Lamellar Bodies Count (LBC) in Amniotic Fluid from Vaginal Pool as a Predictor for Fetal Lung Maturity in Preterm Premature Rupture of Membranes

Thesis

Submitted for partial fulfillment of the Master Degree
in Obstetrics and Gynecology

By

Peter Zarif Shaker Eskander
M.B.B.Ch, (2009) – Ain Shams University
Resident at El-Monira General Hospital

Under the supervision of

Prof. Mohamed Nabegh El Mahallawi
Professor of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Dr. Dina Yahia Mansour
Lecturer of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University

Faculty of Medicine
Ain Shams University
Cairo – 2016

سورة البقرة الآية: ٣٢

Acknowledgments

First and forever, thanks to ***Allah****, Almighty for giving me the strength and faith to complete my thesis and for everything else.*

I would like to express my sincere gratitude to ***Prof. Mohamed Nabegh El Mahallawi,*** *Professor of Obstetrics and Gynecology Faculty of Medicine – Ain Shams University, under his supervision, I had the honor to complete this work, I am deeply grateful to him for his professional advice, guidance and support.*

My deep gratitude goes to ***Dr. Dina Yahia Mansour,*** *Lecturer of Obstetrics and Gynecology Faculty of Medicine – Ain Shams University, for her invaluable efforts and tireless guidance and meticulous supervision throughout this work.*

Last but not least, I like to thank all my ***Family****, especially my beloved* ***Parents*** *for their kind care, help and encouragement.*

Peter Zarif Shaker Eskander

List of Contents

List of Abbreviations

Abbr.	Title

AF.....: Amniotic Fluid

AFI .....: AF index

AFP ..... Alpha-feto protein

AM .....: Amniotic membrane

β-hCG .....: Beta human chorionic gonadotropin

BMI.....: Body mass index

BPD.....: Biparietal diameter

BPD.....: Bronchopulmonary Dysplasia

CDP.....: Continuing distending pressure

CPAP .....: Continuous positive airways pressure

DAO.....: Di amine oxidase

DPPC .....: Dipalmitoyl-phosphatidylcholine

ER .....: Endoplasmic reticulum

FDA.....: Food and Drug Administration

FFN .....: Fetal fibronectin

FHR.....: Fetal heart rate

FSI.....: Foam stability index

GA.....: Golgi apparatus

GBS.....: Group B streptococcal

HFOV .....: High frequency oscillatory ventilation

IGFBP-1 ....: Insulin-like Growth Factor Binding Protein-l

IL-6 .....: Interleukin-6

IPPV.....: Intermittent positive pressure ventilation

IVH .....: Intraventricular hemorrhage

IVH .....: Intraventricular hemorrhage

L/S.....: Lecithin/sphingomyeline

LBC.....: Lamellar body counts

LBS .....: Lamellar bodies

MMPs-3.....: Matrix metalloproteinase-3

MV .....: Mechanical ventilation

NEC.....: Necrotizing enterocolitis

NEC.....: Necrotizing enterocolitis

PAMG-1 ....: Placental alpha microglobulin-1

PC.....: Phosphatidylcholine

PEEP.....: Positive end-expiratory pressure

PG .....: Phosphatidyl-glycerol

PGE2.....: Prostaglandin E 2

PPROM .....: Preterm premature rupture of membranes

RDS.....: respiratory distress syndrome

ROC .....: Receiver operating characteristic

ROM .....: Rupture of membranes

RR .....: Relative risk

SD.....: Standard deviation

SP .....: Surfactant proteins

SP-B .....: Surfactant protein B

SPSS.....: Statistical Program for Social Science

List of Tables

List of Figures

Abstract

Background: The purpose of this study was to validate a non-invasive fetal lung maturity test by counting lamellar bodies from a vaginal pool among women with preterm premature rupture of membranes. **Aim of the Study:** This study is designed 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. **Patients and Methods:** This study was conducted as a prospective cohort study (accuracy of a diagnostic test).at Ain Shams University Maternity Hospital from October 2015 till August 2016. **Results:** The study showed that using 38.131/ml as a cut-off point for LBC it is a good predictor for fetal lung maturity with sensitivity 96% and specificity 97.22%. **Conclusion:** Lamellar body count (LBC) is an effective, safe, easy, cost-effective method to detect fetal lung maturity (FLM). It does not need a highly equipped laboratory or specially trained personnel, it just need the conventional blood count analyzer. Measurement of LBC is now replacing the conventional Lecithin/Sphyngomyelin L/S ratio. LBC cut-off value of 38.131/ml can be used safely to decide fetal lung maturity with sensitivity 96% and specificity 97.22%. **Recommendations:** Lamellar body count (LBC) has taken its place in many laboratories and feto-maternal centers worldwide to confirm fetal lung maturity (FLM) in high and low risk cases. The clinical outcome and the cost-effectiveness of LBC should be prospectively evaluated. 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.

Key words: Lamellar bodies count, fetal lung maturity, PPROM

Introduction

Preterm premature rupture of membranes (PPROM) defines spontaneous rupture of the fetal membranes before completed 37 weeks gestation and before labor onset ***(American College of Obstetricians and Gynaecologists, 2013).***

Preterm premature rupture of membranes may occur for a variety of risk factors. Infection has been shown to be commonly associated with preterm PROM, especially at earlier gestational ages. A history of preterm PROM is a major risk factor for preterm PROM or preterm labor in a subsequent pregnancy. Additional risk factors associated with preterm PROM are similar to those associated with spontaneous preterm birth and include short cervical length, second-trimester and third-trimester bleeding, low body mass index, low socioeconomic status, cigarette smoking, and illicit drug use. Although each of these risk factors is associated with preterm PROM, it often occurs in the absence of recognized risk factors or an obvious cause ***(American College of Obstetricians and Gynaecologists, 2013).***

Several studies have been done to ascertain the incidence of infection-induced premature membranes rupture. Bacterial cultures of amnionic fluid support a role for infection in a significant proportion. A review of 18 studies

comprising almost 1500 women with PPROM found that in a third, bacteria were isolated from amnionic fluid. Accordingly, High risk women have given prophylactic antimicrobial treatment to prevent premature rupture of membranes ***(Miyazaki, 2012; Phupong, 2012).***

Neonatal respiratory distress syndrome (RDS) is a disorder due to pulmonary immaturity with a high mortality characterized by low levels of pulmonary surfactant. Gestational age determines risk based on concentration of pulmonary surfactant, i.e., as gestation progresses the concentration of pulmonary surfactant increases. As a result, new-borns delivered at less than 28 weeks have more than 60% risk of RDS, whereas those delivered at more than 34 weeks have less than 5% risk of RDS. In situations where gestational age alone is not sufficient to determine RDS risk and preterm delivery is medically needed, amniotic fluid analysis can be performed to determine pulmonary surfactant concentration ***(Alter and Grenache, 2009).***

Laboratory assessment of the fetal lung maturity assists obstetricians in estimating the risk of respiratory distress syndrome (RDS) when premature delivery of an infant is being considered ***(Lu et al., 2008).***

There are common methods as the lecithin-sphingomyelin ratio, phosphatidylglycerol measurement and surfactant-albumin

ratio. All of these tests have excellent negative predictive values but poor positive predictive values, i.e., they are great at confirming maturity but poor at confirming immaturity ***(Alter and Grenache, 2009).***

Most of them are either complex, expensive, or with low diagnostic efficiency ***(Grenache et al., 2010).***

Surfactant is stored in the form of lamellar bodies. They are secreted into alveolar space and passed into amniotic fluid where they can be found. The similarity of lamellar body size to platelet size permits the use of a standard automated hematologic cell counter to estimate the number of lamellar bodies in amniotic fluid ***(Visnjevac et al., 2010).***

Lamellar bodies are essentially small packages of lung surfactant which are found in intracellular storage granules in lung cells or pneumocytes. The lamellar bodies are released (exocytosed) and unfold to form a surfactant monolayer in the alveolar space. Surfactant and lamellar bodies are released into amniotic fluid due to fetal breath movements beginning around 28 to 32 weeks of fetal development, with levels increasing exponentially as the fetus matures. The risk of respiratory distress syndrome due to insufficient surfactant levels is significant during gestational weeks 32 to 36, and more accurate assessment of that risk is facilitated by measurement of surfactant phospholipid ratios or, as has

recently been shown, by Lamellar body counts (LBC) ***(Lu et al., 2008).***

Amniotic fluid lamellar body counts performed on cell-counting equipment available in most clinical laboratories is a simple, rapid, inexpensive, and the most practical antenatal method for the efficient evaluation of fetal lung maturity and prediction of neonatal RDS ***(Štimac et al., 2012).***

Aim of the Study

This study is designed 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.

Fetal Membranes and Preterm Premature Rupture of Membranes

Fetal membranes are composed of two layers: an outer layer (chorion), which contacts maternal cells and an inner layer (amniotic membrane; AM) ***(Mamede et al., 2012).***

Anatomy of the fetal membranes:

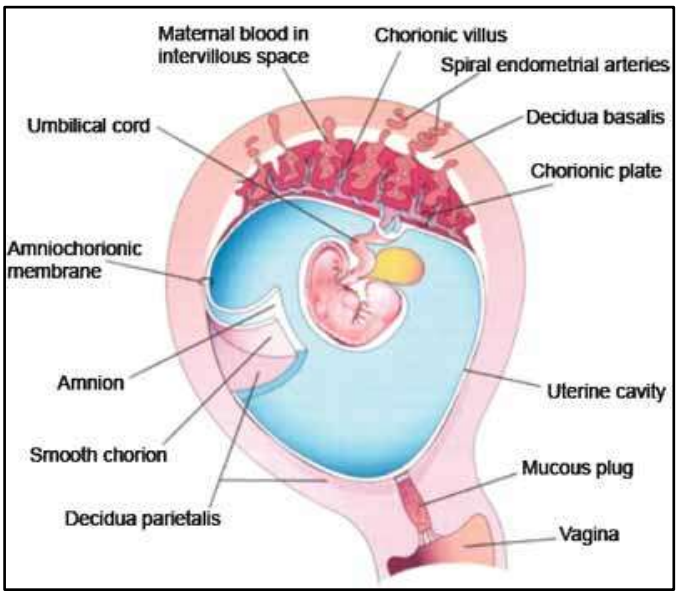

Figure (1): Fetal membranes: Anatomy ***(Seth Guller, 2006)***

Anatomy of the amnion:

AM or amnion is a thin membrane on the inner side of the placenta; it completely surrounds the embryo/fetus and delimits the amniotic cavity, which is filled by amniotic fluid ***(Mamede et al., 2012).***