Sonographic Prediction of Fetal Lung Maturity

Thesis
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Abstract

Study was performed on 40 cases (10 normal full term pregnancies and 30 high risk patients) , five items of sonographic prediction of fetal lung maturity (composite age, placental grade, amniotic fluid turbidity, lung/liver ratio and distal femoral epiphysis) correlated to development of respiratory distress syndrome (RDS) in newborns. Statistical analysis of results found that RSD is more predicted with small femur length (FL) measurement, and using 7.3 cm cut off point for FL is a good predictor for fetal lung maturity with sensitivity 86% and specificity 84% in our study.

Key Words :(sonographic prediction)-(fetal lung maturity)-(femur length)

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List of Abbreviations

AC: Abdominal Circumference
ACOG: American College of Obstetrics & Gynecology
BP: Blood Pressure
BPD: Biparietal Diameter
BV: Bacterial Vaginosis
CS: Cesarean Section
CBC: Complete Blood Picture
DFE: Distal Femoral Epiphysis
DM: Diabetes Mellitus
DPPC: Dipalmitoyl- Phosphatidyl Choline
FBS: Fasting Blood Sugar level
FFN: Fetal Fibronectin
FFPs: Free-Floating Particles
FL: Femur Length
FLM: Fetal Lung Maturity
FSI: Foam Stability Index
FT: Full Term
GA: Gestational Age
GDM: Gestational Diabetes Mellitus
HMD: Hyaline Membrane Disease
HUAM: Home Uterine Activity Monitoring
HTN: hypertension
IDDM: Insulin-Dependent Diabetes Mellitus
IFG: Impaired Fasting Glucose
IGT: Impaired Glucose Tolerance
IUGR: Intra-Uterine Growth Restriction
LBC: Lamellar Body Count
LGA: Large for Gestational Age
L/L ratio: Lung/ Liver ratio
L/S ratio: Lecithin / Sphingomyelin ratio
MgSO4: Magnesium Sulphate
OGTT: Oral Glucose Tolerance Test

PG: PhosphatidylGlycerol
PPBS: Post Prandial Blood Sugar level
PTE: Proximal Tibial Epiphysis
RBS: Random Blood Sugar
RDS: Respiratory Distress Syndrome
RH: Rhesus Factor
SBP: Systolic Blood Pressure
SGA: Small for Gestational Age
SOGC: Society of Obstetricians and Gynecologists of Canada
SP-B: Surfactant Protein B
US: Ultrasonography

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Introduction

Normal fetal lung development is a sequential process that involves several phases. It begins at the 24th menstrual week and extends into postnatal life **(Hadlock FP et al., 1985).**

From 34 to 37 weeks there is a transitional phase in which varying degrees of fetal lung maturity can be expected **(Kulovich MV et al., 1979).**

There are two major clinical situations in which it is useful to have an accurate assessment of fetal lung maturity in utero. One is the preterm patient or in whom early delivery is mandated by maternal or fetal indications. Second is uncomplicated pregnancy with unknown dates in which a cesarean is necessary **(Hadlock FP et al., 1985).**

Prior to this time, the baby is at risk for developing respiratory distress syndrome(RDS).RDS occurs in about 1% of all pregnancies, and it can have serious short-and long-term consequences, involving both the lungs and other organs, that can extend beyond the neonatal period in its most severe forms **(Halliday HL. et al., 2005).**

Later in pregnancy "near term", severe RDS can also occur **(Fantz CR. et al., 2002).**

The diabetic pregnancy is characterized by a delay in the process of fetal lung maturation **(Ira H et al., 1993).**

One of the leading causes of prematurity and respiratory distress in the newborn was iatrogenic prematurity by cesarean section **(Sher G. et al., 1997).**

Fetal lung maturity can be assessed by biochemical analysis of amniotic fluid, but it carries the potential for serious complications **(Gluck et al., 1971).**

Efforts have been made to use prenatal diagnostic ultrasonography as a means of evaluating fetal lung maturity **(Williamson RD et al., 1985).**

Ultrasound items of evaluate fetal lung maturity are: composite age (by BPD, HC, AC, FL), placental grade, fetal bowel pattern, lung/liver ratio, and distal femoral epiphysis **(Salman & Quetel, 1985).**

Fetal bipraietal diameter (BPD) has been related to FL, with accuracy ranging from 78 to 100% (**Prakash KN et al., 2002**).

Placental grading is a reliable ultrasonographic scale that can help to predict fetal lung maturity (**Loret De Mola et al., 1998).**

Amniotic fluid turbidity is a predictor of fetal lung maturity. It had 91% positive value (**Adair CD et al., 1995).**

The incidence of lung to liver echogenicity ratio >1 was found in 65% of patients **(Tekasin and his colleagues, 2004).**

Aim of the Work

The aim of this study is to evaluate five items of sonographic prediction of fetal lung maturity (composite age, placental grade, amniotic fluid turbidity, lung/liver ratio, and distal femoral epiphysis) and compare them in diabetic, hypertensive and preterm cases with normal pregnancy.

Fetal Lung Functional Unit

The fetal lungs are the last organ system to "mature" so that survival outside the womb is possible. **(Muth E. et al., 2004).**

Maturity involves several components: first, there must be sufficient surface area within the lung to allow sufficient exchange of gases (oxygen in and carbon dioxide out) to support metabolic functions. This is accomplished by millions of small sacs called alveoli that give the lungs a sponge-like appearance **(Clements JA. et al., 1998).**

Second, the alveoli must develop to the point that the inner lining of cells (epithelial cells) that come in contact with inspired air are very thin gas exchange can only occur over a short distance between the blood vessels in the alveoli and the air that fills the alveoli **(Clements JA. et al., 1998).**

Third, the alveoli must be able to remain open so that the air can get into them and gas exchange can take place. The first two events are generally quite complete by about 32-34 weeks, however, the third is the most essential component from that point on and it is the focus of fetal lung maturity testing as we shall explain **(Clements JA. et al., 1998).**

Alveoli are like little bubbles. The laws of physics predict that because of the high ratio of surface tension to volume of little bubbles, their tendency is to collapse. To prevent this from happening, certain cells in the lungs - the type II alveolar cells - begin to excrete chemicals that can reduce the surface tension in the alveoli. These chemicals are called 'surfactants' and they are a complex combination of phospholipids and Apo proteins **(Ghodrat M.et al., 2006).**

When sufficient surfactants are produced that the alveoli can remain open to function, the fetal lungs are considered 'mature'. Prior to this time, the baby is at risk for developing respiratory distress syndrome (RDS). RDS occurs in about 1% of all pregnancies and it can have serious short- and long-term consequences, involving both the lungs and other organs that can extend beyond the neonatal period in its most severe forms **(Haliiday HL. et al., 2005).**

When babies are very premature, respiratory distress syndrome (RDS) is the result of a combination of both alveolar epithelial cell immaturity (the lining cells have not yet thinned out) and a deficiency of surfactants. later in pregnancy "near term", severe RDS 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 devastator **(Fantz CR. et al., 2002).**

Embryology of the respiratory system

The respiratory system begins at the nasal cavity and consists of a conducting portion and a respiratory portion **(Thomas et al., 2000).**

The conducting portion includes nasal cavity, pharynx, larynx, trachea, bronchi, and bronchioles. The respiratory portion consists of the respiratory bronchioles, alveolar ducts, alveolar sacs and the alveoli. Gaseous exchange occurs in the alveoli. The development of the respiratory system involves the endoderm and the mesoderm that surrounds it **(Thomas S. et al., 2000).**

The larynx is first seen as an outgrowth from the foregut called the respiratory diverticulum or the lung bud. The lung bud is a ventral diverticulum of endoderm that arises from the floor of the foregut caudal to the pharynx. The diverticulum forms a groove in the floor of the pharynx called the laryngotracheal groove. Cephalic to the laryngotracheal groove is the epiglottal swelling. On either side of this groove are the developing arytenoids swellings **(Thomas S. et al., 2000).**

The trachea develops caudal to the larynx. The epithelium develops from the endoderm and the tracheal cartilage and muscles develop from splanchnic mesoderm. Early in development the trachea bifurcates into the left and right bronchi, as the bronchi develop they continue to branch. The right bronchus gives off three diverticula and the left bronchus gives off two divertlcula. These diverticula become the lobar bronchi. Each of the bronchi at this stage will divide into smaller bronchi. The branching of the bronchi continues until the bronchioles begin to form. There are 17 divisions of the bronchi until the sixth fetal month is reached. However, by early childhood there will be a total of 24 generations of divisions of the bronchi **(Thurlbeck W, 1992).**

As the lungs develop and divide into smaller divisions there are changes in the vascular supply of the lungs as well. The lungs can be described as undergoing four Phases of development. During the first phase of development, the pseudoglandular period, the bronchi are dividing into smaller and smaller units, the bronchioles. This period occurs from the 2^{nd} month through the end of the 4^{th} month. During the

next two and half months the respiratory bronchioles are formed. They will give rise to alveolar ducts. This is called the canalicular period. During this time period the epithelium remains as a cuboidal epithelium and the capillaries while proliferating do not approach the respiratory epithelium. The next phase of development occurs from the 7th month until birth and is called the terminal sac phase **(Thomas S. et al., 2000).**

The number of capillaries increases and the capillaries reach the respiratory epithelium. At the same time the terminal sacs form. These results in the formation of squamous epithelium made up of type 1 alveolar epithelial cells, which will permit gaseous exchange. Hence, from the 7th month on the fetus is capable of survival. It is also starting with the 7th month that type 2 alveolar epithelial cells develop. These type 2 cells produce surfactant, the fluid that reduces the surface tension at the alveolar cell surface. The alveolar lining layer is thought to consist of continuous duplex layer, i.e., an aqueous hypo phase covered by a thin surfactant film which is a monolayer with dipalmitoyl-phosphatidylcholine (DPPC) as it is the most important component **(Ikegami M. et al., 2003).**

Findings obtained by electron microscopy and results from in vitro experiments suggest, however, that the structure and hence the structure-function relations of surfactant films are more complex **(Ikegami M. et al., 2003).**

Surfactant protein B (SP-B) is essential for maintenance of biophysical properties and physiological function of pulmonary surfactant. SP-B mRNA expression is restricted to alveolar type 2 epithelial cells and bronchiolar epithelial cells (Clara cells) of adult lung **(Ashood ER, 2005).**

Finally from the 8th month on, the mature alveoli continue to be formed with an increase in the amount of surface area where capillaries and alveolar cells are in contact. This period of lung development is the alveolar period and actually can last through age ten. The growth of the lungs after birth is mainly the result of increases in the number of alveoli during this time **(Thurlbeck W, 1992).**

Histological Structure of Alveoli

The wall of the alveoli is formed by a thin sheet (2 um) of tissue separating two neighbouring alveoli. This sheet is formed by epithelial cells and intervening connective tissue. Collagenous (few and fine), reticular and elastic fibres are present. Between the connective tissue fibres we find a dense, anastomosing network of pulmonary capillaries. The wall of the capillaries are in direct contact with the epithelial lining of the alveoli. The basal laminae of the epi- and endothelium may actually fuse. Neighbouring alveoli may be connected to each other by small alveolar pores **(Mulugeta and Beers, 2006).**

The epithelium of the alveoli is formed by two cell types:

1. Alveolar type I cells (small alveolar cells or type I pneumocytes) are extremely flattened (the cell may be as thin as 0.05 um) and form the bulk (95%) of the surface of the alveolar walls. The shape of the cells is very complex, and they may actually form part of the epithelium on both faces of the alveolar wall **(Mulugeta and Beers, 2006).**

2. Alveolar type II cells (large alveolar cells or type II pneumocytes)are irregularly (sometimes cuboidal) shaped. They form small bulges on the alveolar walls. Type II alveolar cells contain large number of granules called cytosomes (or multilamellar bodies), which consist of precursors to pulmonary surfactant (the mixture of phospholipids which keep surface tension in the alveoli low). There are just about as many type II cells as type I cells. Their small contribution to alveolar area is explained by their shape **(Mulugeta and Beers, 2006).**

Cilia are absent from the alveolar epithelium and cannot help to remove particulate matter which continuously enters the alveoli with the inspired air. Alveolar macrophages take care of this job. They migrate freely over the alveolar epithelium and ingest particulate matter. Towards the end of their life span, they migrate either towards the bronchioles, where they enter the mucus lining the epithelium to be finally discharged into the pharynx, or they enter the connective tissue septa of the lung **(Mulugeta and Beers, 2006).**