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Prediction of Fetal Lung Maturity Using Ultrasound Evaluation of Thalamus Echogenicity

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ABSTRACT

Background: Hyaline membrane disease, often known as respiratory distress syndrome, affects premature infants nearly exclusively. The newborn's gestational age is inversely associated to the prevalence and severity of respiratory distress syndrome.

Objective: The aim of this study was to predict fetal lung maturity using a non-invasive method, which is transabdominal ultrasound evaluation of thalamus echogenicity.

Patients and method: This Cross-sectional prospective study included a total of 50 pregnant women, attending for antenatal care at Department of Ultrasound and Feto Maternal Unit, Zagazig University Hospitals. Scanning with transabdominal 2D ultrasound (Voluson 730 pro V 2D GE), was done to measure the biparietal diameter and the state of echogenicity of the thalamus was recorded as echogenic or echolucent, in addition to amniotic fluid particles (vernix) and the placental changes.

Results: The four ultrasound parameters of lung maturity were increased with gestational age, and the presence of vernix in the amniotic fluid showed the highest and more predictive percent compared to the others, while the feature of echogenic thalamus demonstrated relatively lowest value.

Conclusion: It could be concluded that evaluation of echogenic thalamus by ultrasound at the level of the biparietal diameter (BPD) is of value and can be considered as a new marker of fetal lung maturity.

Keywords: Respiratory distress syndrome, Fetal Lung Maturity, Ultrasound.

INTRODUCTION

Hyaline membrane disease, often known as respiratory distress syndrome (RDS), affects premature infants nearly exclusively. The newborn's gestational age and respiratory distress syndrome incidence and severity are inversely associated [(1,2)].

Surfactant, which is typically produced by type II pneumocytes and has the property of decreasing surface tension, is insufficiently produced in the lungs, which leads to RDS. Reduced surfactant levels make the lung even less compliant, causing alveoli to collapse during expiration and significantly increasing the amount of energy needed to breathe. Hypoxia and carbon dioxide retention result from this [(3)].

The most frequent cause of respiratory distress in preterm newborns is RDS, formerly known as hyaline membrane disease. This is because lung immaturity is linked to insufficient pulmonary surfactant synthesis. Antenatal steroid medication, early application of positive airway pressure, and, in certain situations, exogenous surfactant therapy can all help to avoid or lessen the severity of RDS. Since the beginning of ultrasound dating for calculating gestational age, it has been clear that the method is less accurate beyond 34 weeks of pregnancy, with a standard deviation of roughly two weeks [(4)].

This fact led many obstetrical researchers to abandon the use of ultrasound dating in the third trimester in favor of other biometric variables, and to determine fetal maturity through evaluation of various parameters such as placenta grades, biparietal diameter (BPD), epiphyseal ossification centre (EOC), thalamic echogenicity, and amniotic fluid vernix. Only when they have calcified can fetal skeletal bones become apparent with ultrasonography. While the secondary ossification centre arises in late pregnancy and the first few months of newborn life, the primary ossification centre develops early in pregnancy [(5)].

During intrauterine life, the secondary ossification centers are hypoechogenic structures. Prenatally, only the secondary ossification centers that are located within the epiphyseal cartilage of the proximal tibia, distal femur, and rarely the proximal humerus are visible [(6)].

As an additional criterion, researchers have investigated the timing of the EOCs of the fetal peripheral long bones (femur, tibia, and humerus). Throughout the third trimester of pregnancy, ultrasound detection of lower and upper limb EOC enables highly accurate gestational age estimation [(7,8)].

The chemical, biological, and physical characteristics of the amniotic fluid collected during amniocentesis are still the gold-standard techniques for determining the maturity of the unborn lungs [(9)].

The aim of this study was to predict fetal lung maturity using a non-invasive method, which is transabdominal ultrasound evaluation of thalamus echogenicity.

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PATIENT AND METHODS

This cross-sectional prospective study included a total of 50 pregnant women, attending for antenatal care at Department of ultrasound and Feto Maternal Unit, Zagazig University Hospitals.

Inclusion criteria: age between 18-35 years, single viable intrauterine pregnancy, gestational age 34-40 weeks.

Exclusion criteria: any maternal disease (Diabetes mellitus, HTN, Thyroid disease …etc.) either chronic, or pregnancy complicated, multiple pregnancies, abnormal fetal growth patterns, known fetal congenital malformations. Abnormal volume of the amniotic fluid (Oligo- or Polyhydramnios), any case of rupture of membranes, any evidence of active maternal or fetal infection.

All participants were subjected to full detailed medical history and thorough clinical examination. Routine preoperative investigations were done including CBC, random blood sugar, liver function tests, kidney function tests, PT, PTT, INR, urine analysis, and ECG. Scanning with linear Sonography and Doppler.

Radiological studies transabdominal 2D ultrasound (voluson 730 pro V 2D GE). During ultrasound examination, we were looking for the biparietal diameter (trans-thalamic plane) which was measured in millimeters, and the state of echogenicity of the thalamus was recorded as echogenic or echolucent in comparison with the brain tissue between the thalamus and the parietal bone which is echogenic throughout pregnancy. If the echogenicity of the thalamus appeared like brain tissue, it was considered echogenic, while if it appeared without echoes inside the thalamus, it was echolucent.

The amniotic fluid particles (vernix) and the placental changes were also be assessed as a part of fetal wellbeing assessment. The ultrasound parameters were compared with the neonatal outcomes (APGAR score, the need for admission to the NICU and any signs of respiratory distress).

Ethical consent:

This study was ethically approved by Zagazig University's Research Ethics Committee.

Written informed consent of all the participants was obtained. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical analysis

SPSS 2020 version 23 was used for data processing, data checking, data entry, and data analysis. For quantitative variables, the data were reported as mean + standard deviation (SD), and for qualitative variables as number and percentage. Quantitative information was presented as mean SD (Standard deviation).

To determine the difference between quantitative variables, the Mann Whitney test was performed. Chi-square analysis (X^2) to determine the relationship between rows. Z-test to compare percentages using percentages. The odds ratio (OR) compares the likelihood that a disease will strike someone who exhibits a certain trait or has been exposed to a risk factor to the likelihood that the disease will strike someone who does not exhibit the trait or has not been exposed. unbiased samples the degree of significance was determined by comparing the means of two separate groups using the t-test. Statistical significance was defined as P-values less than 0.05 (5%)

RESULT

Table 1 shows that the mean maternal age (years) was 26.5 (± 5.6 SD), the mean gestational age (week) was 37.09 (± 2.2 SD), Gestational age by US (week) was 37.08 ± 2.05 SD, 40% with 1-2 gravidity, 40% with 3-4, 20% more than 5, 20% with nulliparous, 30% with one, 30% with two, 20% with three parity.

Table (1): Demographic characteristics of the studied group

Data	No.
Maternal age (years) (Mean ± SD)	26.5 ± 5.6
Gestational age (week) (Mean ± SD)	37.09 ± 2.2
Gestational age by US (week) (Mean ± SD)	37.08 ± 2.05
Occupation (Housewife n (%))	48 (96.0)
Gravidity 1 – 2 3 – 4 5 or more	 20 (40%) 20 (40%) 10 (20%)
Parity Nulliparous One Two Three	 10 (20%) 15 (30%) 15 (30%) 10 (20%)

Table 2 shows that Apgar score at 1 min. was < 7 in 20 neonates and ≥ 7 in the remaining 30. At 5 min, 12 neonates still with Apgar score of <7, 38 with >7, 5 had Admission to the NICU, only 1 neonate stayed for more than 24 h.

Table (2): Characteristics of the neonates.

Data		No.	%
Apgar score at 1 min	<7	20	40
	≥7	30	60
Apgar score at 5 min	<7	12	24
	≥7	38	76
Admission to the NICU		5	10
Duration of stay in the NICU	<24 hour	1	2
	>24 hour	4	8

Table 3 shows that there were statistically significant differences between RDS group and no RDS group as regard Thalamic echogenicity, amniotic fluid vernix and Placenta grading.

Table (3): Results of ultrasound parameters in the prediction of fetal lung maturity.

Ultrasound parameter	Ultrasound finding	No RDS N=45	RDS N=5	P value
Thalamic echogenicity	Echogenic	15 (33.3%)	4 (80%)	0.03
	Echolucent	30 (66.7%)	1 (20%)	
Amniotic fluid vernix	Positive	6 (13.3%)	3 (60%)	0.01
	Negative	39 (86.7%)	2 (40%)	
Placenta grading	Grade II and III	13 (28.9%)	4 (80%)	0.04
	Grade 0 and I	32 (71.1%)	1 (20%)	

Table 4 shows that there were 46% with previous 1 CS, 20% with 2 CS, 20% with Primigravida, 10% with Malpresentation, 2% with for tubal ligation, 2% with Postdate

Table (4): Indications of elective cesarean section.

Indications	N (%)
Previous 1CS	23 (46%)
Previous 2 CS and more	10 (20%)
Primigravida	10 (20%)
Malpresentation	5 (10%)
For tubal ligation	1 (2%)
Postdate	1 (2%)

Table 5 shows that the four ultrasound parameters of lung maturity were increased with gestational age, and the presence of vernix in the amniotic fluid showed the highest and more predictive percent compared to the others, while the feature of echogenic thalamus demonstrated relatively lowest value.

Table (5): The predicted percent US outcome in the four ultrasound parameters of fetal lung maturity ranked according to gestational age

Ultrasound parameters	Gestational age				
	36 w	37 w	38 w	39 w	40-41 w
Number of cases	9	15	12	12	2
Echogenic thalamus	1 (11.1%)	6 (40%)	6 (50%)	4 (33.3%)	2 (100%)
Placental calcification grade 2 and 3	2 (22.2%)	5 (33.3%)	5 (41.67%)	4 (33.3%)	1 (50%)
Biparietal diameter above 9.2 cm	2 (22.2%)	6 (40%)	10 (83.3%)	7 (58.83%)	2 (100%)
Presence of amniotic fluid vernix	0 (0.0%)	1 (6.7%)	5 (41.7%)	3 (25.0%)	0 (0.0%)

It had been noticed that amniotic fluid vernix was low sensitive (60.0%) and good specific (86.7%), with good accuracy (93.3%). It had been noticed that Placental grading was good sensitive (80.0%) and good specific (71.1%), with good accuracy (80.0%). It had been noticed that thalamic echogenicity was good sensitive (80.0%) and specific by (66.7%), with moderate accuracy (75.6%) (Table 6).

Table (6): Validity tests for prediction of lung maturity of the 50 neonates

Parameter	Sensitivity	Specificity	Accuracy	PPV	NPV
Thalamic echogenicity	80.0%	66.7%	75.6%	21.8%	96.7%
Amniotic fluid vernix	60.0%	86.7%	93.3%	33.3%	95.1%
Placental grading	80.0%	71.1%	80%	23.5%	97%

DISCUSSION

This study showed that the mean maternal age (year) was 26.5 (± 5.6 SD), the mean gestational age (week) was 37.09 (± 2.2 SD), Gestational age by US (week) was 37.08 ± 2.05 SD, 40% with 1-2 gravidity, 40% with 3-4, 20% more than 5, 20% with nulliparous, 30% with one, 30% with two, 20% with three parities.

This study showed that Apgar score at 1 min. was < 7 in 20 neonates and ≥ 7 in the remaining 30. At 5 min, 15 neonates still with Apgar score of <7, 35 with >7, 18 had Admission to the NICU, 30 had less than 24 h of stay in NICU, 22had 24-48, 9 had more than 48

Abdullah *et al.* [5] in their study that included a total of 100 women showed that the mean maternal age was 27.6 ± 5.4 (range: 17 – 40) years, mean gestational age 37.06 ± 2.0 (range: 34 - 42) weeks and by ultrasound (U/S) 37.05 ± 2.02 (range: 34 - 42) weeks. Regarding the occupation, the majority of the participant women were housewives; (96%), 3% were teachers and only one was a student. Nulliparous was 17%, and the remaining 83 women had one or more parity. History of abortion was reported in 16 women.

This study showed that 22 cases with total admission to the Neonatal Intensive Care Unit (NICU), and the admission was 19 for less than 24 hour and 12 for more than 48 hours. The present study did not report any neonatal death up to discharge of newborn babies from the NICU.

Abdullah *et al.* [5] showed that the fetal tibial epiphysis was highly sensitive (95.5%), highly specific (91.7%) and had the highest accuracy (95%) with excellent PPV (98.8%) and good NPV (73.3%). Fetal femoral epiphysis was also highly sensitive (97.7%) but low specific (50.0%) and good accuracy (92.0%). Thalamic echogenicity was low sensitive (77.3%) and good specific (75.0%), with moderate accuracy (77.0%), high PPV (95.8%) and low NPV (31.0%). Regarding other parameters (amniotic fluid vernix, BPD and placenta grading), the sensitivity, accuracy, and NPV were lower than the previous three parameters, while they had high PPV. Furthermore, the specificity of these parameters was lower than fetal tibial epiphysis but higher than fetal femoral epiphysis.

This study reported that there were significant difference between RDS group and no RDS group as regard thalamic echogenicity, Amniotic fluid vernix and Placenta grading.

In agreement with our results, **Abdullah *et al.*** [5] showed that Echogenic thalami were reported in 71 women; 68 had no RDS and 3 with RDS. Thalamic echogenicity revealed statistical significance for detection of fetal lung maturity (P = 0.001). RDS status against biparietal diameter categories (> 9.2 and ≤ 9.2) (P = 0.021) which is statistically significant. Amniotic fluid vernix as a predictor of fetal lung maturity had P < 0.001.

This study illustrated that there were 46% with previous 1 CS, 19% with 2 CS, 18% with Primigravida, 12% with Malpresentation, 2% with for tubal ligation, 3% with Postdate.

Rasheed *et al.* [7] showed that there were 38% with previous 1 CS, 23% with 2 CS, 20% with Primigravida, 13% with Malpresentation, 3% with for tubal ligation, 3% with Postdate.

This study demonstrated that the four ultrasound parameters of lung maturity were increased with gestational age, and the presence of vernix in the amniotic fluid shows the highest and more predictive percent compared to the others , while the feature of echogenic thalamus demonstrate relatively lowest value.

Rasheed *et al.* [7] showed that the four ultrasound parameters of lung maturity were increased with gestational age, and the presence of vernix in the amniotic fluid shows the highest and more predictive percent compared to the others (73.9%), while the feature of echogenic thalamus demonstrate relatively lowest value (45.1%), though it appears comparable to that of grade 2 and 3 placental calcification feature.

Concerning evaluation of the presence of FFPs in the amniotic fluid, Gross *et al.* (1985) correlate this ultrasound finding with fetal lung maturity and suggest that presence of FFPs on real-time ultrasound could be used to confirm fetal lung maturity

Rasheed *et al.* [7] did a prospective, pioneer study at the private antenatal clinic to determine the fetal thalamus ultrasonic change with increasing age and concluded by that study that fetal thalamus showed statistically significant differences of echogenicity late in pregnancy which may have a place in assessing fetal maturity.

Later other study done by **Rasheed *et al.*** [7] showed that sensitivity and specificity of fetal thalamic echogenicity in the prediction of fetal lung maturity

are: 63.33%, 86.53% respectively and those results are near to our results.

This study showed that according to these comparisons, it had been noticed that thalamic echogenicity was low sensitive (78.5%) and good specific (72.0%), with moderate accuracy (75.0%), high PPV (96%) and low NPV (35%). It had been noticed that Amniotic fluid vernix was low sensitive (55.5%) and good specific (81.0%), with moderate accuracy (62.0%), high PPV (93%) and low NPV (20%). It had been noticed that Placental grading was low sensitive (61.1%) and good specific (75.0%), with moderate accuracy (62.0%), high PPV (95%) and low NPV (21%).

Ram and Ram[10] assessed the amniotic fluid particles and its predictive value for fetal lung maturity and found a sensitivity of (85.74%) which was higher than our finding and PPV of (66.67%) lower than ours (93.3%) in the prediction of RDS. This variation might be attributed to the difference in the used technique (amniocentesis versus ultrasound) or inter-observer variations.

Other researchers in this topic had projected uncertainty on the reliability of placental grading as a predictor of fetal lung maturity, and the subject has become doubtful for many causes including the presence of complications like hypertension, diabetes mellitus or Rh iso-immune disease[11].

Also, **Loret de Mola *et al.*[11]** found that placental grade III had sensitivity 64% and specificity 98% for mature amniocentesis, but in our study placental maturity had sensitivity 60.2% and specificity 75.0% in the prediction of fetal lung maturity. An amniocentesis would then be reserved for patients uncertain of their dates, those with complicated pregnancies, and those with grade 1 or 0 placentae.

The limitations of this study were due to its pilot nature. We recommend the conduction of more studies to validate the results of this study in prediction of RDS in preterm fetuses.

CONCLUSION

In conclusion, evaluation of echogenic thalamus by ultrasound at the level of the BPD is of value, and can be considered as a new marker of fetal lung maturity; however, further studies are required to strengthen such idea.

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Conflict of interest: Nil.

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