Different Grey scale and Color Doppler Ultrasonographic Fetal Parameters in Prediction of Fetal Lung Maturity and its correlation with Neonatal Outcome

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Abstract

Background: Several methods were presented to estimate fetal lung maturity (FLM), including the lecithin/sphingomyelin ratio measurement, the phosphatidylglycerol existence or deficiency, and the lamellar body count in amniotic fluid (AF). However, all of these methods necessitate amniocentesis, which is an invasive process. Non-invasive ultrasound (US) methods have been studied to predict FLM.

Objectives: This study objective was to assess the various grey scale and color doppler US parameters accuracy and to identify the most sensitive and specific parameter as a non-invasive approach for predicting FLM.

Patients and methods: This prospective study was conducted on 100 pregnant women, aged 18 to 37 years old, who were experiencing a normal singleton pregnancy with a viable fetus and routine fetal surveillance between 34 and 40 weeks of gestation. All patients were investigated to: History taking, sonographic assessment, conventional 2D US, Epiphyseal ossification centers (EOC), placental grading, AF index and free-floating particles, thalamus echogenicity, fetal lung echogenicity, and doppler examination.

Results: Ultrasound parameters we found that EOC of the tibia has the highest accuracy 94% followed by EOC of the femur with accuracy 92 % then free-floating particles presence in AF with accuracy 83% and thalamic echogenicity with accuracy 80% and the least accuracy was for humerous OC 54% and lung echogenicity 45%. In concerning to doppler indices we noticed that Main pulmonary artery acceleration time / ejection time (MPA AT/ET) ratio cutoff value of 0. 295 showed the highest accuracy 94. 9% followed by Middle cerebral artery resistive index (MCA RI), Umbilical artery pulsatility index (UA PI), Umbilical artery resistive index (UA RI) and Main pulmonary artery resistive index (MPA RI) respectively.

Conclusions: Utilizing US and doppler to assess FLM is helpful. However, no single parameter alone could demonstrate definite sign of fetal lung maturity.

Keywords: Ultrasonographic; Color Doppler; Fetal Parameters; Fetal Lung Maturity; Neonatal Outcome.

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Introduction

Neonatal respiratory failure and mortality are frequently precipitated by respiratory distress syndrome (RDS). It was previously assumed that RDS was primarily observed in premature infants; however, the RDS increased awareness has resulted in its neonates more common diagnosis.**(Moety et al.,2015)**

There are a variety of methods available to estimate fetal lung maturity (FLM), such as phosphatidylglycerol (PG) presence or absence and the lamellar body count in amniotic fluid (AF), lecithin/sphingomyelin measurement (L/S) ratio which requires amniocentesis. **(Abd EL-Fattah et al., 2018)**

Nevertheless, amniocentesis is an invasive procedure that carries a small but significant risk to the pregnancy. These risks include preterm premature rupture of membranes, preterm labor, placental abruption, feto-maternal haemorrhage, fetal injury, and, in rare cases, fetal or maternal mortality. **(Abdelhamid et al., 2020)**

Non-invasive ultrasound (US) techniques that can differentiate between immature and mature fetal lungs would be valuable in clinical settings. Several US methods have been investigated, with various degrees of success. **(Ghorayeb et al.,2017)**

The accuracy of US dating is diminished after 34 weeks of gestation, as evidenced by the standard deviation (SD) of approximately ± two weeks, which was evident in the primitive days of utilizing it for gestational age (GA) control. This fact has motivated numerous obstetrical researchers to employ alternative biometric variables as an alternative to enhance US dating in the late 3th trimester and to determine fetal maturity through the evaluation of various parameters, such as placenta grades, biparietal diameter (BPD), thalamic echogenicity , epiphyseal ossification center (EOC), and AF vernix. **(Abdullah et al.,2018)**

Utilizing ultrasound exclusively when the fetal skeletal bones are calcified enhances their visibility. Primary ossification centers are formed during the early stages of pregnancy, while secondary ossification centers are formed during later pregnancies and early neonatal life. Secondary ossification centers were observed exclusively in the epiphyseal cartilage of the, distal femur, proximal tibia, and, on occasion, the proximal humerus, through out the prenatal period. The high degree of certainty that lower and upper limb EOC ultrasonographic detection provides for the GAs expectation throughout pregnancy the 3th trimester. **(Alkashty et al.,2021)**

The numerous variables related to fetal hemodynamic assessment is facilitated by the Doppler effect. These measurements have assisted the numerous vessels characterization in the maternal-fetal circulation, thereby enabling the both the mother and the fetus medical status and wellness monitoring. Various studies have provided reference values for variables related to gestational age, including, ejection time (ET), pulsatility index (PI), acceleration time (AT), systolic and diastolic velocities, and deceleration time, some of these have been employed for practical uses, such as predicting FLM methods. **(Sosa-Olavarria et al.,2019)**

The purpose of this study was to assess the various grey scale and color doppler US parameters precision and to identify the most sensitive and specific parameter as a non-invasive method for predicting FLM.

Patients and methods

The subject of this prospective study was 100 pregnant women, aged 18 to 37 years old (Mean± SD: 25. 61 ± 5. 19), who were experiencing a normal singleton pregnancy with a viable fetus and regular fetal surveillance between 34 and 40 weeks of gestation (Mean± SD: 36.76 ± 1. 27).

Informed written consent was granted by the patient or their family. The investigation was conducted from December 2021 to November 2022 after Tanta University Hospitals of the Ethical Committee approval.

Exclusion criteria: macrosomic fetuses, intrauterine growth restriction, fetal malformations, or multiple gestations, high-risk pregnancy (e.g., hypertensive and diabetic mothers), antepartum hemorrhage or the meconium-stained fluid presence, and difficult labour that may end in respiratory distress.

All cases were subjected to: History taking [last menstrual period, chronic disease history, any complications during pregnancy and parity, women with any pregnancy-related diseases, due to fetal condition], sonographic assessment [Utilizing US equipment is able to achieve -resolution gray-scale, pulsed-wave and color Doppler modes, (Edan U2) equipped with a 3–5-MHZ probe transducer], traditional 2D US, EOC, placental grading, AF index and free-floating particles, thalamus echogenicity, fetal lung echogenicity, and doppler examination [MPA doppler, Fetal umbilical artery and middle cerebral artery MCA].

Conventional 2D US: The protocol involved collecting data of GA, FL, BP, AC, expected fetal weight (EFW), EOC (tibia, humerus, and femur), AFI, thalamus echogenicity, free floating particles in the AF, placental grading, and fetal lung-to-liver echogenicity.

The epiphysis was measured in an axial plane along the epiphysis mediolateral surface from the outer-to-outer margins. The transducer was guided along the largest axis of the femoral diaphysis to ensure precise identification, thereby averting oblique sectioning. The maximum diameter was recorded after the femur distal EOC was detected, and the measurement was taken in the axial plane. This process was repeated three times. **(Awad et al.,2020)**

The proximal tibial and humeral epiphysis measurements were obtained in a similar way. **(Awad et al.,2020)**

Placental grading

The transducer was held perpendicular to the chorionic plate when scanning to grade the placenta, particularly when studying a laterally positioned placenta. Any angulation would have altered the appearance and impacted the interpretation. **(Bowman and Kennedy,2014)**

Regarding to Grannum classification Grading was completed as follow: The chorionic plate is uniformly smooth in grade I, the basal plate is well-defined by small linear highly reflective areas, and the indentations of the chorionic plate do not extend to it in grade II. In grade III, the basal plate is reached by the chorionic plate indentations, which contain highly reflective areas. In the basal layer, echogenic densities persist and increase in size and density. **(Moran et al.,2011)**

Amniotic fluid index and free-floating particles

Utilizing the four-quadrant techniques, the deepest, unobstructed, vertical length of each fluid compartment in each quadrant was measured in centimeters and subsequently gathered to estimate AFI. **(Ali ,2009)**

Four quadrants were utilized to observe the linear densities (Vernix) in the AF, which were measured in millimeters. The number, size, and distribution of the free-floating particles in four quadrants were utilized to determine the AF turbidity. Upon the gentle shaking of the mothers' abdomen by a probe, they were realized with their full mobility. **(Buyuk et al.,2021)**

Thalamus echogenicity

The thalamus' echogenicity is documented as either echogenic or echolucent in the transthalamic plane throughout an ultrasound examination, in contrast to the brain tissue located between the thalamus and the parietal bone, which remains echogenic throughout pregnancy. The thalamus is regarded as echogenic if its echogenicity is comparable to that of brain tissue, and echolucent if it displays no echoes within the thalamus. **(Rasheed et al.,2012)**

Fetal lung echogenicity

The embryonic thorax and upper abdomen are imaged using ultrasound imaging to obtain longitudinal and transverse sections. The thoracic and upper abdominal sections are used to identify the fetal lung and liver, respectively. It was taken into account to prevent the presence of any discernible vascular structures in the liver. The 'venetian blind' effect of the ribs is minimalized whenever feasible, and the lung is imaged through the heart or the liver is imaged through a fluid-filled fetal stomach. The reason for this is that the organ parenchyma would inevitably appear falsely echogenic as a result of acoustic enhancement posterior to these cystic structures. **(Tekesin et al.,2004).**

Compared to the foetal liver, the fetal lung echogenicity was categorized as hyper-echoic hypo-echoic, or iso-echoic. **(kandil et al.,2021)**

Doppler examination

Doppler measurements were obtained from a free-floating segment of umbilical cord in close proximity to the fetal abdominal insertion site. Resistance measurements conducted in close proximity to the placental insertion exhibit a lower resistance than those conducted in close proximity to the abdominal insertion. From the umbilical artery, the flow velocity waveforms were recorded as RI and PI. **(Zalud and Broady, 2016)**

As the major anterolateral branch of the circle of Willis, the MCA vessels can be identified with color or power Doppler US overlying the anterior wing of the sphenoid bone near the base of the cranium. The pulsed Doppler sample gate is subsequently affixed to the middle section of this vessel. The angle of insonation (AoI) should be less than 15°; an angle that is almost 0° can be attained by repositioning the transducer on the maternal abdomen. In the absence of fetal respiratory movement, waveforms of the umbilical and middle cerebral arteries were obtained. **(Liu and Li ,2021)**

The fetal heart was initially examined in a systematic manner. The transducer was subsequently rotated from the four-chamber view to the short-axis view of the fetal heart, thereby demonstrating the bifurcation of the right and left branches of the pulmonary artery and the pulmonary valves. Hence, the fetal MPA was observed. The fetal MPA's pulsed Doppler sample gate was situated in the center, between the pulmonary artery and valves bifurcation, and was placed away from the arterial walls. The AoI (the angle between the sound beam and the direction of blood flow) was maintained at <20, and the sample gate was adjusted to 3 mm. a specific "spike and dome" pattern was generated by the Doppler velocity waveform in the fetal MPA. The germane Doppler velocity variables were measured three times utilizing a manual trace after the optimal fetal MPA waveform was obtained, and the average has been determined. **(Azpurua et al.,2010)**

Neonatal outcome

Before delivery, the time interval between the US assessment and delivery was documented, as well as the period of admission to the neonatal intensive care unit (NICU) for RDS.

Statistical analysis

The statistical analysis was performed using SPSS v28 (IBM©, Armonk, NY, USA). The data distribution's normality was assessed using the Shapiro-Wilks test and histograms. The unpaired student t-test was employed to analyze the quantitative parametric data, which were then presented as the mean and standard deviation. Mann Whitney-test was employed to analyze quantitative non-parametric data, which were presented as the median and interquartile range (IQR). When applicable, qualitative variables were examined utilizing the Chi-square test or Fisher's exact test and stated as percentage (%) and frequency. The

Receiver Operating Characteristic curve (ROC-curve) analysis was utilized to evaluate the overall diagnostic efficacy of each test. The overall test performance is assessed by the area under the curve (AUC), with an AUC > 50% indicating adequate performance and an area of approximately 100% indicating the greatest performance for the test. Diagnostic Performance Evaluation: Incidence of true positive (TP) results in patient groups is quantified by diagnostic sensitivity. TP): the number of diseased patients that the test accurately classified, and false negative (FN): diagnostic specificity is a metric that quantifies the true negative results frequency in a healthy group, while the number of diseased cases precisely misclassified by the test is measured by TN (true negative) and FP (false positive). A two-tailed P value that was less than 0.05 was considered statistically significant.

Results

(Table.1) shows the participants' age ranged from 18 to 37 years, with a mean of 25. 61 ± 5. 19 years. The gravidity was with a median of 3, and the parity was with a median of 2. The GA mean at delivery was 36. 76 ± 1. 27 weeks. The BPD was with a mean of 90. 91 ± 2. 94 mm, the AC was with a mean of 326. 79 ± 15. 5 mm, the FL was with a mean of 71. 7 ± 3. 3 mm, and the AFI was with a mean of 10. 17 ± 2. 28 cm. the US assessment revealed that the ossification center was absent from femur, tibia, and humorous in 6 (6%), 10 (10%), and 54 (54%) fetuses, respectively. Fetal brain assessment showed echogenic thalamus in 72 (72%) fetuses and echolucent thalamus in 28 (28%) fetuses. The fetal lung was hyperechoic to liver in 45 (45%) fetuses, hypoechoic to liver in 28 (28%) of fetuses, and isoechoic in 26 (26%) fetuses. Regarding the placental grade, grade 1 in 8 (8%) fetuses, grade 2 in 40 (40%), and grade 3 in 52 (52%) fetuses. There were floating particles in 75 fetuses (75%). Regarding the doppler data, the MPA RI was with a mean of 0. 76 ± 0. 03, the MPA (AT/ET) ratio was with a mean of 0. 32 ± 0. 02, the UA RI was with a mean of 0. 64 ± 0. 04, the UA PI was with a mean of 1. 03 ± 0. 13, the MCA RI had a mean of 0. 76 ± 0. 04, the MCA PI was with a mean of 1. 4±0. 12. After delivery, acute respiratory distress syndrome (ARDS) was encountered in 12 (12%) fetuses.

Table 1. Participants' demographic, clinical data, obstetric measurements, ultrasound data, doppler data, and fetal outcome (n = 100)

Variables		Patients (n = 100)
Age (years)	Mean± SD	25. 61 ± 5. 19
	Median (IQR)	24 (21-30)
Gravidity	Mean± SD	2. 8 ± 1. 54
	Median (IQR)	3 (2-4)
Parity	Mean± SD	2. 18 ± 0. 56
	Median (IQR)	2 (2-3)
GA (weeks)	Mean± SD	36. 76 ± 1. 27
	Median (IQR)	36. 57 (35. 86-37. 86)
Obstetric measurements		
BPD (mm)	Mean± SD	90. 91 ± 2. 94
	Median (IQR)	91 (88-93)
AC (mm)	Mean± SD	326. 79 ± 15. 5
	Median (IQR)	325 (314-341)
FL (mm)	Mean± SD	71. 7 ± 3. 3
	Median (IQR)	71 (69. 5-75)
AFI (cm)	Mean± SD	10. 17 ± 2. 28

	Median (IQR)	10 (8-12)
Ultrasound data		
Femur OC	**Absent**	6 (6. 0%)
	Present	94 (94. 0%)
Tibia OC	**Absent**	10 (10. 0%)
	Present	90 (90. 0%)
Humerous OC	**Absent**	54 (54. 0%)
	Present	46 (46. 0%)
Thalamic echogenicity	**Echogenic**	72 (72. 0%)
	Echolucent	28 (28. 0%)
Lung echogenicity compared to liver	**Hyperechoic**	45 (45. 0%)
	Hypoechoic	29 (29. 0%)
	Isoechoic	26 (26. 0%)
Placental grade	**1. 00**	8 (8. 0%)
	2. 00	40 (40. 0%)
	3. 00	52 (52. 0%)
Floating particles	**Absent**	25 (25. 0%)
	Present	75 (75. 0%)
Doppler data		
MPA RI	**Mean± SD**	0. 76 ± 0. 03
	Median (IQR)	0. 76 (0. 73-0. 78)
MPA AT/ET	**Mean± SD**	0. 32 ± 0. 02
	Median (IQR)	0. 32 (0. 3-0. 33)
UA RI	**Mean± SD**	0. 64 ± 0. 04
	Median (IQR)	0. 64 (0. 61-0. 67)
UA PI	**Mean± SD**	1. 03 ± 0. 13
	Median (IQR)	1 (0. 93-1. 12)
MCA RI	**Mean± SD**	0. 76 ± 0. 04
	Median (IQR)	0. 75 (0. 73-0. 79)
MCA PI	**Mean± SD**	1. 4 ± 0. 12
	Median (IQR)	1. 4 (1. 31-1. 47)
Fetal outcome		
ARDS	**Absent**	88 (88. 0%)
	Present	12 (12. 0%)

Data are presented as mean ± SD, median (IQR), or frequency (%). IQR: interquartile range, GA: gestational age, AC: Abdominal circumference, BPD: biparietal diameter, FL: Femur length, AFI: Amniotic fluid index, MPA: Main pulmonary artery, MCA: Middle cerebral artery, ARDS: Acute respiratory distress syndrome.

There was statistically significant lower GA, smaller BPD, AC, and FL, AFI, and MPA AT/ET ratio in participants with distressed fetuses than those with non-distressed fetuses (P < 0. 05). There was statistically significant higher percentage of absent ossification centers in femur, tibia, and humerous, echolucent thalamus, and placental grade 1, absent floating particles, in the context of the Doppler indices, there were statistically higher mean values of MPA RI, UA RI, and UA PI, and MCA RI, and lower mean value of MPA AT/ET ratio in participants with RDS fetuses than those with non-RDS fetuses (P <0. 05), (**Table. 2).**

Table 2. Comparison between the study participants' demographic, obstetric data, ultrasound data, and doppler data according to the occurrence of fetal ARDS

Variables		Participants with fetal ARDS (n= 12)	Participants without fetal ARDS (n= 88)	p-value
Age (years)		27. 67 ± 5. 87	25. 33 ± 5. 06	0. 144
Gravidity		3 (1-4)	3 (2-3)	0. 795
Parity	Primi	0 (0)	8 (9. 1)	0. 276
	Multi	12 (100)	80 (90. 9)	
GA		36. 02 ± 0. 72	36. 86 ± 1. 3	0. 003*
BPD (mm)		88. 67 ± 2. 06	91. 22 ± 2. 92	0. 004*
AC (mm)		319. 17 ± 6. 91	327. 83 ± 16. 07	0. 002*
FL (mm)		70. 5 ± 1. 98	71. 86 ± 3. 42	0. 028*
AFI (cm)		9. 47 ± 2. 51	12. 67 ± 3. 31	0. 007*
Ultrasound data				
Femur OC	Absent	4 (33. 3)	2 (2. 3)	<0. 001*
	Present	8 (66. 7)	86 (97. 7)	
Tibia OC	Absent	8 (66. 7)	2 (2. 3)	<0. 001*
	Present	4 (33. 3)	86 (97. 7)	
Humerous OC	Absent	10 (83. 3)	44 (50)	0. 03*
	Present	2 (16. 7)	44 (50)	
Thalamic echogenicity	Echogenic	2 (16. 7)	70 (79. 5)	<0. 001*
	Echolucent	10 (83. 3)	18 (20. 5)	
Lung echogenicity compared to liver	Hyperechoic	6 (50)	39 (44. 3)	0. 585
	Hypoechoic	2 (16. 7)	27 (30. 7)	
	Isoechoic	4 (33. 3)	22 (25)	
Placental grade	1. 00	8 (100)	0 (0)	<0. 001*
	2. 00	3 (7. 5)	37 (92. 5)	
	3. 00	1 (1. 9)	51 (98. 1)	
Floating particles	Absent	10 (83. 3)	15 (17)	<0. 001*
	Present	2 (16. 7)	73 (83)	
Doppler data				
MPA RI		0. 79 ± 0. 04	0. 75 ± 0. 03	0. 007*
MPA AT/ET		0. 27 ± 0. 01	0. 32 ± 0. 02	<0. 001*
UA RI		0. 69 ± 0. 04	0. 63 ± 0. 04	<0. 001*
UA PI		1. 17 ± 0. 1	1 ± 0. 09	<0. 001*
MCA RI		0. 82 ± 0. 04	0. 75 ± 0. 03	<0. 001*
MCA PI		1. 42 ± 0. 11	1. 39 ± 0. 12	0. 204

Data are presented as mean ± SD, median (IQR), or frequency (%). IQR: interquartile range, GA: gestational age, AC: Abdominal circumference, BPD: biparietal diameter, FL: Femur length, AFI: Amniotic fluid index, MPA: Main pulmonary artery, MCA: Middle cerebral artery. *: significant as P value < 0. 05.

ROC analysis to assess the validity Doppler indices in the prediction of cases that would develop RDS in fetuses is demonstrated in (**Table.3**). MPA RI, MPA AT/ET ratio, UA RI, UA PI, and MCA RI exhibited good to excellent diagnostic performance for prediction in RDS cases. (MPA RI) cutoff value of 0. 765 showed an (AUC) of 0. 721, sensitivity of 68. 7%, specificity of 59%, and a p value of 0. 003. MPA AT/ET ratio cutoff value of 0. 295 showed an AUC of 0. 994, sensitivity of 100%, specificity of 94. 2%, and a p value of <0. 001. Umbilical artery RI cutoff value of 0. 688 showed an AUC of 0. 830, sensitivity of 85. 3%, specificity of 69. 8%, and a p value of <0. 001. Umbilical artery PI cutoff value of 1. 145 showed an AUC of 0. 888, sensitivity of 83. 3%, specificity of 92. 2%, and a p value of <0. 001. MCA RI cutoff value of 0. 795 showed an AUC of 0. 936, sensitivity of 83. 7%, specificity of 94. 2%, and a p value of <0. 001. Evaluation of accuracy of doppler indices showed that MPA RI, MPA AT/ET ratio, UA RI, UA PI, and MCA RI exhibited good to excellent diagnostic performing for prediction in RDS cases. MPA AT/ET ratio showed the highest accuracy of 94. 9% followed by MCA RI with accuracy of 93. 2% and UA PI with accuracy of 90. 9% and the least accuracy was for UA RI with accuracy of 73% and MPA RI with accuracy of 62%.

Table 3. Validity and accuracy of Doppler indices in prediction of fetal lung maturity

Variables	AUC	P	95% C. I	Cut off	Sensitivity	Specificity	Accuracy
MPA RI	0. 721	0. 003*	0. 574 - 0. 867	0. 765	68. 7%	59%	62%
MPA AT/ET	0. 994	<0. 001*	0. 984 -1. 005	0. 295	100%	94. 2%	94. 9%
UA RI	0. 830	<0. 001*	0. 732 -0. 927	0. 6880	85. 3%	69. 8%	73%
UA PI	0. 888	<0. 001*	0. 761 -1. 015	1. 1450	83. 3%	92. 2%	90. 9%
MCA RI	0. 936	<0. 001*	0. 861 -1. 010	0. 7950	83. 7%	94. 2%	93.2%

AUC: Area Under a Curve, CI: Confidence Intervals, MPA: Main pulmonary artery, MCA: Middle cerebral artery, ARDS: Acute respiratory distress syndrome. *: Statistically significant at p ≤ 0. 05.

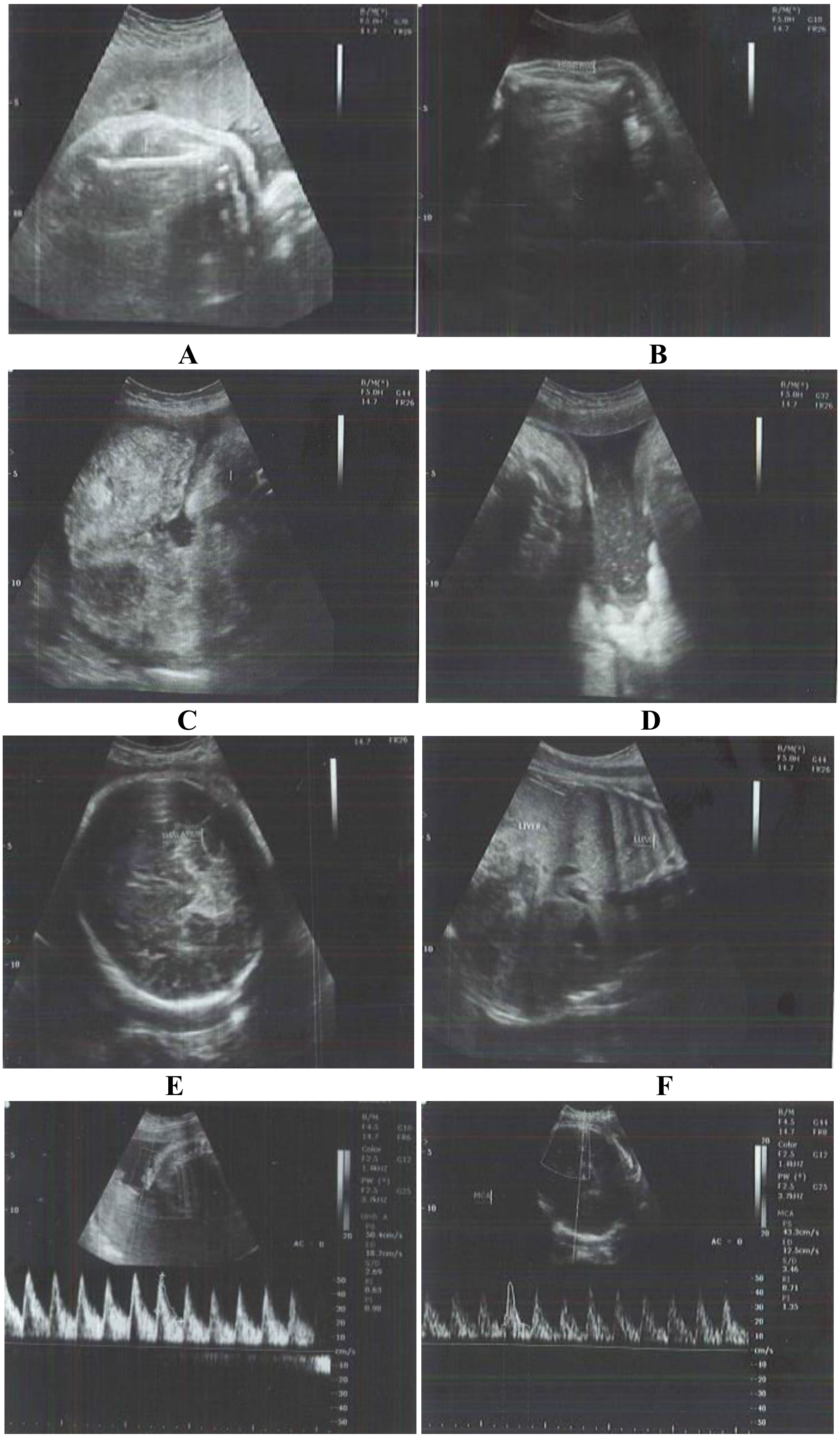
Calculating the accuracy of the US data in the diagnosis of fetal ARDS revealed that the highest accuracy was for the tibia OC (94%), femur OC (92%) with presence of femur OC ≥ 4mm predict FLM, floating particles (83%), and thalamic echogenicity (80%), and the least accuracy was for humerous OC (54%) and the lung echogencity compared to liver (45%), **(Table .4).**

Table 4. Accuracy of ultrasound parameters in prediction of fetal lung maturity

Variables	TP	FP	TN	FN	Accuracy
Femur OC	4	2	86	8	92%
Tibia OC	8	2	86	4	94%
Humerous OC	10	44	44	2	54%
Thalamic echogenicity	10	2	70	18	80%
Lung echogenicity compared to liver	6	6	39	49	45%
Placental grade	11	37	51	1	66%
Floating particles	10	15	73	2	83%

Data are presented as number. TP: true positive, FP: false positive, TN: true positive, FN: false positive.

Cases (Fig.1 &2).



A B

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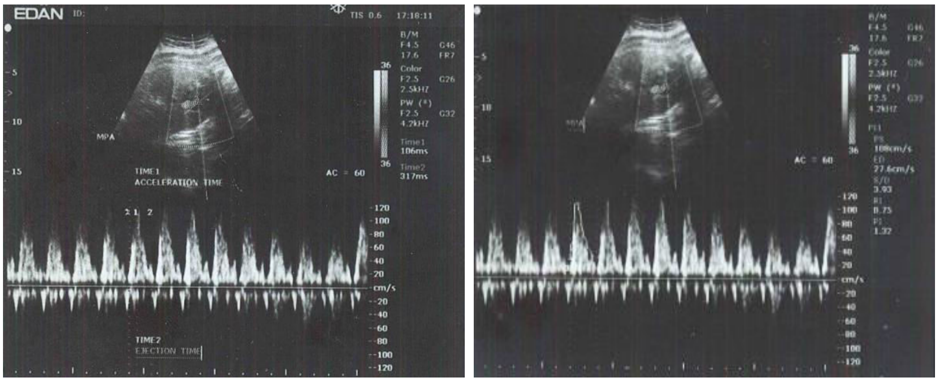

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Fig.1. A 30 years old pregnant female G3P2 admitted for standard prenatal ultrasound assessment, Average GA: 39 weeks, 3days. **Fetal biometry**: BPD: 97. 8 mm, AC: 354mm, FL: 76. 4mm, EFW: 3740 gm, AFI: 11. 5 cm. **Ultrasonic markers of lung maturity**: **(A)** EOC of the femur is present and measures 7mm, **(B)** EOC of humerus is present, **(C)** placental grading: grade III, **(D)** Free-floating particles existence in amniotic fluid, **(E)** thalamus is echogenic, **(F)**fetal lung is iso echoic in relation to liver echogenicity. **Doppler examination**: **(G)**UA RI 0. 63, UA PI 0. 98, **(H)** MCA RI 0. 71, MCA PI 1. 35, **(I)** MPA AT\ET Ratio: 0. 334, **(J)** MPA RI 0. 75. **Neonatal outcome**: Delivery within 24 hours of US assessment, **mode of delivery:** cesarean section (CS), **NICU admission**: NO, and clinical diagnosis: No RDS indicating FLM.

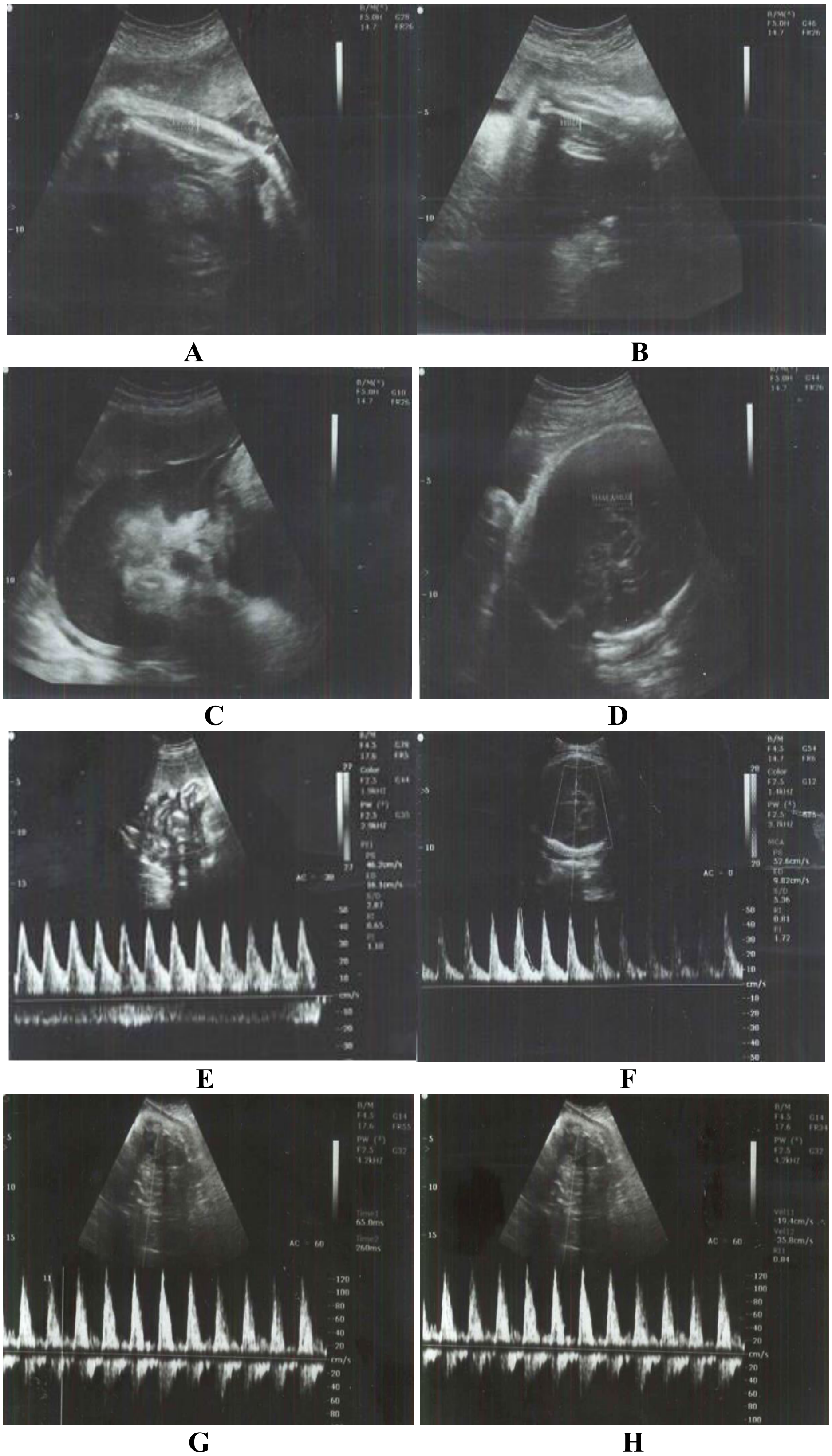

Fig. 2. 23 years old female G3P2 admitted for standard prenatal ultrasound assessment , Average GA: 34 weeks, 4 days. **Fetal biometry**: BPD: 87.9 mm, AC: 303 mm, FL: 66.1mm, EFW: 2430 gm, AFI: 10 cm, **Ultrasonic markers of lung maturity: (A)** EOC of the femur is absent, **(B)** EOC of the tibia is absent, **(C)** Placental grading: grade I, Amniotic fluid is clear and show no free-floating particles, **(D)**Thalamus is echolucent.
Doppler examination: **(E)** UA RI: 0.65, UA PI:1.10, **(F)** MCA RI:0.81, **(G)** MPA AT\ET

ratio:0.25, **(H)** MPA RI:0.84. **Neonatal outcome**: Delivery within 48 hours of **US** assessment. **Mode of delivery**: CS, the new born was admitted to NICU for 2weeks after birth diagnosed as RDS indicating fetal lung immaturity.

Discussion

It seems that RDS is a significant contributor to neonatal mortality and morbidity. **(Monica et al.,2017)** Therefore, the assessment of FLM is a critical component of the management of expectant women. **(Vafaei et al 2021)**

RDS was employed as an indicator of FLM status in the present investigation, which included 12 patients (12% of neonates had RDS). Comparable outcomes were demonstrated by **Abdulla et al. (2018)**. who noted 12%prevalence for RDS. Also, **Hibbard et al .(2010)** stated prevalence of 10. 5%. A diverse array of RDS incidences has been documented on a global scale., where **Ghafoor et al. (2013)** reported an even lower incidence of 3.7%.

The present study showed significantly lower GA in participants with distressed fetuses. This reflected on significantly smaller BPD, AC, and FL. This is in line with the previous reports(**Moety et al.,2015; Schenone et al.,2014; Khalil et al., 2019; EL-omda and Elboghdady 2022)** making GA and, consequently, prematurity a critical reason in the neonatal RDS development. **Wang et al. (2019)** concluded that as GA increases the RDS rate reduces. This can be attributed to the fact that premature neonates have either an insufficient or pulmonary surfactant lack production, which is responsible for the gas exchange by coating the healthy alveoli interior lining. **(Wang et al.,2019)**

AF volume continues to be a critical element of any obstetric ultrasonographic examination. The AFI was the most frequently employed method for quantifying AF. The AFI of participants with RDS neonates was considerably lower than that of those without RDS neonates in the present study. These findings are corroborated by (**Alkashty et al.,2023; Khalil et al.,2019 and Hassan et al.,2023).** In contrast to our outcomes, **Moety et al. (2015)** study determined that neonatal RDS was significantly correlated with polyhydramnios.

Statistically significant higher percentage of absent ossification center in the femur, tibia, and humerus of the participants in this study's US data. The research conducted by **Kandil et al. (2021)** is consistent with our findings emphasized the significance of the prenatal tibia epiphysis and the femur epiphysis as indicators of lung maturity. Such findings are in line with **Abdou et al. (2020)** who reported that the mean EOC were significantly reduced in neonates with RDS.

These findings suggested that by visualizing and measuring the epiphyseal ossification of the fetal knee and shoulder prior to labor, it may be possible to differentiate between fetuses with a mature lung amniocentesis profile. Nevertheless, several of critical variables should be taken into account. Though these centers presence is a lung maturity sign in the neonatal lung, their absence does not preclude lung maturity. Furthermore, it is imperative to utilize extreme caution when identifying these epiphyseal centers in order to prevent them from being confused with other cartilaginous structures. **(Kandil et al., 2021)**

The current study indicates that neonates with RDS have a significantly greater percentage of echolucent thalamus in terms of fetal thalamic echogenicity. Matching findings were reported by **Kandil et al. (2021)** who detected that with the age of the neonate the thalamic density increased in the daily practice and reported the accuracy of thalamic echogenicity in the prediction of RDS. **Abdullah et al. (2018)** reported similar findings with respect to the usage of thalamic echogenicity as a FLM US indicator.

Participants with RDS fetuses exhibited a significantly higher placental grade 1 in this study. Such finding is in harmony with **Das et al. (2016)** who reported that the RDS was discovered to be linked to grade 0 and grade I placenta.

The study also evaluated the AF floating particle's role, which demonstrated a significantly reduced occurrence in cases with RDS neonates. Several researchers have emphasized the significance of this discovery in lung maturity prediction, which is consistent with our findings (**Ram and Ram.,2010; Kandil et al.,2021** and **Mohamed et al.,2022).**

Close to figures found in the current study regarding the UA RI, **Kandil et al., (2021)** demonstrated a correlation between neonatal RDS and UA RI > 0.69 and **Scopesi et al. (1994)** concluded that increased UA RI values (>0.70) can be considered a cut-off value that can predict which fetuses are at low/high risk for respiratory disorders. Furthermore, Doppler velocimetry analysis can offer more dependable information regarding fetal conditions and can predict the appropriate timetable for delivery and admission to the unit care.

In the context of the Doppler indices, our investigation utilized parameters that were not significantly influenced by the angle of insonation, including MPA At/Et, PI, and RI. This work showed statistically significant higher mean values of MPA RI, UA RI, and UA PI, and MCA RI, and lower mean value of MPA AT/ET ratio in participants with RDS fetuses than those with non-RDS fetuses. These parameters showed good to excellent diagnostic performance for prediction in RDS cases.

In the current study we found that increase MCA RI in participants with RDS fetuses than those with non-RDS fetuses with cut off value 0. 795, our findings agree with **Elrashedy et al. (2022)** and **kandil et al . (2021)** who showed higher values of MCA RI in fetuses affected by neonatal RDS.

As for the MPA RI, **Kandil et al. (2021)** exhibited higher values in fetuses afflicted by neonatal RDS with a cut point of MPA RI > 0.78 that was correlated with RDS. **Laban et al., (2019)** reported a cut-off value of pulmonary artery (PA) RI > 0. 77 for prediction of neonatal RDS and this agrees to our results.

Concerning the MPA AT/ ET, our findings agree with **Khalil et al. (2019)** who reported a cut of point of 0. 3 to predict the development of neonatal RDS with a high sensitivity, specificity, negative predictive value and accuracy (77. 78%,83. 87%, 92. 9% and 82. 5 % respectively). Our results are also matching with **Schenone et al. (2014)** have reported that MPA At/Et ratio was positively correlated, which means that an increased At/Et ratio is associated with a more mature lung and a less risk of developing RDS, which supports our findings.

However, our results contradicted **Mohamed et al. (2022)** who discovered that the MPA At/Et ratio was inversely correlated with FLM. The discordance may be attributed to a difference in the study population or the specifics of the US measurements and apparatus.

Doppler is readily accessible on many ultrasound machines , and the results can be obtained instantly. However, it is a technique that is quite challenging, largely reliant on the operator, and necessitates a significant amount of experience. Consequently, the test is severely hindered by an important degree of inter-observer variability, which is an important disadvantage. Consequently, it is advisable to incorporate it into the other parameters. Additionally, the angle of insonation influences Doppler parameters. In our study we depended on parameters that were not significantly influenced by the angle of insonation, such as, MPA AT/ET, PI and RI.

We recommended additional studies on larger number of participants with different conditions and GA, also other US and doppler parameters should be included, group study should be divided to allow accuracy better assessment in expecting neonatal outcomes and monitoring.

Limitations: However, the sample size was relatively modest. There was only one center where the investigation was conducted. The patients were followed up on for a relatively short period.

Conclusions

Utilizing US and doppler to assess FLM is helpful. However, no single parameter alone could demonstrate FLM definite sign.

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