Prediction of Neonatal Respiratory Distress Syndrome in Preterm Fetuses by Assessment of Fetal Lung Volume by Vocal and Pulmonary Artery Resistance Index

Thesis

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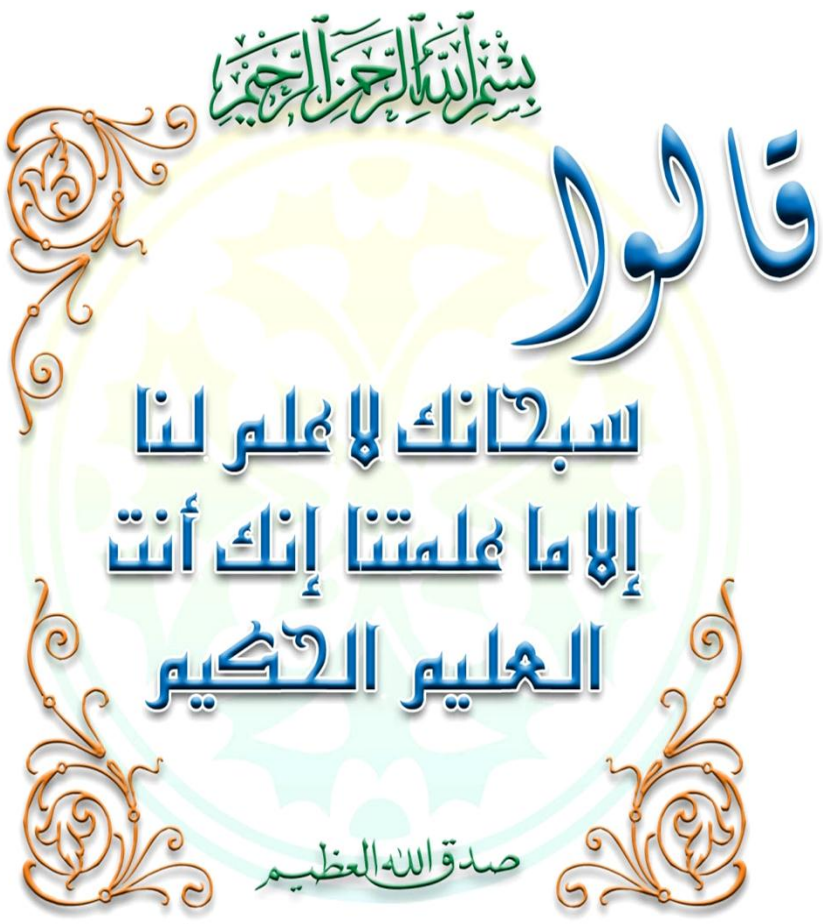

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Abdel Rahman Saleh

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List of Abbreviations

Abbr.	Full-term
ACOG	: American College of Obstetricians and Gynecologists
CBC	: Complete blood count
CNS	: Central nervous system
CPAP	: Continuous positive airway pressure
CS	: Cesarean section
FI	: Flow Index
FI	: Flow intensity
FLV	: Fetal lung volume
GER	: Gastroesophageal reflux
hCG	: Human chorionic gonadotropin
ICU	: Intensive care unit
IVH	: Intra ventricular hemorrhage
kHz	: Kilohertz
L/S	: Lecithin-to-sphingomyelin ratio
LMP	: Last menstrual period
NEC	: Necrotizing enterocolitis
PaO_2	: Partial pressure of oxygen
PDA	: Patent ducts arteriosus
PEEP	: Positive end-expiratory pressure
PGDH	: Hydroxy-prostaglandin dehydrogenase
PIE	: Pulmonary interstitial emphysema

PPROM : Preterm premature rupture of membranes
PTL : Preterm labour
PVL : Periventricular leukomalacia
RDS : Respiratory distress syndrome
SD : Standard deviation
SONAR : Sound Navigation and Ranging
TTN : Transient tachypnea of the newborn
UAE : Uterine Artery Embolization
US : Ultrasound
V/Q : Ventilation-perfusion
VI : Vascularization Index
VOCAL : Virtual Organ Computer-aided Analysis
WBC : White blood cell
2DUS : Two-dimensional ultrasound
3D : Three-dimensional

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Introduction

Neonatal respiratory distress syndrome (RDS) is defined as respiratory failure that occurs after birth due to absence of lung surfactant, a substance that is required to prevent alveolar collapse and for inflation of the lungs. This condition is a leading cause of neonatal morbidity and mortality: estimates suggest that 80.000 cases of neonatal RDS occur every year in the USA alone, with 8500 neonatal deaths ***(Angus et al., 2001).***

Respiratory distress syndrome (RDS) is a major contributor to neonatal mortality worldwide. However, little information is available regarding rates of RDS-specific mortality in low-income countries, and technologies for RDS treatment are used inconsistently in different health care settings ***(Kamath et al., 2011).***

Risk of neonatal RDS decreases as gestational age increases, because the lungs are the final fetal organs to functionally mature. Therefore, neonatal RDS is often considered to be a disease of premature newborns, although it does not exclusively occur after preterm deliveries ***(American College for Obstetrics and Gynecology (ACOG), 2008).***

Biochemical tests have been developed to determine the risk of neonatal RDS and help obstetricians to decide when to deliver a neonate. The chemical, biological, and physical properties of amniotic fluid represent the gold-standard measures of fetal lung maturity. Nevertheless, amniotic fluid can be obtained only by performing amniocentesis, an invasive procedure that poses potential risks to the pregnancy, such as premature rupture of membranes, preterm labor, placental abruption, fetomaternal hemorrhage, fetal injury, and even fetal or maternal death ***(Gordon et al., 2009).***

Indeed, previous studies reported that the frequency of fetal lung maturity testing had decreased in the USA between 1998 and 2008, often because of concerns about amniocentesis ***(Grenache et al., 2010).***

A non-invasive test to assess fetal lung maturity would be a more acceptable option for pregnant women. Fetal lung maturity has been in-directly assessed by ultrasonic evaluation of gross morphology and the use of Doppler blood flow waveforms ***(Gerards et al., 2008).*** However, as yet, there is no reliable non-invasive test to predict fetal lung maturity before delivery ***(Moshiri et al., 2013).***

Measurement of fetal lung volume (FLV) and pulmonary artery pressure could potentially be used to

predict neonatal RDS. Structural and functional progress of fetal lung development with increasing gestational age correlates with a change in the pattern of sonographic echogenicity of this organ ***(Tekesin et al., 2004).*** Furthermore, fetal pulmonary artery flow velocity waveforms were found to change with increasing gestational age. Finally, pulmonary artery pressure measured by Doppler decreased among newborns with RDS after administration of surfactant ***(Olavarria and Guerrero, 2000).***

Several other non-invasive procedures could potentially have value for prediction of fetal lung maturity. For example, 2D ultrasonography has been used to assess the length, area, diameter, and circumference of the fetal lung. Nevertheless, sensitivities and specificities associated with the use of such measures to predict the development of pulmonary hypoplasia have been inconsistent ***(Merz et al., 1995).***

The ratio of chest to trunk length has also been used to predict pulmonary hypoplasia among fetuses with congenital anomalies: a ratio of 0.32 or less had a sensitivity of 92% and a specificity of 95.9% for the prediction of postnatal lung hypoplasia in a previous study ***(Ishikawa et al., 2003).***

Among various quantitative imaging methods, texture analysis has been proposed as a powerful approach to extract quantitative features directly from medical images.

Nevertheless, none of these methods has yet been widely applied, either because their efficacy is unproven or the technique is too complicated for routine clinical practice ***(Castelano et al., 2004).***

Aim of the Work

The aim of the present study is to investigate the reliability and validity of fetal lung volume assessed by VOCAL and pulmonary artery resistance index (PA-RI) as noninvasive measures that could be used to predict the development of neonatal RDS in preterm pregnancies.

Preterm Labour

Definition:

Preterm labour infers to birth between the onset of viability and 37 completed weeks gestation. It is a common problem occurring in 5-25% pregnancies and is a major cause of death or disability in newborns ***(Steer, 2005).***

Preterm labour could also be categorized by its clinical presentation: medically induced, preterm premature rupture of membranes (PPROM) and spontaneous preterm labour leading to preterm delivery. Several etiologies and/or risk factors have been reported for each of the three categories although none completely explain all preterm births. Recent investigations, more directed to defined plausible biological pathways, may reconcile the apparent heterogeneity of preterm birth ***(Behrman et al., 2007)***.

It's estimated that the preterm delivery contributes to 70% of perinatal morbidity and mortality excluding those related to congenital malformations ***(Challis et al., 2000)***. The incidence of preterm birth has risen over the past 20 years ***(Joseph et al., 1998)***.

Spontaneous preterm labor can be understood as a syndrome with a number of underlying causes including infection, maternal stress, uterine distention, placental

hypoxia, bleeding and lack of prostaglandin dehydrogenase ***(Hagberg and Wennerholm, 2000)***.

Impact of preterm Labor:

Low birth weight is the term used to define infants who are born too small while preterm or premature birth are the terms used to define infants who are born too soon. In 1990's, in the United States, of the thousands of premature infants born, most are quietly laid away with little if any effort was made for their rescue. As the 20th century progressed, there was increasing awareness that preterm infants required special care, as evidenced by the development of incubators and ICU ***(Cunningham et al., 2001)***.

It is more logic to use gestational age than birth-weight as a threshold since:

1. Outcome is more closely related to gestational age especially before 30 weeks' gestation.

2. Normal range of birth weight varies between populations and is dependent on number of factors such as hypertension and smoking.

3. Prior to delivery, an obstetrician can more accurately determine gestational age than estimated birth weight ***(Mathews et al., 2004)***.