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Relationship Between Ultrasonic Marker of Fetal Lung Maturity and Lamellar Body Count: A Review

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ABSTRACT

Background & Objective: In this study, the relationship between ultrasonic marker of fetal lung maturity and lamellar body number was studied.

Materials & Methods: A comprehensive literature review was performed on papers published from 2004 to 2016 by searching databases including NCBI, Science Direct, Springer, and Web of Science as well as native databases such as Iran DAC, Islamic science citation (ISC), and Magiran with a special focus on presented articles. Keywords used include body count, fetal lung, and ultrasonic.

Results and Conclusion: In this study we used ultrasonic marker of fetal lung maturity and related this to lamellar body count and neo natal outcome. The ultrasonic marker of fetal lung maturity can reduce mortality and morbidity in neonate

A limited study has been performed in the field of ultrasonic marker of fetal lung maturity and it is suggested that detailed studies be performed in this field in other parts of Iran as well.

Keywords: Body count, Fetal Lung, RDS, Ultrasonic

Introduction

Respiratory distress syndrome (RDS), also known as hyaline membrane disease, is a respiratory disorder in premature infants. A soap-like substance called surfactant covers small alveoli (sacs responsible for exchanging air in the lungs) in healthy infants' lungs reducing the surface tension and making lung inflation easier. In premature infants' lungs however, breathing can be problematic due to lack of surfactant secretion.

Epidemiology, Prevalence, Economic Burden, and Vulnerable Populations

Respiratory distress syndrome affects about 1% of premature infants and is their leading cause of death (1). Reports show that about 12% of all babies born in the United States are born prematurely, and about 10% of these babies have RDS (2).

Younger premature infants are more likely to have RDS. Babies born at 29 weeks have a 60% chance of being born with RDS (3). Various factors cause preterm delivery in pregnant women including low prenatal care, previous preterm birth, low maternal body mass, poverty, periodontal disease, etc.

In 2003, the number of live births in the United States was 4,089,950, of which about 0.6% had RDS (about 24,000 or 6:1000 live births). In 2005, the number of live births in the United States was reported 4,138,000 and the rate of preterm births increased from 6.11% to 12.7% due to increasing birth rates (34 to 36 weeks of gestation) (4-6).

Infant mortality rates declined sharply in the United States from 2,500 infant deaths in 1960s to 860 in 2005 due to application of surfactant replacement therapy; however, there was an increase in the number of infants born with RDS (7).

RDS mortality in early African American infant was 2.6 times higher than Caucasian infants, although Caucasian infants were at higher risk. Thousands of infants have been saved with this treatment, but newborns still suffer from pulmonary bronchial

dysplasia. Part of the problem is that surfactant replacement therapy and other medical advances and intensive care have kept very premature babies alive whom may face long-term complications of RDS.

It seems that in the current situation, preventing premature birth is the main way to eliminate RDS.

Proper nutrition and delivering intensive care medication to infants will also improve the outcomes. Surfactant replacement therapy is not effective in treating the type of RDS caused by a genetic mutation in *SP-B*. In most of the cases however, it has been surprisingly successful. Fetal lung maturation has always been a challenge for obstetricians in cases of preterm delivery and premature rupture of membranes (PROM).

Hyaline membrane disease has always been the main cause of infant death and fetal lung immaturity is one of the main health concerns.

Suggested by Liggins and Howie **(5)**, corticosteroid therapy in patients at risk of preterm delivery was an important milestone in fetal lung maturity and reducing RDS morbidity and mortality in neonates. Nowadays, the main treatment applied in the intensive care unit (ICU) is maintaining oxygen saturation and preventing respiratory acidosis using sodium bicarbonate.

This treatment put a heavy financial burden on the patients since the length of neonatal ICU stay was considerable, while the outcomes were not satisfactory. Meanwhile, Liggins and Howie's **(5)** treatment (using glucocorticoids to improve fetal lung maturation), not only reduces neonatal mortality and complications from RDS, but also reduces the need for neonatal intensive care and exogenous surfactant therapy which results in economic savings. Steroids may cause the premature release of alveolar surfactant by stimulating an enzyme involved in surfactant biosynthesis.

The steroids used are usually dexamethasone or betamethasone. They are biologically identical, and easily cross the placenta. They have low mineralocorticoid activity and are relatively weak in suppressing immunity. Doses recommended by Howie and Liggins include two doses of 12 mg betamethasone with an interval of 24 hours or four doses of 6 mg of dexamethasone with an interval of 12 hours. **(6)**. Betamethasone is widely used due to patient adaptation between 24 and 34 weeks of pregnancy. Before 24 weeks, type II pneumocytes are not developed enough to release surfactant, and after 34 weeks, the risk of RDS is lower and less severe. Prenatal corticosteroids reduce intraventricular bleeding and infant mortality as well as reducing RDS **(7)**.

The best respiratory results in infants appear after a full period of treatment, and delivery is ideal 3-7 days after this period. The protocol can be used simultaneously to delay labor to allow steroids fully function. The above recommendations are in line with the Royal College of Obstetricians and Gynecologists (RCOG) guidelines **(7)** and the American College of Obstetricians and Gynecologists (ACOG) Committee **(8)**.

Some physicians believe that the reduction in RDS rate associated with prenatal steroids is not statistically significant in the subgroup of infants who are delivered more than 7 days after a course of treatment. Therefore, the course of treatment is repeated at weekly intervals for women who do not give birth but are at risk of preterm delivery.

This state of repeated steroids has never been properly randomized and there is no evidence that multiple steroid cycles are more effective than a single cycle. Interestingly, both the RCOG guidelines and the ACOG committee emphasized that there was no evidence that state repeated doses were useful after 7 days. In a randomized controlled trial on 502 pregnant women between 24 and 30 weeks, weekly antenatal steroid courses did not reduce the combined neonatal complications in comparison with one course of treatment **(8)**.

Materials and Methods

A comprehensive literature review was performed on paper that have been published from 2004 to 2016 in databases such as NCBI, Science Direct, Springer, Web of Science as well as local databases such as Iran DAC, Islamic science citation (ISC) and Magiran with a special focus on reported articles using the following keywords: Body count, Fetal Lung, Ultrasonic.

Results and Discussion

There has been limited research in this area but all the results reviewed showed an association between ultrasonic markers of fetal lung maturity.

Behzadmehr conducted a study on pregnancy and its diagnostic values in Amir Al-Momenin Hospital in Zabol from 2015 to 2016. The results suggested that out of 300 patients, 148 patients (49.3%) were between 20-30 years old, 96 patients (32%) were pregnant for the third time, 112 patients (37.3%) had less than a high school diploma, and 68 patients (22.7%) had a university degree. Out of those surveyed, 223 patients (74.3%) stated that ultrasound was able to diagnose fetal physical problems, and 71 patients (23.7%) believed that ultrasound could identify fetus chromosomal and genetic abnormalities in the second trimester of pregnancy **(9)**.

In a study by Keikhaei, Fetal lung maturation was predicted using ultrasonic markers and contrast with lamella body number and fetal outcome. The results show that out of 100 patients, 8 were admitted to the NICU (neonatal ICU) including 6 boys and 2 girls. All of the admitted infants had lamellar body count<14000

(10000-14000), and fortunately no maternal mortality was reported in this study **(10)**.

The results of Kars indicated that RDS was observed in 12 of 56 infants (21.4%). Sensitivity and specificity of impact testing were 91% and 88%, respectively. While the sensitivity was 83% and the specificity was 65% for the turbidity test **(11)**. Management of women with elective cesarean section requires confirmation of pregnancy history and fetal lung maturation **(12, 13)**. A large number of studies compared deviant markers of fetal lung maturation with amniocentesis **(14)**. Using biparietal diameter (BPD) is possible in the timing of elective cesarean section **(16)**, and BPD greater than 9.2 cm demonstrated fetal lung maturity in 90% of the cases **(15)** and BPD_8.7 cm showed RDS in 80% of the cases (Destro *et al*., 1975). BPD>9.2 cm was 92% specific and 87% sensitive. Grade 2 and 3 placentas have been reported to be associated with fetal lung maturation **(17-19)**. In this study, grade 3 placenta was associated with lack of RDS. In 2011, Chen studied the Relationship between premature placental calcification and maternal and fetal outcomes **(20)**.

Farris *et al.* identified the thalamus echogenicity as an indicator of fetal lung maturity using ultrasound **(21)**. In this study we show that the thalamic echogenicity is 70%.

Crosst *et al.* suggested that free-floating particles in amniotic fluid (FFPS) detected by reading-time ultrasound can confirm fetal lung maturation **(22)**.

The results of the present study are consistent with a previous study by Mario Zilianti *et al.* indicating that the ultrasound image of the fetal intestine correlates with Gestational age (GA) and fetal maturity.

The latest article published by French *et al*. **(23)** in Western Australia, indicated that after a period of pre-pregnancy steroid use, the improvement of respiratory function is very high, but among women who have two, three or more weekly courses, no improvement is observed. Although the risks of recurrent steroids are low for the mother, they occur at any dose therefore multiple medications should always be avoided. Multiple-dose therapy is associated with weight loss at birth **(24)**. A study by Dunlop *et al.* **(25)** found that repeated prenatal steroids delayed myelination of CNS axons in sheep. Further research has shown that repeated doses are harmful to the fetus because of great myelin damage. Computed tomography (CT) and magnetic resonance imaging (MRI) studies on fetuses have shown flattening of the cerebral hemispheres **(26)**.

A. Rasheed's study, compared to other ultrasound manufacturers, uses ultrasound as a possible indicator of fetal lung maturation.

The presence of echogenic thalamus as a sign of fetal lung maturity had a specificity of 86.53%, which is greater than the other three signs of lung maturity. The predictive value was positive (89.6%) which is higher than the other three symptoms, but the sensitivity was 63.33% and the negative prediction was 57.69%, which is less than the presence of vernix in amniotic fluid, 86.66 and 67.56 respectively **(27)**.

Another study on 155 individuals found that prenatal diagnosis reduced neonatal mortality by 95% **(28)**. These results can inspire other clinical groups **(29)**. Many studies on ultrasound prediction of fetal lung maturation were performed to compare ultrasound parameters with amniocentesis tests to evaluate this symptom with lung maturation **(30)**.

Beck's study assesses lung maturity using ultrasound, comparing mental histogram techniques, and the gray scale histogram (GSH). The subjective assessment recognize 41 cases (53.2%) correctly and 36 (46.8%) incorrectly, while GSH found 58 (75.3%) correctly and 19 (24.7%) incorrectly (P=0.006). There was an important difference in mean lung/hepatic echogenicity among the groups with and sans respiratory distress (1.05 vs 1.26, P=0.002). In the 28 to 35+6 weeks group, GSH had 61.9%, 89.1%, and 81.6% sensitivity, specificity, and accuracy in predicting respiratory distress, respectively **(31)**.

Conclusion

A limited study has been performed in the field of ultrasonic marker of fetal lung maturity and it is suggested that detailed studies be performed in this field in other parts of Iran.

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Conflict of Interest

The authors declare no conflicts of interest.

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