

Evaluation of thalamus echogenicity by ultrasound as a marker of fetal lung maturity

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ABSTRACT

The present study evaluated fetal thalamic echogenicity by ultrasound as a possible marker of fetal lung maturity in comparison with other ultrasound makers. A prospective longitudinal study performed in Al-Elwiya Maternity Teaching Hospital in Baghdad, Iraq during the period from April 2010 to March 2011. One hundred and forty two pregnant women (36 to 42 weeks of gestation) who were admitted for elective cesarean section and referred for an obstetric ultrasound scan at the same day of their elective cesarean section were included. Scanning with linear ultrasound with convex transducer frequency of 3.5 MHz was utilized to measure the biparietal diameter and the state of echogenicity was recorded as echogenic or echolucent, in addition to amniotic fluid vernix and the placental changes. The presence of echogenic thalamus as a sign of fetal lung maturity had a specificity of 86.53% which is higher than the three other signs of lung maturity; the positive predictive value was (89.6%) which is also higher than the three other signs, but the sensitivity was 63.33% and negative predictive value was 57.69% which is lower than the presence of vernix in the amniotic fluid, 86.66 and 67.56 respectively. In conclusion, evaluation of echogenic thalamus is beneficial, and can be considered as a new marker of fetal lung maturity; however, further studies are required to strengthen such idea.

Keywords: Fetal Lung Maturity; Thalamic Echogenicity; Ultrasound

1. INTRODUCTION

Fetal lung immaturity is a major problem in the management of elective birth with respect to predicting the development of infant respiratory distress syndrome

(IRDS) in the neonate after birth. Although gold-standard measures of fetal lung immaturity were the chemical, biological and physical properties of amniotic fluid [1], the fluid was obtained by invasive technique through amniocentesis. Moreover, lamellar body count was evaluated and found to be an easy, rapid and cost-effective as a predictive measure fetal lung maturity [2]. Fetal lung maturity was indirectly assessed by ultrasonic fetal lung morphology [3], fetal respiratory movement or fetal nasal respiratory flow imaging by Doppler ultrasound [4], ripening of the placental image [5], Doppler blood flow wave forms [6] or the intrauterine amniotic fluid choline by magnetic resonance spectroscopy [7]. Noninvasive direct assessment of fetal lung maturity was studied by the ultrasonic fetal lung frequency component [8], B-mode image texture [9] and special mean gray level [10], where the ultrasonic methods should rely on a special computer system or the mean gray level was so unstable to the device gain and the depth of the subjects that every measurement needed test piece calibration. Ultrasonography has contributed by the use of chest circumference and area [11] or by comparison with other fetal measurements [12]. Attempts have also been made to correlate the ultrasonic appearances of the placenta with fetal lung maturity. In all of these studies, however, the sensitivity and positive predictive value were poor, although the non-invasive nature of this approach and rapidity of evaluation were attractive [13]. Estimates of direct fetal lung volume have been made using 3-D ultrasound [14], but these methods may be affected by liquor volume and do not provide any additional physiological information relating to potential function. In an attempt to establish further non-invasive method for evaluation of fetal lung maturity, the present study was designed to evaluate the validity of measuring fetal thalamic echogenicity by ultrasound as a marker of fetal lung maturity.

2. MATERIAL AND METHODS

2.1. Patients and Study Design

The present prospective longitudinal study involved 142

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pregnant women (age 31.0 ± 5.2 years) from 36 to 42 weeks of gestation (38.8 ± 2.6 weeks) who were admitted for elective cesarean section for many indications (**Table 1**) in Al-Elwiya Maternity Teaching Hospital/Baghdad during the period from April 2010 to March 2011; after being fully familiarized with study protocol and techniques; the protocol was in compliance with the principles of the 1996 amendment the Declaration of Helsinki, and the study was approved by both the Ministry of Health ethical committee and institutional review board of Al-Kindy College of Medicine; the protocol was compatible with the safety guidelines published by the National Radiological Protection Board [15] and informed written consent was obtained from each woman prior to evaluation.

The inclusion criteria include women with single viable pregnancy, uncomplicated pregnancy (hypertension or diabetes), normal amount of liquor approved by ultrasound and Rh positive mothers. All included women were examined by linear ultrasound with convex transducer frequency of 3.5 MHz (Braun, UK) at the Radiology Department at the same day of their elective cesarean section. During ultrasound examination we look for the biparietal diameter (transthalamic 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 through out pregnancy; if the echogenicity of the thalamus appears like brain tissue, it is considered echogenic, while if it appears without echoes inside the thalamus it is echolucent. The amniotic fluid particles (vernix) and the placental changes were also measured as a part of fetal wellbeing assessment. All cases with complicated pregnancy, multiple pregnancy and pregnancy with known fetal malformations, or those with oligohydramnios or polyhydramnios were excluded.

2.2. Statistical Analysis

Statistical analysis was performed using the Statistical Package for Social Sciences version 17.0 (SPSS Inc.,

Table 1. Indications of elective cesarean section.

Indications	
Previous 1CS	38%
Previous 2 CS and more	23%
Primigravida	20%
Malpresentation	13%
For tubal ligation	3%
Postdate	3%

Chicago, IL, USA). The results of the study were analyzed statistically using descriptive statistics to describe the observed frequencies with their percentages (Cross tabulations). The validity of the US indicators compared with fetal lung maturity were analyzed for validity of the screening test through calculating sensitivity and specificity; the sensitivity is defined as the probability of testing positive if the disease is truly present and is calculated by: Sensitivity = (True positive by the test)/(True positive + false negative) $\times 100\%$, while specificity is defined as the probability of screening negative if the disease is truly absent and is calculated by: Specificity = (True negative by the test)/(True negative + false positive) $\times 100\%$ [16].

3. RESULTS

The changes in thalamic echogenicity in different gestational stages are demonstrated in **Figures 1-4**, which represent the outcome in 64 cases (45.1%) of the evaluated women.

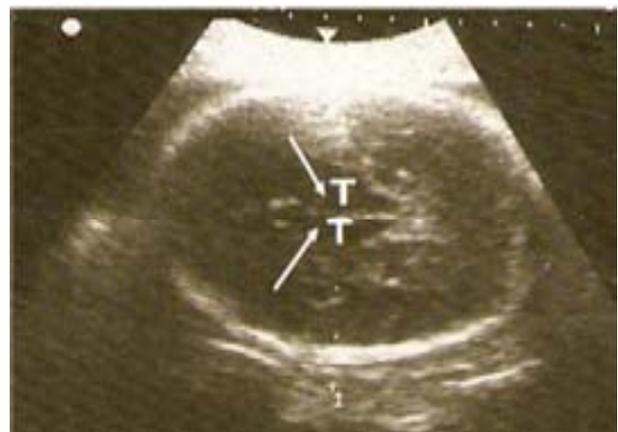


Figure 1. Ultrasonograph shows echolucent fetal thalamus (T) at 36 weeks of gestation (white arrows).



Figure 2. Ultrasonograph shows echolucent fetal thalamus (T) at 36 weeks of gestation (white arrows).



Figure 3. Ultrasonograph shows echogenic thalamus (T) at 38 weeks of gestation (white arrows).



Figure 4. Ultrasonograph shows echogenic thalamus (T) at 38 weeks + 3 days of gestation (white arrows).

Table 2 showed that for the 4 ultrasonic criteria measured during the present study, the specificity and the positive predictive values are higher for the thalamic density. However, the presence of vernix in the amniotic fluid showed more sensitivity (86.66%) versus 63.33% in the thalamic density. Meanwhile, **Table 3** 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 the neonatal outcome of the present study, **Table 4** showed that neonatal morbidity mostly occurs at early stages of the gestational age (less than 39 weeks) and represents 35/52 of total admission to the Neonatal Intensive Care Unit (NICU), and the admission was 19/52 for less than 24 hour and 5/52 for more than 48 hours. The present study did not report any neonatal death up to discharge of new born babies from the NICU.

4. DISCUSSION

It would be convenient to predict fetal lung immaturity before an elective birth noninvasively to allow therapeutic protection against possible respiratory distress syndrome (RDS) in the neonate, or in some cases, to estimate the effect of adrenal steroid treatment of a preterm fetus by repeated tests that can be freely performed by noninvasive techniques. Prenatal diagnosis permits delivery by planned caesarean section sufficiently early to

Table 2. Comparison between the sensitivity and the specificity of the four ultrasound parameters in our study as a sign of fetal lung maturity.

Ultrasound parameters	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Echogenic thalamus	63.33	86.53	89.6	57.69
Placental calcification grade 2 and 3	51.11	71.15	75.40	45.67
Biparietal diameter above 9.2 cm	62.22	42.30	65.11	39.28
Presence of amniotic fluid vernix	86.66	48.07	74.28	67.56

Table 3. The predicted percent US outcome in the four ultrasound parameters of fetal lung maturity ranked according to gestational age.

Ultrasound parameters	Gestational age						Total
	36 week	37 week	38 week	39 week	40 week	41 - 42 week	
Number of cases	12	31	45	38	13	3	142
Echogenic thalamus	2 (16.7)	14 (45.2%)	14 (31.1%)	21 (55.3%)	10 (76.9%)	3 (100%)	64 (45.1%)
Placental calcification grade 2 and 3	3 (25%)	13 (41.4%)	16 (35.6%)	19 (50%)	8 (61.5%)	2 (66.7%)	61 (43%)
Biparietal diameter above 9.2 cm	1 (8.3%)	8 (25.8%)	30 (66.7%)	33 (86.8%)	11 (84.6%)	3 (100%)	86 (60.6%)
Presence of amniotic fluid vernix	4 (33.3%)	22 (71%)	31 (68.9%)	34 (89.5%)	11 (84.6%)	3 (100%)	105 (73.9%)

Table 4. Neonatal outcome according to evaluation of thalamic echogenicity.

Neonatal outcome	Gestational age						Total
	36 week	37 week	38 week	39 week	40 week	41 - 42 week	
Number of cases	12	31	45	38	13	3	142
Good neonatal outcome (not needed to be admitted to the NICU)	5 (41.6%)	18 (58.1%)	30 (66.7%)	24 (63.2%)	10 (76.9%)	3 (100%)	90 (63.4%)
Total admission to the NICU	7 (58.3%)	13 (41.9%)	15 (33.3%)	14 (36.8%)	3 (23.1%)	0	52 (36.6%)
Admission to the NICU less than 24 hrs	1 (8.3%)	8 (25.8%)	10 (22.2%)	9 (23.7%)	3 (23.1%)	0	31 (21.8%)
Admission to the NICU from 24 to 48 hrs	4 (33.3%)	4 (12.9%)	3 (6.7%)	5 (13.2%)	0	0	16 (11.3%)
Admission to the NICU more than 48 hrs	2 (16.7%)	1 (3.2%)	2 (4.4%)	0	0	0	5 (3.5%)
TTN or RDS	3 (25%)	10 (32.3%)	13 (28.9%)	14 (36.8%)	3 (23.1%)	0	43 (30.3%)
RDS	4 (33.3%)	3 (9.6%)	2 (4.4%)	0	0	0	9 (6.3%)
Treated hypoglycemia	1 (8.3%)	1 (3.2%)	2 (4.4%)	0	0	0	4 (2.8%)
Neonatal mortality	0	0	0	0	0	0	0

NICU: Neonatal Intensive Care Unit; TTN: Transient Tachypnea of the Newborn; RDS: Respiratory Distress Syndrome.

avoid the possible complications. A review of 155 cases found that prenatal diagnosis results in a 95% reduction in late fetal and neonatal mortality [17]. Such observations have inspired several clinical groups [17-20] and parents to recommend routine identification of umbilical cord insertion at 20 weeks of gestation and targeted screening for vasa praevia in women identified as at high risk for the condition. Many studies of ultrasound prediction of fetal lung maturity were used to compare ultra-sound parameters with tests of amniocentesis to assess that sign with lung maturity [10]. Amniocentesis is not available in our practice, so in the present study we compare the ultrasound parameters with the neonatal outcomes (APGAR score, the need for admission to the NICU and any sign of respiratory distress). From clinical practice it has been noticed that thalamic density increased with gestational age, so the present study; for the best of our knowledge, was carried out to assess this sign and try to adopt it as an indicator for lung maturity; this subject was presented for the first time and not previously reported elsewhere. In the present study, through non-invasive technique, we try to evaluate fetal thalamic echogenicity by ultrasound as a new indicator for lung maturity and compare it with other previously known signs of fetal lung maturity such as biparietal diameter, amniotic fluid vernix and placental changes. The data showed that the thalamus is echogenic in 64 cases (45%) and echolucent in 78 cases (55%) and the echogenicity increases with the increase in the gestational age; this result seems comparable to a previously reported data that correlate thalamic echogenicity with gestational age by the same author [21]. The presence of echogenic thalamus as a

sign of fetal lung maturity by ultrasound was found to be of high specificity in detecting fetal lung maturity and demonstrates high positive predictive value compared to other ultrasound parameters utilized in the present study; however, the sensitivity and negative predictive value were reported to be lower compared to the signs of vernix in the amniotic fluid. Although the utilized technique is simple and can be easily performed in all obstetrics units, the echo reflection is not measurable and depends on the experience of the examiner, which represents a major difficulty in interpretation of data.

It has been reported that both grade II and III placenta predicted fetal lung maturity in 100% of cases [22], suggesting that placental grading could replace estimation of the *L/S* ratio and thereby avoid amniocentesis and its complications. However, subsequent workers in this field have cast doubt on the reliability of placental grading as a predictor of fetal lung maturity [23,24], and the subject has become controversial for a many reasons including presence of complications like hypertension, diabetes mellitus or Rh iso-immune disease. Accordingly, the search for novel signs and markers for prediction of lung maturity became an interested discipline in the obstetrics field. The present study confirmed the previously reported data that grades II and III placentas were highly associated with fetal lung maturity [25]. Meanwhile, the finding of fetal lung maturation in 83.3% of infants in grade III group justifies using this group to indicate fetal lung maturity before repeat caesarean section in woman with reasonable certainty to reach 38 weeks of gestation and has no complicating diseases. However, because only 18% of our patients had a grade

III placenta, those with grade II placenta satisfying the provisos mentioned above should be managed in the same way as those in grade III on the basis of our findings, and even with this group 75.4% of fetuses had achieved lung maturity, such finding seems compatible with that reported previously [22]. Hadlock *et al.* (1985) utilized amniocentesis for determination of fetal lung maturity and ultrasonographic (US) evaluation of the biparietal diameter (BPD) and placental grade were performed simultaneously and concluded that the ability of the sonographic parameters to predict fetal lung maturity was closely related to menstrual age and the best use of US for predicting fetal lung maturity is in establishing menstrual age early in pregnancy [26]; the results obtained in the present study support the previously mentioned idea. 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 [27]. The data presented in this study support the previously mentioned one and more than one ultrasound markers may be better correlated for prediction of fetal lung maturity. Moreover, the present study demonstrates that a BPD greater than or equal to 92 mm predicted 56 of 90 (62.22%) cases with mature lung, while the presence of FFPs predicted 78 of 90 (86.66%); when utilized together, a BPD equal to or greater than 92mm and/or the presence of FFPs predicted 83 of 90 (92.22%) of cases with mature fetal lung, and such finding complies with data reported by others, where BPD greater than or equal to 92 mm and the presence of free-floating particles are independent, and considered as complimentary predictors of fetal lung maturity [28]. Subjective approach during measurement of echogenicity and lack of a method to measure the gain of echoes are the limitations of the present study, in hope that we can overcome in future studies. 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.

5. ACKNOWLEDGEMENTS

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