrasound during second trimester of pregnancy.
2- The fetus is alive with regular heart beats by ultrasound.
3- Delivery within two days after amniotic fluid sampling.

Exclusion criteria:

1- Uncertain gestational age.
2- Inadequate sample volume of amniotic fluid.
3- When the samples contain obvious mucous or blood.
4- Samples with haematocrit value exceeding 1%.
5- Samples stained with meconium because its presence usually provides a compelling reason for prompt termination of pregnancy irrespective of fetal lung maturity status.
6- Intra uterine fetal death.
7- Presence of clinical amnionitis (preterm premature rupture of membranes accompanied with fever, uterine tenderness and leukocytosis).
8- Occurrence of placental abruption.
9- Delivery more than two days after amniotic fluid sampling.

Methods:

All pregnant women involved in the trial will have:-

- Detailed history.
- Complete clinical examination.

- Investigations:-

a- Trans- abdominal ultrasound.
b- Collection and procession of vaginal amniotic fluid samples:

1- Amniotic fluid will be collected by a sterile speculum inserted into the posterior fornix of the vagina.
2- Only one specimen will be included per subject.
3- Specimen will be about 0.5 ml or more and will be directly transferred to a test tube and processed within an hour after collection or stored at 4 degrees and will be processed within 24 hours after collection through a

platelet channel of an electronic cell counter (type of the counter) without centrifugation.

4- Lamellar bodies will be counted using the electronic cell counter.

- **After labor,** the newborn will be assessed for Respiratory Distress Syndrome. The diagnosis of RDS is based on the presence of 3 of the following items:
  a- Physical signs (nasal flaring, chest retractions, grunting and tachypnoea)
  b- Supplementary oxygen requirement longer than 24 hours.
  c- Radiographic findings (reticulogranular opacification of lung fields with superimposed air bronchogram) ***(Khazardoost et al., 2005).***

  Neonates classified as having transient tachypnea of the newborn will not be considered to have RDS ***(Salim et al., 2009).***

Results:-

All the collected data will be tabulated for further statistical analysis.

Statistical analysis:

- Quantitative data e.g. age are presented as mean ± standard deviation. Independent t test is used to compare such data between two groups and one-way ANOVA is used when more than two group are to be compared.
- Qualitative data e.g. sex, are presented as count and percentage. Chi-squared test is used to compare such data between two or more groups.

Binary Logistic regression is used to predict the outcome from the test. It is suited to models where the dependent variable is dichotomous. Logistic regression