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Accuracy of Ultrasound Markers in Prediction of Lung Maturation

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ORIGINAL ARTICLE

Accuracy of Ultrasound Markers in Prediction of Lung Maturity

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Abstract

Background: **Because of accurate dating of gestational age, ultrasound imaging is attractive tool in avoiding maternal & perinatal mortality, particularly when done in the first trimester. Ultrasound is used to monitor foetal growth.**

Aim of the work: To assess the accuracy of ultrasound markers in the prediction of lung maturation by measuring certain parameters and comparing the results with the neonatal outcome by using APGAR score at 1 min and 5 min, neonatal respiratory distress syndrome, and NICU admission.

Patients & methods: This study is a cohart study on 120 pregnant women (37:39 wks gestation) with the previous one to three (1: 3) caesarean sections at Al Hussein and Mansheyet Al Bakri Hospitals during the period from October 2021 to June 2022.

Results: **The Biparietal Diameter≥92 mm was associated with foetal lung maturation and was found to have Sensitivity (63.6%) and good Specificity (80.6%). The amniotic fluid particles (Vernix) were found to have good Sensitivity (72.7%) and low Specificity (56.3%). The placental maturation grade III were found to have good Sensitivity (72.7%) and low Specificity (59.2%). The colon echogenicity grade III was found to have good Sensitivity (72.7%) and lowest Specificity (52.4%). The kidney length was found to have low Sensitivity (63.6%) and good Specificity (76.7%). The lung/liver echogenicty was found to have Sensitivity (63.6%) and good Specificity (88.3%).**

Conclusion: **Because of accurate dating of gestational age, ultrasound imaging is attractive tool in avoiding maternal & perinatal mortality.**

Termenation of pregnancy after the age of 39 weeks was the best time to exclude TTN and NRDS.

Keywords: Lung maturation, Neonatal RDC, Ultrasound

1. Introduction

Normal foetal lung development is a sequential process that involves several phases. It begins at the 24th menstrual week and extends into post-natal life.[1]

From 34 to 37 weeks there is a transitional phase in which varying degrees of foetal lung maturation can be expected.[2]

There are 2 major clinical situations in which it is needed to have an accurate assessment of foetal lung maturation in utero. First is a preterm studied case, or studied case for whom early delivery is required due to maternal or foetal indications. 2nd, uncomplicated pregnancy with unknown due dates necessitates caesarean section.[1]

The baby is at risk of developing respiratory distress syndrome before this time. RDS affects approximately 1% of all pregnancies & can have serious short & long-term consequences, involving both lungs & other organs that can extend beyond the neonatal period in its most severe forms.[3]

Later in pregnancy ‘near term’, severe RDS can happen.[4]

Diabetic pregnancy is characterized by a delay in process of foetal lung maturation.[5]

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Iatrogenic prematuration by caesarean section was one of the top reasons for newborn prematuration & respiratory distress.[6]

Foetal lung maturation can be evaluated by biochemical analysis of amniotic fluid, but it carries the potential for serious complications.[7]

Attempts have been made to use prenatal diagnostic ultrasonography to assess foetal lung maturation.[8]

Ultrasound items to evaluate foetal lung maturation are composite age (by BPD, HC, AC, FL), placental grade, foetal bowel pattern, lung/liver ratio, and distal femoral epiphysis.[9]

Foetal bipraietal diameter (BPD) has been related to FL, with accuracy ranging from 78 to 100%.[10]

Placental grading is a reliable ultrasonographic scale that can help to predict foetal lung maturation.[11]

Amniotic fluid turbidity is a predictor of foetal lung maturation. It had a 91% positive value.[12]

Neonatal RDS is frequently regarded as a prematuration disease caused by a lack of surfactant (phospholipid mixture -predominantly de saturated palmitoyl phosphatidylcholine) that decreases alveolar surface tension, which reduces the pressure required to keep alveoli inflated, & preserves alveolar stability, resulting in progressive & diffuse atelectasis. Although it can happen in term pregnancies, the risk of occurrence decreases as gestational age rises.[13]

Furthermore, the amniotic fluid vernex was evaluated & considered easy, quick & cost-effective predictor of foetal lung maturation.[14]

It would be convenient to predict foetal lung immaturation non-invasively before elective birth to enable therapeutic protection against possible respiratory distress syndrome in the neonate, or some cases, to estimate the impact of steroid therapy on preterm foetus using repeated exams that can be freely done by noninvasive methods. Prenatal diagnosis allows for planned caesarean section delivery to occur early enough to avoid potential problems.[15]

2. Patients and methods

Study setting: This research is a randomized clinical trial at Al Hussein Hospital and Mansheyet Al Bakri Hospital during the period from October 2021 to June 2022.

Type of study and study population: This is a cohart study on 120 pregnant women (37:39 wks gestation) with the previous (1: 3) caesarean sections.

Inclusion criteria of the cases: Age: 18–35 yrs. Pregnant women with Gestational age: 37–39 wks. Previous (1: 3) caesarean sections.

Exclusion criteria of the cases: Women with chronic diseases. Women with uterine masses. Women with recurrent vaginal infections. Women with a risk of preterm labor. Any type of cardiovascular disease. Multiple pregnancies in previous pregnancies had congenital malformed foetus. Macrosomic fetuses Oligohydramnios Meconium stained fetuses.

Sample size calculation: MedCalc version 12.3.0.0 program 'Ostend, Belgium' was used for calculations of sample size, statistical calculator based on 95% confidence interval & and power of research 80% with α error 5%.

Ethical and legal consideration: Approval from the Department of Obstetrics & Gynecology, Al-Hussien Hospital, and Mansheit Al Bakry General Hospital, to review the records was obtained.

Confidentiality: Women are identified by their names in the data collection sheet, which is kept in privacy by the investigator.

2.1. Methods

Patients were subjected to:

Complete history taking: Menstrual history: including menarche age, menstrual disturbance, dysmenorrhea, & related symptoms. Obstetric history, such as parity & delivery mode Current medical history: chronic diseases & medications. HTN and diabetes history there is a family history of similar conditions or diabetes. Any medication allergy history surgical history, laparoscopic interference, laser therapy of hirsutism.

2.2. Examination

General examination: Evaluation of vital signs, Measurement weight, height.

Abdominal & local clinical examination: To determine the fundal level & gestational age, scars from previous operations, masses, tenderness or rigidity and any clinically detectable pathology in the abdomen or pelvis.

2.3. Investigations

Laboratory: CBC, coagulation profile, albumin detection in urine samples via boiling or urine analysis & liver and kidney function examinations are all available.

Abdominal U/S: Abdominal U/S was used for obstetric ultrasound. The single sonographer used the same machine to perform all measurements.

Foetal biometry, Amniotic Fluid Index measurement, & anomaly scan were performed to look for any congenital anomalies. Once congenital anomalies are suspected, the studied case is referred to foetal medicine specialist for an anomaly scan using the 4D US.

Elective caesarean section: at 37/39 weeks.

Follow-up: The patients were followed up after caesarean section. Assessment of the baby by the paediatrician: APGAR score. Symptoms of respiratory difficulties. Weight. Foetal sex.

Analysis of data: All data was collected and tabulated and statistically analyzed.

Outcome measures: Gestational age at the duration of delivery. APGAR score at one & 5 min. Neonatal birth weight. Neonatal ICU admission lessor more than 24 h.

Ethical Consideration: The research protocol had been submitted to the Institutional Research Board of Al Azhar University's faculty of medicine for approval. Each research participant had given their verbal consent after being informed. Confidentiality and personal privacy were respected at all stages of research.

2.4. Statistical analysis

Collected data was tabulated & statistically analysed using SPSS software version 20.0. Descriptive statistics were computed for numerical parametric data as mean ± SD & minimum & maximum of range, for numerical non parametric data as median & first & third inter-quartile ranges, and for categorical data as number & percentage. Level of significance was set at P value < 0.050, which indicates that data is significant; or else, it is not. *P* value is statistical measure of likelihood that outcomes of research could have happened by chance.

3. Results

Fig. 1, Tables 1–5.

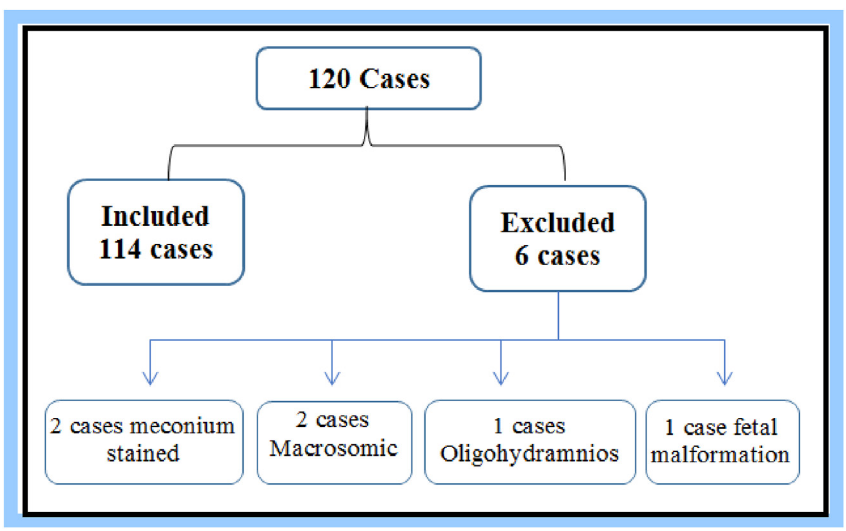

Fig. 1. Flowchart of Selection of studied cases.

Table 1. Comparison according to APGAR-1<7 regarding immaturation predictors.

Predictors	APGAR-1<7 (*N* = 42)	APGAR-1≥7 (*N* = 72)	*P* value
Proximal tibia epiphysis <5 mm	19 (45.2%)	1 (1.4%)	#<0.001*
Distal femur epiphysis <6.25 mm	29 (69.0%)	28 (38.9%)	#<0.001*
Proximal humerus epiphysis (absent)	14 (33.33%)	1 (1.4%)	#<0.001*
Thalamic echogenicity (echolucent)	19 (45.2%)	11 (15.3%)	#<0.001*
Biparietal diameter <92 mm	18 (42.8%)	9 (12.5%)	#<0.001*
Colon grading I-II	25 (59.5%)	32 (44.4%)	#<0.001*
Kidney length	20 (47.6%)	11 (15.3%)	#<0.001*
Lung/liver echogenicity	14 (33.33%)	5 (6.9%)	#<0.001*
Amniotic fluid vernix (absent)	35 (83.33%)	18 (25%)	#<0.001*
Placenta grading 0-I-II	35 (83.33%)	19 (26.4%)	#<0.001*

#Chi square test.
*Significant.

Table 2. Comparison according to APGAR-5 <7 regarding immaturation predictors.

Predictors	APGAR-5<7 (*N* = 29)	APGAR-5 ≥7 (*N* = 85)	*P* value
Proximal tibia epiphysis <5 mm	15 (51.7%)	5 (5.9%)	#<0.001*
Distal femur epiphysis <6.25 mm	21 (72.4%)	36 (42.4%)	#<0.001*
Proximal humerus epiphysis absent	21 (72.4%)	33 (38.8%)	#<0.001*
Thalamic echogenicity (echolucent)	16 (55.1%)	14 (16.4%)	#<0.001*
Biparietal diameter <92 mm	13 (44.8%)	14 (16.4%)	#<0.001*
Colon grading I −II	20 (69.0%)	37 (43.5%)	#<0.001*
Kidney length	19 (65.5%)	12 (14.1%)	#<0.001*
Lung/liver echogenicity	12 (41.4%)	7 (8.2%)	#<0.001*
Amniotic fluid vernix (absent)	20 (69.0%)	33 (38.8%)	#<0.001*
Placenta grading 0-I- II	19 (65.5%)	32 (37.6%)	#<0.001*

#Chi square test.
*Significant.

Table 3. Comparison according to RDS regarding immaturation predictors.

Predictors	RDS (*N* = 11)	No RDS (*N* = 103)	*P* value
Proximal tibia epiphysis <5 mm	10 (90.9%)	10 (9.7%)	#<0.001*
Distal femur epiphysis <6.25 mm	10 (90.9%)	47 (45.6%)	#<0.001*
Proximal humerus epiphysis (absent)	9 (81.82)	8 (7.7%)	#<0.001*
Thalamic echogenicity (echolucent)	8 (72.7%)	22 (21.4%)	#<0.001*
Biparietal diameter <92 mm	7 (63.6%)	20 (19.4%)	#<0.001*
Colon grading I − II	8 (72.7%)	49 (47.6%)	#<0.001*
Kidney length <4 cm	7 (63.6%)	24 (23.3%)	#<0.001*
Lung/liver echogenicity	7 (63.6%)	12 (16.6%)	#<0.001*
Amniotic fluid vernix (absent)	8 (72.7%)	45 (43.7%)	#<0.001*
Placenta grading 0-I- II	8 (72.7%)	43 (41.7%)	#<0.001*

#Chi square test.
§Fisher's Exact test.
*Significant.

Table 4. Comparing according to NICU admission concerning immaturation predictors.

Predictors	NICU Admission (*N* = 19)	No NICU Admission (*N* = 95)	*P* value
Proximal tibia epiphysis <5 mm	14 (73.7%)	6 (6.3%)	#<0.001*
Distal femur epiphysis <6.25 mm	16 (84.2%)	41 (43.2%)	#<0.001*
Proximal humerus epiphysis (absent)	15 (78.9%)	2 (2.1%)	#<0.001*
Thalamic echogenicity (echolucent)	13 (68.4%)	17 (17.9%)	#<0.001*
Biparietal diameter <92 mm	10 (52.6%)	17 (17.9%)	#<0.001*
Colon grading I-II	11 (59.9%)	46 (48.4%)	#<0.001*
Kidney length <4 cm	9 (47.3%)	22 (23.2%)	#<0.001*
Lung/liver echogenicity	16 (84.2%)	3 (3.2%)	#<0.001*
Amniotic fluid vernix (absent)	16 (84.2%)	37 (38.9%)	#<0.001*
Placenta grading 0- I- II	15 (78.9%)	36 (37.9%)	#<0.001*

#Chi square test.
*Significant.

Table 5. Comparison according to NICU admission ≥24 h regarding immaturation predictors.

Predictors	NICU≥24 h (*N* = 5)	NICU <24 h (*N* = 14)	*P* value
Proximal tibia epiphysis <5 mm	4 (80.0%)	10 (71.4%)	§0.999*
Distal femur epiphysis <6.25 mm	4 (80.0%)	11 (78.6%)	§0.999
Proximal humerus epiphysis absent	5 (100%)	10 (71.4%)	§0.999*
Thalamic echogenicity (echolucent)	4 (80.0%)	10 (71.4%)	§0.999*
Biparietal diameter <92 mm	4 (80.0%)	6 (42.8%)	§0.044*
Colon grading I −II	3 (60.0%)	8 (57.1%)	§0.999
Kidney length <4 cm	2 (40.0%)	4 (28.6%)	§0.999
Lung/liver echogenicity	4 (80.0%)	10 (71.4%)	§0.999*
Amniotic fluid vernix (absent)	4 (80.0%)	8 (57.1%)	§0.115
Placenta grading 0-I- II	4 (80.0%)	10 (71.4%)	§0.999

§Fisher's Exact test.
*Significant.

4. Discussion

Foetal lung immaturation is the most important complication in the management of elective birth with the prediction advance of infant respiratory distress syndrome in the neonate after delivery. It is best to predict the lung maturation of the prenatal fetus before birth to avoid respiratory distress syndrome and find out the impact of steroid therapy on a preterm fetus by non-invasive procedure to avoid any complications.[16]

In the present research, RDS was cross-tabulated against a ultrasound finding of each parameter.

Gestational age rather than maternal age was shown to be a main risk factor for both improvements of RDS and NICU admission with a *P* value of 0.001 and 0.863, respectively.

Hence, after applying the appropriate statistical methods, regarding the prediction of RDS, the thalamic echogenicty was found to have moderate Sensitivity (72.7%) moderate Specificity (78.6%), positive Predictive value of (26.7%), negative predictive (96.4%), & diagnostic accuracy (77.3%).

The epiphyseal ossification centers (PTE and DFE) were found to have the highest Sensitivity (90.9%), high Specificity (90.3%) for PTE and lowest specificity (54.4%) for DFE, positive Predictive value of (50%) for PTE, low positive predictive value (17.5%) for DFE and the highest negative predictive value (98.9%) for PTE, high negative predictive value (98.9%), diagnostic accuracy (90.1%) for PTE and about (61.2%) for DFE.

The appearance of PHE correlates with foetal lung maturation was found to have very good Sensitivity (90.9%), very good Specificity (92.2%), positive Predictive value of (52.9%) negative predictive (97.9%), and diagnostic accuracy (91.2%).

The Biparietal Diameter $\geq$**92** mm was associated with foetal lung maturation and was found to have Sensitivity (63.6%), good Specificity (80.6%), positive Predictive value of (25.9%) negative predictive (95.4%), and diagnostic accuracy (78.5%)

The amniotic fluid particles (Vernix) were found to have good Sensitivity (72.7%), low Specificity (56.3%), a low positive Predictive value of (15.1%), negative predictive (95.1%), and diagnostic accuracy (65.5%)

The placental maturation grade III was found to have good Sensitivity (72.7%), low Specificity (59.2%), positive Predictive value of (15.7%) negative predictive (95.2%), and diagnostic accuracy (66.2%).

The colon echogenicity grade III was found to have good Sensitivity (72.7%), lowest Specificity (52.4%), lowest positive Predictive value of (14.1%) negative predictive (94.7%), and diagnostic accuracy (63.2%).

The kidney length was found to have low Sensitivity (63.6%), good Specificity (76.7%), positive Predictive value of (22.6%) negative predictive (95.2%), and diagnostic accuracy (71.4%).

The lung/liver echogenicty was found to have Sensitivity (63.6%), good Specificity (88.3%), highest positive Predictive value of (36.8%) negative predictive (95.8%), and diagnostic accuracy (86.1%).

This outcome agrees with the research of *Abdulla* et al.[17] in which foetal tibia epiphysis was the best predictor compared to other 5 parameters (with sensitivity, specificity, & precision of 95.5%, 91.7%, & 95%), next to tibia epiphysis is foetal femoral epiphysis (sensitivity of 97.7%, specificity 50%, & precision of 92%). ***Mahony*** et al.,[18] Sonographic epiphyseal ossification centres were evaluated in the evaluation of foetal lung maturation about amniocentesis profile of the lung and They discovered that proximal tibia epiphysis had a positive predictive accuracy of (100%) and specificity of (100%), whereas sensitivity & accuracy of prediction of immature amniocentesis profile of the lung were low (22–25%) for the same epiphyseal parameters.

Moreover, some researchers used EOC as markers of foetal gestational age & to forecast foetal maturation indirectly.

In *Abdulla* et al.,[17] It was discovered that the sensitivity, specificity, & accuracy of foetal thalamic echogenicity in predicting foetal lung maturation are 77.3%, 75%, and 75; which had the same results as the present study.

In ***2001, Faris***[19] did prospective pioneer research at a private maternity clinic to decide foetal thalamus ultrasonic modification with advancing age & found that foetal thalamus found statistically significant variations in echogenicity late in pregnancy, which may have a role in evaluating foetal maturation.

Research done by ***Rasheed*** et al.[15] found that the sensitivity & specificity of foetal thalamus echogenicity in prediction of foetal lung maturation are: 63.33%, 86.53% & those outcomes are near to this study's outcomes.

Saba et al.,[20] discovered that proximal humeral epiphysis was not observed before thirty-sixth week of GA & was noticed in a small proportion of foetuses 14% at thirty-sixth week of GA, increasing to 25% at thirty-seventh, it 66% at thirty eighth, & 100% at thirty-ninth & fortieth weeks. The presence of proximal humeral epiphysis indicates that foetus has reached maturation. Similar findings are found in ***Mahony*** et al.[21] According to research, all foetuses with visible proximal humeral epiphysis had mature amniocentesis, which is a good indicator of foetal lung maturation based on the L/S ratio & phosphatidyl glycerol in amniotic fluid. Similar findings are also found in ***Kumari*** et al.,[22] who discovered that proximal humeral epiphysis was not seen throughout ultrasonography with a gestational age of fewer than thirty-five weeks. And also similar results are in the same line with our results in ***Mongolli*** et al.,[29] Examination of ossification centres may confirm foetal maturation. Distal femoral epiphysis appears at a mean gestational age of thirty-two-thirty-three weeks. Its size grows linearly with gestational age. Identification of proximal humeral epiphysis by ultrasound has been linked to mature amniocentesis lung profile.

Patil et al.[23] found that the sensitivity & specificity of foetal thalamic echogenicity in predicting foetal lung maturation are: 81.2% and 77.7%, and diagnostic accuracy is 80.9% and these results were close to this study's results.

The present research found that Biparietal Diameter ≥**92** mm was associated with foetal lung maturation. In another research done by ***Slocum*** et al.[24] BPD of 92 mm or larger in all parturients who underwent elective repeat caesarean delivery was connected to no hyaline membrane disease. Additionally, ***Prakash*** et al.[10] Sonographically determined parameters, such as foetal biparietal diameter & placental grading, have been linked to foetal maturation with an accuracy range of 78%–100%. Current research found that amniotic fluid vernix has a sensitivity of 72.7% & specificity of 56.3% for predicting foetal lung maturation. In ***Abdulla*** et al.,[17] it was discovered that amniotic fluid vernix played role in predicting foetal lung maturation, with a sensitivity of 63.6% & specificity of 66.3%. Other researchers found different results.

Research by ***Shweni*** et al.[25] All foetuses with placental grades II & III had lung maturation, implying that the estimation of lecithin/sphingomyelin ratio could be replaced by placental grading could & decrease the number of cases that need amniocenteses.

However, ***Clair*** et al., and ***Kazzi*** disagreed with these results, and Numerous factors call into question the reliability of placental grading as a predictor of foetal lung maturation, such as the existence of problems such as hypertension, diabetes, or Rh iso-immune disease, which will impact foetal lung maturation in the existence of placental maturation grade III.[26,27]

Also, ***Kandil*** et al.[28] found that lung/liver echogenicity had a sensitivity of 63.1% and specificity of 30.8%, but in the present study lung/liver echogenicity had a sensitivity of 63.6%and specificity of 88.3% in the prediction of foetal lung maturation.

Loret de Mola et al.[11] Placental grade III had a sensitivity of 64% & specificity of 98% in predicting foetal lung maturation, however in current research, placental maturation had a sensitivity of 72.7% & specificity of 59.2%.

Also, ***Kandil*** et al.[28] showed that colon echogenicity grade III had a sensitivity of 68.4% & specificity of 45.7%, but in the present research placental maturation had a sensitivity of 72.7% & specificity of 52.4% in the prediction of foetal lung maturation.

Ugur et al.[21] studied kidney length as a useful adjunct parameter for better purposes of gestational age.

No study before was found to determine the effect of kidney length on lung maturation.

4.1. Conclusion

Because of accurate dating of gestational age, ultrasound imaging is beneficial in avoiding maternal & perinatal mortality, particularly when acquired in the first trimester. Ultrasound is used to monitor foetal growth & well-being to intervene early if needed. Termenation of pregnancy after the age of 39 wks was the best time to exclude TTN and NRDS.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Conflict of interest

There are no conflicts of interest.

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