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Evaluation of Fetal Lung Maturity Correlated by Various Ultrasound Parameters as Noninvasive Method

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Abstract
Background: Neonatal respiratory distress syndrome (RDS) continues to be a major problem in perinatology, contributing to the morbidity and death of preterm babies. To lower the risk of newborn RDS, the major objective of this study was to measure fetal lung maturity utilizing various color Doppler and multiple ultrasonography characteristics. **Methods:** This research was conducted on a cohort of 100 pregnant women who gave birth at Benha University Hospitals between February 26, 2022 and August 25, 2022, spanning six months. According to the occurrence of RDS, we categorized our study subjects into two groups: Group RDS+: n = 13; group RDS-: n = 87. Regarding (Maternal age, Parity, Type of delivery), there was no statistically significant difference between the two groups, but there was a statistically significant difference between the two groups regarding (Gestational age at Birth and NBW). **Results:** According to ultrasonography measurements, the Mann-Whitney test revealed no significant changes in the main pulmonary artery diameter (MPA), trans cerebellar diameter, or placental thickness between the study groups. The chi-square test revealed significant differences between proximal tibial epiphysis and thalamic echogenicity (p 0.001). Positive PTE results were seen in 91.95 percent of the non-RDS group compared to 7.69 percent of the RDS group. Thalamic echogenicity was seen in 88.5% of the non-RDS group compared to 15.38% of the RDS group. **Conclusions:** The development of newborn RDS may be accurately predicted using certain acoustic characteristics. The ultrasonic identification of the proximal tibial ossification sites and thalamic echogenicity demonstrated the highest accuracy in predicting fetal lung maturity.

Keywords: Ultrasound, Fetal Lung Maturity, Parameters, Noninvasive Method.

1. Introduction

Neonatal RDS remains a significant concern in the field of perinatology, contributing to the morbidity and mortality of premature infants [1]. It is a condition characterized by inadequate lung maturation and surfactant deficiency, leading to respiratory compromise and potential long-term complications. Early identification of fetal lung maturity plays a crucial role in determining the optimal timing and management of delivery, ensuring the best possible outcomes for both the mother and the new-born [2].

Traditionally, the assessment of fetal lung maturity has relied on invasive methods such as amniocentesis and analysis of the fetal lung fluid for surfactant components. While effective, these invasive procedures carry inherent risks and are often performed late in pregnancy, limiting their predictive value in preterm births [3]. Therefore, there is a need for non-invasive methods that can accurately evaluate fetal lung maturity at earlier gestational ages, enabling timely interventions to reduce the risk of neonatal RDS [4].

Ultrasound has emerged as a valuable tool in obstetric practice, providing detailed anatomical and functional information about the developing fetus. Advances in ultrasound technology, particularly the utilization of color Doppler and multiple ultrasound parameters, offer the potential to assess fetal lung maturity noninvasively [5, 6]. By evaluating specific ultrasound markers associated with lung development, such as lung parenchymal echogenicity, pulmonary artery Doppler flow, and lung volume measurements, it may be possible to predict the maturity of fetal lungs and identify those at increased risk for RDS [7].

The objective of this study is to evaluate fetal lung maturity using multiple color Doppler and ultrasound parameters as a non-invasive method. By investigating the correlation between these ultrasound markers and actual neonatal outcomes, we aim to assess the feasibility and reliability of ultrasound-based fetal lung maturity assessment.

2. Methods

This study was carried out on a cohort of 100 pregnant women who underwent delivery at Benha University Hospitals over a period of six months, from February 26, 2022, to August 25, 2022. The inclusion criteria for this study were pregnant women with a GA ranging from 32 to 37 weeks and a single pregnancy. Exclusion criteria included maternal diseases such as preeclampsia, diabetes mellitus, coagulation disorders, chronic renal disorders,

and psychiatric disorders. Other exclusion criteria involved premature rupture of membranes (PROM), chorioamnionitis, placental invasion anomalies, multiple pregnancies, and known chromosomal abnormalities or major congenital anomalies identified after delivery.

Patients provided informed consent prior to enrolment in the trial. Benha Faculty of Medicine Research Ethics Committee permission was received.

The study was conducted at Benha University Hospitals, where all the enrolled subjects underwent various assessments and evaluations. A detailed history was taken from each participant, including information on parity and previous cesarean sections or abdominal surgeries. Clinical examinations were performed, encompassing general assessments such as vital signs (pulse, blood pressure, capillary filling time, respiratory rate, and temperature) before and after the operation, as well as systemic examinations covering cardiovascular, respiratory, gastrointestinal, and neurological assessments.

Investigations were conducted, including routine laboratory investigations such as complete blood count, prothrombin time (Pt), partial thromboplastin time (Ptt), international normalized ratio (INR), random blood sugar, kidney function tests, liver function tests, and urine analysis. Sonographic assessments were also performed, focusing on specific parameters. These parameters included the presence or absence of the tibia epiphysis, main pulmonary artery diameter, thalamus echogenicity, trans cerebellar diameter, and placental thickness.

In this research, the outcome measures of interest were recorded at delivery. The delay between the ultrasound examination and birth was recorded, as well as the admission to the NICU for RDS.

Statistical analysis:

The obtained data was processed and displayed in tables and graphs (SPSS). The quantitative data were represented as mean standard deviation and range. Variables of qualitative nature, such as frequency and %. The significance threshold was p0.05.

3. Results

This study was a cross-sectional study which was done in Benha University Hospital on 100 pregnant women undergoing delivery period of six months (from February 2022 to August 2022).

The mean maternal age was 29.6 years and 69% of mothers were multigravida. At delivery, mean GA was 36.21 ± 1.31 week. Mode of Delivery was elective caesarean section in 55% (55) pregnancies while 45% (45) was vaginal delivery. **Table 1**

Table (1) Demographic Data, Parity, gestational age and Mode of Delivery in all studied group

N = 100			
Maternal Age	Mean		29.6
	SD		4.52
	20-30		69 (69%)
	31-40		31 (31%)
parity	Mean		3.15
	SD		1.30
	Primigravida		31 (31%)
	Multigravida		69 (69%)
gestational age	Mean		36.21
	SD		1.31
	35-36 week		89 (89%)
	≥36 week		11 (11%)
Mode of Delivery	Normal vaginal delivery	45	45%
	Caesarean section	55	55%

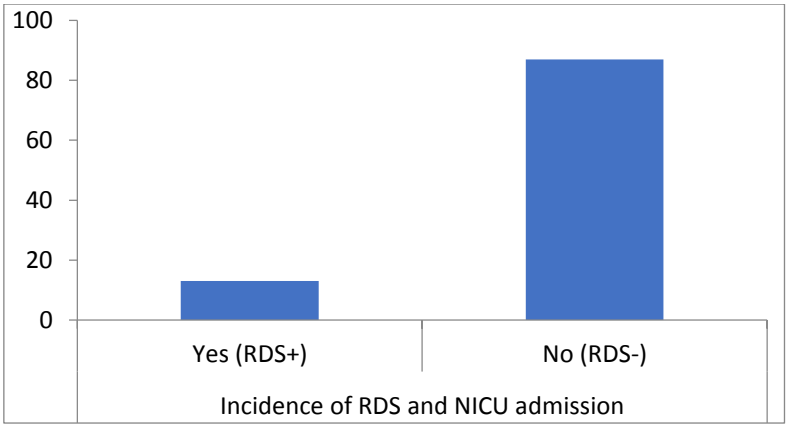

Fig. (1) Incidence of RDS and NICU admission in all studied cases

According to the occurrence of RDS, we categorized our study subjects into two groups: Group RDS+: n = 13; group RDS-: n = 87. Regarding (Maternal age, Parity, Type of delivery), there was no statistically significant difference between the two groups, but there was a statistically significant difference between the two groups regarding (GA at Birth and NBW). **Table 2**

Table (2) comparison between both groups according to basic parameters

	RDS- N=87	**RDS + N=13**	**P-value**
Maternal age	29.37±6.55	30.60±5.46	0.521
Parity			
Primigravida	25(25.0%)	6(6%)	0.205
Multigravida	62(62.0%)	7(7%)	
Type of delivery			
VD	39(39%)	6(6%)	0.862
CS	47(47%)	8(8%)	
Neonatal data			
Gestational age at Birth	39.8±1.4	38.2±1.1	0.0002
NBW (gram)	2641.27±693.81	1973.65±664.50	0.0012

According to ultrasound parameters there was no significant differences between the studied groups using Mann-Whitney test in main pulmonary artery diameter (MPA), trans cerebellar diameter and placental thickness. Significant differences were noticed in proximal tibial epiphysis and thalamic echogenicity ($p < 0.001$) using chi-square test. Positive PTE was noticed in 91.95% of non RDS group and 7.69 % in the RDS group. Thalamic echogenicity was present in 88.5% of the non RDS group while 15.38% in the RDS group. **Table 3**

Table (3) Ultrasound parameters in both groups

Ultrasound parameters	RDS- N=87	RDS+ N=13	Test	p
MPA (mm)				
M±SD	7.89±1.15	8.39±0.85	1.558	0.119
Range	6-9.97	6.91-9.73		
TCD (mm)				
M±SD	50.96±1.71	50.98±1.79	0.102	0.918
Range	48.04-53.91	48.14-53.38		
PT (mm)				
M±SD	39.65±3.05	38.83±3.38	0.881	0.378
Range	34.05-44.93	34.26-43.65		
PTE, n (%)				
Positive	80(91.95%)	1(7.69%)	3.841	<0.001*
Negative	7(8.04%)	12(92.3%)		
Thalamic echogenicity, n(%)				
Present	77(88.5%)	2(15.38%)	3.624	<0.001*

Absent	10(11.49%)	11(84.61%)

4. Cases

Case 1:

We discuss the case of a 35-year-old primigravida who gave birth vaginally without problems. The GA was 36 weeks and 4 days at the time of examination, and 37 weeks and 5 days at the time of delivery. The EFW was determined to weigh 2524 grams. During the ultrasound assessment, several parameters were evaluated. The tibia epiphysis was observed and found to be present. However, there was no echogenicity detected in the thalamus. The trans cerebellar diameter was measured at 4.6 mm, indicating a normal value. The main pulmonary artery diameter was measured at 49 mm, which falls within the expected range. Additionally, the placental thickness was measured at 39 mm. No RDS was reported in this case, and there was no need for admission to the NICU. These findings suggest that the fetal lung maturity was adequate, and the baby did not experience any respiratory complications.

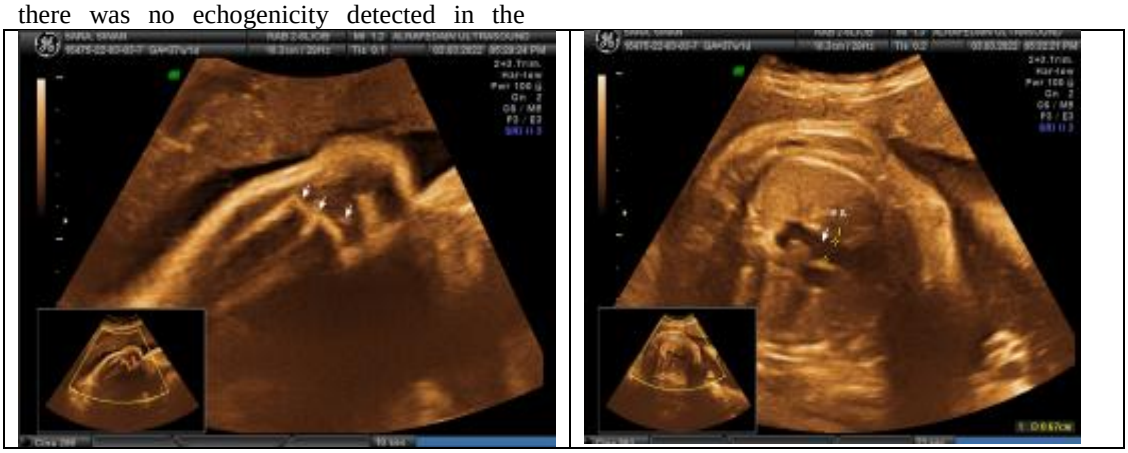

Fig. (2) Case 1

Case 2:

A case of a 35-year-old primigravida woman who underwent a CS delivery. The GA at the time of examination was 35 weeks and 5 days, and the GA at the time of delivery was also 35 weeks and 5 days. The EFW was measured at 2570 grams. During the ultrasound assessment, several parameters were evaluated. The tibia epiphysis was not visualized in this case. Additionally, there was no echogenicity observed in the thalamus. The trans cerebellar diameter was measured at 48 mm, indicating a normal value. However, the main pulmonary artery diameter was measured at 4.4 mm, which suggests a smaller than expected size. The placental thickness was measured at 37 mm. The new-born in this case experienced RDS and required admission to the NCU. This indicates an immature lung function and the need for medical intervention to support breathing. The CS was performed, likely due to the presence of RDS and other associated factors.

Fig. (2) Case 2

5. Discussion

In the current study, the mean maternal age was 29.6 years and 69% of mothers were multigravida. At delivery, the mean GA was 36.21 ± 1.31 week. Mode of Delivery was elective cesarean section in 55% (55) pregnancies while 45% (45) was vaginal delivery.

In a prospective cohort research, Essam et al. (2022) evaluated the usefulness of ultrasonographic measurement of amniotic fluid in predicting fetal lung maturity and its

impact on fetal outcome. Their outcomes are similar to ours. Three hundred pregnant women participated in their research. Participants were divided into RDS and non-RDS categories. They discovered that the average age of moms was 30,58 years and that cesarean section was the most prevalent birth mode [8].

Kandil et al. performed a prospective cohort study to reduce the incidence of neonatal respiratory distress by measuring fetal lung maturity using ultrasonography and Doppler rather than amniocentesis, which is consistent with our findings. 200 females were examined in all. Using a combination of ultrasound and Doppler measures, they identified the most accurate and appropriate method for evaluating the maturity of the fetal lungs. It was discovered that the average age of mothers is 27.89 4.37 years (range: 20–37). Mean GA was 35.45 weeks ± 1.72 (range 30–37) [9].

Parity did not differ significantly between the RDS and non-RDS groups, according to Essam et al. (P = 0.577), while maternal age was significantly lower in the RDS group than in the non-RDS group (P = 0.015). They also discovered a statistically significant difference between the RDS group and the non-RDS group in terms of birth weight (P value 0.05) [8].

Kandil et al. (2021) found, with a P value greater than 0.05, that there was no statistical correlation between RDS status and maternal age, parity, and number of births. The average age of RDS moms was 27.84, whereas that of non-RDS mothers was 28.01. The average GA of moms carrying newborns with respiratory distress syndrome was 2.42 weeks, compared to 2.12 weeks for mothers carrying infants with well-formed lungs. The average number of pregnancies for moms of newborns with RDS was 1.42, whereas it was 1.37 for mothers of fetuses with fully formed lungs [9].

Peacock et al. found in a prior research that male preterm newborns are more likely to have RDS than female preterm infants of the same GA, necessitating more urgent respiratory and circulatory care. In addition, males are more susceptible to infant mortality and respiratory illnesses [10]. This considerable risk was explained as a consequence of the fact that estrogen controls the development of surfactant proteins and enhances specific growth factors throughout the fetal period [11].

In our study, there was a statistically significant difference in the ultrasound parameters of the two groups (Thalamic echogenicity, Proximal tibia Epiphysis; P-value 0.05). There was no statistically significant difference in the diameter of the main pulmonary artery (MPA), the thickness of the placenta, or the transcerebellum diameter (TCD) between the two groups. In terms of thalamic echogenicity and the existence of proximal tibia epiphysis, however, there was a statistically significant difference between the two groups (P-value 0.05).

Our study showed that there were no significant differences between the studied groups using Mann-Whitney test in main pulmonary artery diameter (MPA), trans cerebellar diameter and placental thickness. we can add to these results that neonate RDS will decrased if we see the two significant ultrasound parameters (proximal tibia epiphysis and thalamic echogenicity) in addition to placental thickness more than 35 mm and transcerebellum diametr more than 45 mm.

In the current work, significant differences were noticed in proximal tibial epiphysis and thalamic echogenicity (p <0.001) using chi-square test. Positive PTE was noticed in 91.95% of non RDS group and 7.69 % in the RDS group. Thalamic echogenicity was present in 88.5% of the non RDS group while 15.38% in the RDS group.

The specificity of the existence of echogenic thalamus as an indicator of fetal lung maturity was 77.2 percent, which was lower than the specificity of the presence of PTE (90.4 percent). 77.3 percent diagnostic accuracy was also lower than PTE (90.8 percent). 78.9 percent sensitivity was lower than the PTE (99.5 percent). Negative predictive value was 97.7 percent for thalamic echogenicity and 99.5 percent for PTE.

According to our findings, Thalamic echogenicity, Proximal tibia Epiphysis, was considerably greater in the non RDS group than in the RDS group (P-value 0.05).

Concerning a comparison of the Doppler waveform levels of fetuses with and without RDS. The Doppler values between the two groups were statistically significant (P = 0.001), according to Kandil et al. A mean UA RI value larger than 0.69 was related with lung maturation delay and RDS in newborns. In RDS, the UA PI values were significantly higher (0.92–1.32) than in non-RDS (0.86–1.12). Similarly, MCA RI values are larger in RDS (0.77–0.88) than they are in non-RDS (0.74–0.79). The MCA PI values were lower in RDS (0.89–1.56) due to the brain sparing effect than in non-RDS (1.21–1.68). The UtA RI values for RDS and non-RDS fetuses were 0.43–0.66 and 0.42–0.55, respectively. Between the two groups of fetuses, the MPA RI values ranged from 0.74 to 0.88 in RDS and

from 0.71 to 0.75 in fetuses with developed lungs [9].

FLM was assessed by counting lamellar bodies (LBs) in amniotic fluid using amniocentesis in a study by Piazze et al. in which fetal lung maturity (FLM) indices were correlated with Doppler velocimetry results. They discovered a relationship between MCA PI and LBs. MCA PI levels tended to be lower in newborns with RDS than in those without RDS (1.36 0.5 vs. 1.69 0.4, NS). A value of mean Ut RI > 0.64 was also shown to coincide with a delayed biophysical FLM exhibited as a decrease in LBs, with a sensitivity of 90.9 percent and a specificity of 90.3 percent [12].

Similar to our results, Abdou et al. (2020) .'s meta-analysis revealed that the mean epiphyseal ossification centers were considerably lower in neonates with respiratory distress syndrome [13].

In the research conducted by Khalil et al., 2019 nine (22%) of forty eligible pregnancies had new-born RDS. AT/ET was substantially lower (mean 0.27) in the RDS-positive group than in the RDS-negative group (mean 0.34). (P 0.001). Between PI and RI, there was no statistically significant difference. Using a threshold of 0.3 for At/Et, the existence of RDS was predicted (sensitivity: 77.78 percent , specificity: 83.87 percent) [14].

Elkhalik and his colleague found that 46 (23%) of the fetuses had RDS (+ve) whereas 154 (77%) did not (-ve). At/Et and PSV correlated positively with RDS, but PI and RI correlated negatively. The S/D ratio did not significantly alter. The At/Et connection was the most important. AT/ET was considerably lower in the RDS-positive group, and the onset of RDS in infants could be predicted with good sensitivity, specificity, and accuracy using a 0.32 cutoff value (98.0 percent , 92.0 percent , and 95.0 percent , respectively) [15].

According to the results of Nardeen et al., 2022, the main pulmonary artery (At/Et ratio), fetal lung to liver echogenicity, free particles in amniotic fluid, and placental grading were significantly associated with lung maturity. It was determined that the ratio of At/Et in the major pulmonary artery (cutoff >!0.30) was a reliable predictor of newborn RDS (92.5 percent sensitivity, 87.2 percent specificity) [16]. Additionally, our investigation demonstrated that GA, free particles of amniotic fluid, fetal lung to liver echogenicity, and placental grading were substantially connected with the development of newborn respiratory distress syndrome, with GA being lower in those who acquired RDS.

Assessing prenatal lung maturation may significantly improve delivery time in high-risk pregnancies in order to prevent neonatal morbidity and mortality associated with undeveloped lungs. Controlling therapeutic choices on birth planning and prenatal steroid treatment is one of the benefits of noninvasive approaches. The practitioner must weigh the advantages of preterm delivery for both mother and child against the hazards for the baby. Theoretically, a high-risk result might also be utilized as an indication for prenatal steroids in order to enhance fetal lung maturation and assess the adverse consequences of the administered antenatal steroids [3].

6. Conclusion

Our study reveals that measuring fetal lung maturity by ultrasonography is a beneficial noninvasive tool. Using certain auditory parameters, the onset of RDS in newborns may be correctly predicted. The ultrasonic detection of the proximal tibial ossification sites and thalamic echogenicity had the best predictive accuracy for fetal lung maturity.

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