

## Assessment of Fetal Lung Maturity by U/S and its Impact on Fetal Outcome

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### ABSTRACT

**Background:** The presence of an immature foetal lung is linked to a variety of negative consequences, including respiratory distress syndrome. (RDS). The ability to continue or postpone birth is frequently the deciding factor efficiently assess lung maturity in the foetus.

**Aim of the work:** To evaluate the value of assessment of amniotic fluid using ultrasonography in predicting fetal lung maturity and its impact on fetal outcome.

**Patients and methods:** This prospective cohort study included three hundred pregnant women. They were later divided into two groups; RDS group and non-RDS group.

**Results:** Our results indicated the presence of a significant distinction between RDS group as well as non-RDS group regarding gestational age (P value=0.0005). However, there was no statistically significant difference regarding maternal age, gravidity, parity and abortion among RDS & non-RDS fetuses (P value > 0.05). Regarding the fetal biometric measurements, our results indicated a statistically significant decrease in the values of fetal biometric measurements including BPD, FL and AC among RDS group in comparison with the non-RDS group (P value < 0.001).

**Conclusion:** Ultrasound parameters including proximal tibial epiphysis (PTE) followed by distal femoral epiphysis (DFE) then amniotic fluid free floating particles (FFP) are precise predictors in the assessment of RDS with varying degrees of performance.

**Keywords:** Distal femoral epiphyses; fetal lung maturity; fetal outcome.

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### INTRODUCTION

The liquid that surrounds a developing foetus in the amniotic sac, amniotic fluid (AF), is normally clear to pale yellow in colour. The makeup of AF is diverse, containing a variety of maternal and foetal components. The AF's composition varies with gestational age, with an average pH of 7.2 and specific gravity of 1.2. 1.0069–1.008. <sup>13</sup>

In preterm and early term infants, lung immaturity is still the leading cause of morbidity and mortality. Although gestational age (GA) is the strongest predictor of lung maturity, respiratory distress syndrome and transitory tachypnea in the newborn are not limited to premature births (34 weeks). These problems are substantially more common in late preterm (34–36 weeks' gestation) and early term (37–38 weeks' gestation) newborns than in neonates delivered at or after 39 weeks' gestation. <sup>11</sup>

Because lung immaturity is linked to insufficient pulmonary surfactant production, respiratory distress syndrome (RDS), formerly known as hyaline membrane disease, is the most prevalent cause of respiratory distress in premature newborns. With the use of prenatal steroid medication, early provision of

positive airway pressure, and, in some circumstances, exogenous surfactant therapy, RDS can be avoided or its severity reduced. <sup>3</sup>

For nearly a quarter-century, Gray-level measurements, lung tissue mobility, and relative characteristics of lung-to-placenta or -liver imaging, among other things, have been utilised to attempt foetal lung ultrasound images without being invasive. These studies discovered a strong relationship between respiratory illness and death, but the diagnostic accuracy was insufficient to be useful for therapeutic purposes. <sup>4</sup>

The use of foetal ultrasonography to predict foetal lung maturity has long been suggested as a non-invasive alternative to amniocentesis. Gray-scale measurements, lung tissue motility, and the link between imaging features of foetal lung vs. placental or hepatic tissue have all been attempted utilising computer analysis of foetal lung ultrasound pictures over the last 25 years. <sup>20</sup>

## PATIENTS AND METHODS

**Study design and setting:** This was a prospective cohort study that was completed on 300 women coming for labour at El Hussein University and Shibin Elqantar public hospital in obstetrics and gynecology department from December 2019 to August 2021.

**Criteria for inclusion:** All women who are pregnant with a viable foetus and have an uncomplicated singleton pregnancy are eligible. Women have to be certain of their last menstrual cycle date and have it confirmed by ultrasound during the first trimester of pregnancy.

**Criteria for exclusion:** Multiple pregnancies, Malformations of the foetus ,complications (hypertension, diabetes, etc.) Macrosomic foetuses or intrauterine growth restriction Presence of meconium-stained fluid or antepartum haemorrhage.

**Ethical considerations:** Approval of ethical committee was obtained from Al-Azhar university faculty of medicine, Egypt. Verbal consent was taken from all cases before participation in this study. The nature and aims of this work were fully discussed to all women who were included in this study. No funding sources.

### Methods:

**All patients were subjected to the following:**

**Detailed personal, obstetric and medical history including:** Personal history including age, smoking and level of education. Obstetric history including gravidity, parity, number of abortions, modes of delivery in previous pregnancies, first day of the last normal menstrual period and the gestational age, onset, duration. Medical history including Present or Past history

**Examination:** Vital signs are all important factors to consider. Abdominal examination for assessment of fundal level and fetal heart sounds. Palpation of the belly to detect foetal size and presentation, as well as uterine activity.

**Lab assessment:** All investigations obtained according to standard protocol of labour in our hospital including complete blood count, CRP and grouping, liver enzymes, kidney functions, random blood sugar, and urine analysis.

**Ultrasound evaluation:** All mothers were examined by ultrasound prenatally for assessment of amniotic fluid index, umbilical artery Doppler, assessment of estimated fetal weight & fetal maturity sign. The existence and size of epiphyseal ossification centres, placental grading (classification based on chorionic convolutions and calcifications), and other imaging measurements have all been used to determine maturity (19-21). Some mature fetuses may not have these findings at term, and some fetuses having these traits may be immature (e.g., maternal diabetes complicated by macrosomia). In general, ultrasonography assessment of gestational age in the third trimester (indirectly evaluating for maturity) is inferior to other approaches.

**Technique:** Abdominal ultrasound was done using mindray DP20 with center frequency 3.5MHZ. ultrasound examination was done On the same day after their delivery, they went to the radiology department for an obstetric ultrasound scan. The same ultrasonographer performed the ultrasound examination to decrease the intraobserver variability.

**Ultrasound Findings:** The placenta was graded according to Grannum's categorization. Biparietal diameter (BPD): The axial section of the foetal skull was measured with callipers from the outer table to the inner table of the skull, where a clear midline echo of the thalamus and septum pellucidum could be seen. Epiphyseal centres: The foetus' lower limbs were inspected, and callipers were used to measure the distal femoral epiphysis and proximal tibial epiphysis. Amniotic fluid linear densities: Linear densities in the amniotic fluid were observed.

**Postoperative management:** Each neonate was examined by the paediatrician for the following foetal outcomes: foetal sex, weight, APGAR score at one and five minutes, signs of a respiratory problem, admission to the neonatal intensive care unit (NICU) and follow-up by the paediatrician for the duration of the hospitalisation, and any adverse neonatal morbidity or mortality up to discharge.

**Sample size calculation:** Based on previous studies who found that the adjusted the mean significant difference in the Mean FL between the RDS and the non-RDS, were in -RDS ( $1.27 \pm 0.07$ ) and non -RDS ( $1.47 \pm 0.11$ ) (Laban et al., 2015). Based on this assumption, the sample size was determined according to the using the formula:

$$n = 2 \left[ \frac{(Z_{\alpha/2} + Z_{\beta}) * \sigma}{\mu_1 - \mu_2} \right]^2$$

Where

$n$  is the sample size and  $Z/2$  is 1.96. (The key number that separates the 95 percent of the Z distribution in the middle from the 5% in the tail.)

0.84 ( $Z$ ) (The critical value that separates the lower 20 percent of the Z distribution from the upper 80 percent )

= the standard deviation of the mean MCA's estimate RI equals 0.07.  $\mu_1$  = mean in FL in -RDS. (1.27).

$\mu_2$  = mean in FL in non-RDS. (1.47).

The sample size was calculated to be 300 patients in total.

### Statistical analysis and data management

Data was collected, coded, updated, and entered into IBM SPSS version 20 (Statistical Package for Social Science). The qualitative data were given as numbers and percentages, the quantitative data with parametric distribution as mean, standard deviations, and ranges, and the quantitative data with non-parametric distribution as median with inter quartile range (IQR). When comparing two groups with qualitative data, the Chi-square test was utilised, but the Fisher exact test was used instead when the predicted count in any cell

was less than 5. In the comparison of two groups with quantitative data and parametric distribution, the independent t-test was employed, while the Mann-Whitney test was used in the comparison of two groups with quantitative data and non-parametric distribution. The confidence interval was set at 95%, while the

acceptable margin of error was set at 5%. As a result, the following p-value was declared significant: Non-significant if the P value is greater than 0.05. (NS). Significant if the P value is less than 0.05. (S). Highly significant if the P value is less than 0.01. (HS).

**RESULTS**

		Neonatal respiratory distress syndrome (RDS)				Chi square test		
		Positive (No.=47)		Negative (No.=253)		x <sup>2</sup>	p value	
		No	%	No	%			
Maternal age	Mean ± SD	29.62	4.96	31.55	4.97	2.454	0.015	
Gestational age	Mean ± SD	35.68	0.76	36.04	0.81	2.829	0.005	
Residence	Rural	25	53.2%	128	50.6%	0.107	0.743	
	Urban	22	46.8%	125	49.4%			
Gravidity	Once upon a time	4	8.5%	38	15.0%	5.403	0.611	
	At least twice	8	17.0%	31	12.3%			
	At least three times	4	8.5%	34	13.4%			
	At least four times	6	12.8%	35	13.8%			
	At least five times	10	21.3%	30	11.9%			
	At least six occasions	5	10.6%	27	10.7%			
	a total of seven	6	12.8%	33	13.0%			
	a total of eight	4	8.5%	25	9.9%			
	zero times	1	2.1%	18	7.1%			
	Once upon a time	5	10.6%	44	17.4%			6.630
At least twice	11	23.4%	42	16.6%				
At least three times	7	14.9%	32	12.6%				
At least four times	4	8.5%	30	11.9%				
At least five times	7	14.9%	26	10.3%				
At least six occasions	4	8.5%	30	11.9%				
a total of seven	5	10.6%	23	9.1%				
a total of eight	3	6.4%	8	3.2%				
Zero times	28	59.6%	97	38.3%	8.656	0.013		
One time	10	21.3%	106	41.9%				
Two times	9	19.1%	50	19.8%				

**Table 1:** Contrast between neonatal respiratory distress syndrome (RDS) and non RDS groups as regards demographic data

Neonatal respiratory distress syndrome (RDS)						
	RDS (No.=47)		NON-RDS (No.=253)		Independent t test	
	Mean	SD	Mean	SD	T	p value
BPD	82.09	2.59	88.24	3.14	12.665	<0.001
FL	60.67	3.51	67.86	2.86	15.215	<0.001
AC	278.72	13.92	307.96	8.67	19.037	<0.001

**Table 2:** Comparison between neonatal respiratory distress syndrome (RDS) and the non RDS as regards BPD, FL and AC.

		Neonatal respiratory distress syndrome (RDS)					
		RDS (No.=47)		NON-RDS (No.=253)		Chi square test	
		No	%	No	%	x <sup>2</sup>	p value
Placental Grading	0-I	34	72.3%	46	18.2%	59.482	<0.001
	II	8	17.0%	135	53.4%		
	III	5	10.6%	72	28.5%		

**Table 3:** Comparison between neonatal respiratory distress syndrome (RDS) and non RDS as regards placental grading.

		Neonatal respiratory distress syndrome (RDS)					
		Positive (No.=47)		Negative (No.=253)		Chi square test	
		No	%	No	%	x <sup>2</sup>	p value
COLON	I	5	10.6%	19	7.5%	11.466	<b>0.003</b>
	II	28	59.6%	91	36.0%		
	III	14	29.8%	143	56.5%		
Thalamic echogenicity	Echogenic	13	27.7%	194	76.7%	44.528	<0.001
	Echo lucent	34	72.3%	59	23.3%		
Lung/liver echogenicity	Hyper-echoic	13	27.7%	70	27.7%	1.648	0.439
	Hypo-echoic	17	36.2%	70	27.7%		
	Iso-echoic	17	36.2%	113	44.7%		

**Table 4:** Comparison between neonatal respiratory distress syndrome (RDS) according thalamic echogenicity, lung/liver echogenicity and colonic grading.

		Neonatal respiratory distress syndrome (RDS)					
		Positive (No.=47)		Negative (No.=253)		Independent t test	
		Mean	SD	Mean	SD	T	p value
APGAR 1 min		2.98	0.82	5.26	0.79	18.062	0.001
APGAR 5 min		5.91	0.83	7.8	1.14	10.838	0.012

**Table 5:** Comparison between neonatal respiratory distress syndrome (RDS) according Apgar score.

		Neonatal respiratory distress syndrome (RDS)					
		Positive (No.=47)		Negative (No.=253)		Chi square test	
		No	%	No	%	x <sup>2</sup>	p value
NICU admission	No	21	44.7%	221	87.4%	46.276	<0.001
	Yes	26	55.3%	32	12.6%		
Mortality	No	45	95.7%	252	99.6%	5.966	0.015
	Yes	2	4.3%	1	0.4%		

**Table 6:** Comparison between neonatal respiratory distress syndrome (RDS) according NICU admission and mortality.

Item	AUC	Sensitivity	Specificity	-PV	+PV	P value
FFP	0.726	61.70	83.40	92.1	40.8	0.001
DFE	0.874	85.11	89.72	97.0	60.6	0.001
PTE	0.925	93.62	91.30	98.7	66.7	0.001

**Table 7:** Cut of point, sensitivity and specificity of FFP, DFE and PTE among RDS.

This table shows that in FFP, DFE and PTE:

Its sensitivity is 61.7%, 85.11% and 93.62%

Its specificity is 83.4%, 89.72% and 91.30%

The positive predictive value is 40.8%, 60.6% and 66.7%

The negative predictive value is 92.1%, 97% and 98.7%

## DISCUSSION

The pulmonary system is one of the last foetal organ systems to mature in terms of both function and structure. Preterm delivery can result in substantial newborn morbidity or mortality due to the immature pulmonary system's inability to sufficiently oxygenate the preterm neonate.<sup>6</sup>

Respiratory distress syndrome in newborns (RDS) is considered as their lungs are immature, it is a primary cause of mortality and morbidity in newborns. It is more common in neonates that are born prematurely, and it is linked to inversely with gestational age at birth.<sup>18</sup>

The decision to continue or delay delivery depends usually on the ability to efficiently assess fetal lung maturity for ensuring the protection of the fetus from risks such as sequelae of respiratory distress syndrome (RDS), necrotizing enterocolitis, intraventricular hemorrhage, patent ductus arteriosus and neonatal sepsis as much as possible.<sup>16, 11</sup>

Fetal lung maturity can be assessed by biochemical tests such as lecithin/sphingomyelin ratio, absence or presence of phosphatidyl glycerol and amniotic liquid, fluorescent polarization, foam stability or shake test lamellar body that all rely on amniocentesis, which is an invasive method to determine fetal lung maturity that could cause complications.<sup>13</sup>

Ultrasound being the easiest, for routine obstetric scanning, a simple, common, non-invasive, and cost-effective equipment is available. Ultrasound measures include bi-parietal diameter, femur length, epiphyseal centres of the lower limb, placental grading, colon grading, and free-floating particles in the amniotic fluid for assessing foetal lung maturity, with controversial diagnostic accuracy.<sup>4,20</sup>

Therefore, the goal of our research was to assess the value of assessment of amniotic fluid using ultrasonography in predicting fetal lung maturity and its impact on fetal outcome.

This prospective cohort study included three hundred pregnant women. They were later divided into two groups; RDS group and non-RDS group.

Regarding the demographic characteristics of the studied cases, our results revealed the presence of a significant distinction between RDS group as well as non-RDS group regarding gestational age (P value=0.0005). There was no statistically significant difference as regards maternal age, gravidity, parity and abortion among RDS & non-RDS fetuses as illustrated in Table (1).

Such findings were in agreement with studies by Wang<sup>28</sup> *et al.* that indicated that with increasing gestational age, the risk of RDS reduced and Shapiro-Mendoza and Lackritz<sup>25</sup> study that in comparison to babies born at term, babies born between the 34th and 37th week of pregnancy had a higher risk of RDS. Additionally, Abdulla *et al.*<sup>3</sup> study indicated that incidence of RDS was infants born before 40 weeks gestation have a 12 percent chance of dying, whereas those born after 40 weeks have a 0% chance. A previous study by Mehrabadi *et al.*<sup>19</sup> indicated that early gestation RDS was substantially linked with maternal age (35 years) but protective for late gestation RDS.

Our results indicated a statistically significant decrease in the values of fetal biometric measurements including BPD, FL and AC among RDS group in comparison with the non-RDS group (P value<0.001) as illustrated in Table (2).

Such findings were in agreement with a study by Kandil *et al.*<sup>15</sup> indicated the decreased BPD, FL, and AC among RDS group and that by using the fetal biometry values in the prediction of fetal pulmonary maturity, a BPD between 8.28 and 9.35 cm, AC between 29.5 and 32.2 cm, and FL between 6.27 and 7.21 cm correlated with mature fetal lungs.

It was indicated that BPD can be used for the timetable in BPD bigger than 9.2 cm and elective caesarean section showed 90% of foetuses have reached lung maturity, with high specificity and sensitivity (92% and 87% respectively) and in 80% of the cases, BPD 8.7 cm revealed RDS.<sup>19</sup>

Pallavi *et al.*<sup>21</sup> indicated that BPD is an accurate foetal lung maturity marker because the BPD and Correlation > 9.0 cm. The predictability of a positive shake test (in amniocentesis) was 100 percent. Our results indicated a statistically significant difference between RDS group and non-RDS group regarding

placental grading (P value<0.001) as illustrated in Table (3).

Such findings were in agreement with Das *et al.*<sup>7</sup> that indicated that the respiratory distress syndrome was found to be associated with grade 0 and grade I placenta and no cases were detected in grade II or grade III placenta.

Previous studies by Keikhaie *et al.* and Sharma *et al.*<sup>14, 26</sup> indicated that grade III placenta was associated with good fetal pulmonary maturity and the absence of respiratory distress syndrome.

Our results indicated a statistically significant decrease in free-floating particles (FFP), distal femoral epiphysis (DFE) and proximal tibial epiphysis (PTE) values among RDS group in comparison with the non-RDS group (P value<0.001) as illustrated in Table (4).

Such findings are in agreement with Abdou *et al.*<sup>3</sup> that indicated that the mean epiphyseal ossification centers were significantly low in neonatal with respiratory distress syndrome. A previous study by Elsaed *et al.*<sup>9</sup> indicated that as long as the diameter is at least 1 mm.

ultrasonography may identify each epiphyses ossification centre at a much earlier stage. However, Kandil *et al.*<sup>15</sup> indicated that even though the detection of ossification. Although the presence of centres indicates foetal lung maturity, their absence does not rule out lung maturity. Furthermore, to prevent being confused with other neighbouring cartilaginous structures, these epiphyseal foci must be recognised with extreme caution. In difficult pregnancies, DFE detection of any size may not be related with foetal lung maturity.

Our results indicated a difference that is statistically significant between RDS group as well as non-RDS group regarding colon (p value=0.003) and thalamic echogenicity (P value<0.001), however, non-statistically significant between both groups regarding Lung/liver echogenicity as illustrated in Table (5).

Such findings were in agreement with studies by Kandil *et al.*<sup>15</sup> that there was no evidence of a link between prenatal lung echogenicity and liver maturity or newborn RDS. The same research indicated thalamic echogenicity was found to be a reliable predictor of foetal lung maturity with a 77% and 79% for sensitivity and specificity, respectively and Keikhaie *et al.*<sup>14</sup> study that the foetal intestine was divided into four phases. And Grade 4 foetal intestine was found to be a predictor of foetal lung maturity with a good specificity and a low sensitivity (62.5%) (98.9 percent).

A previous study by Rasheed *et al.*<sup>24</sup> indicated that the examination of the echogenic thalamus is advantageous and can be used as a foetal lung maturity measure.

Our results indicated a statistically significant difference between RDS group and non-RDS group regarding birth weight (P value<0.001) and no significant difference between birth groups regarding fetal sex (P value > 0.05) as illustrated in Table (6).

Such findings were in agreement with a study by Fehlmann et al.<sup>10</sup> that indicated that RDS had a high incidence in very low birth weight infants, despite the frequent use of antenatal steroids.

Condò et al.<sup>6</sup> study that indicated that the biggest risk factor for RDS is a low birth weight, but contrarily with our results, the same study indicated that the risk of RDS was high when fetal sex is male.

Our findings were in disagreement with a previous study by Peacock et al.<sup>23</sup> that indicated that Male preterm newborns are more likely than girls of the same gestational age to develop RDS and require more immediate respiratory and circulatory care. Furthermore, men have been linked to a higher risk of neonatal mortality and respiratory disease.

Such high risk was explained as caused by During the foetal phase, oestrogen regulates surfactant protein synthesis and promotes certain growth factors.<sup>12</sup>

Our results indicated the presence of significant decrease in APGAR score at one minute and five minutes post birth among RDS group in comparison with the non-RDS group (P value<0.001) as illustrated in Table (7).

Such results are in agreement with Wang et al.<sup>28</sup> that indicated that an At 5 minutes after birth, the Apgar score was 7. revealed negative role on the development of RDS and indicated poor conditions after delivery due to the impairment of the respiratory function that exacerbates hypoxia

Thavarajah et al.<sup>27</sup> study indicated that Both low and intermediate Apgar scores were substantially related with infant issues such as respiratory distress, feeding difficulty, hypothermia, and convulsions.

A retrospective cohort study by Chen et al.<sup>5</sup> indicated Male infants with low gestational ages and low Apgar scores died at a higher rate than female neonates due to RDS syndrome.

Our results indicated a statistically significant increase in NICU admission, mortality rate and hospital stay among RDS group in comparison with the non-RDS group.

Such findings were in agreement with Edwards et al.<sup>8</sup> that indicated that neonatal respiratory distress is a major reason for increased morbidity and mortality among newborn, causing increased infants being admitted to neonatal units so early recognition of signs and symptoms of neonatal respiratory distress and proper management could improve the prognosis of these babies.

Our results indicated that ultrasound parameters are precise predictors in the assessment of RDS including proximal tibial epiphysis (PTE) followed by distal femoral epiphysis (DFE) then amniotic fluid free floating particles (FFP) that showed sensitivity values (93.62%, 85.11%, and 61.7%) respectively and specificity values (91.30%, 89.72% and 83.4%) respectively .

Such findings were in agreement with a recent study by Kandil et al.<sup>15</sup> that indicated that ultrasound parameters are good predictors in the assessment of

RDS including epiphyses of the proximal tibia that the distal femoral epiphyses had the highest sensitivity (91%) and specificity (95%) after the proximal femoral epiphyses. showed The sensitivity is 90% and the specificity is 84 percent.

A previous study by Patil et al.<sup>22</sup> indicated that The foetal tibial epiphysis exhibited the best sensitivity (98.7%), specificity (88.8%), and accuracy of any of the tests (97.7 percent ) followed by fetal femoral epiphysis that showed high sensitivity (92.8%), whereas low specificity (60%) and a high level of precision (91.0 percent ) in the evaluation of RDS.

## CONCLUSION

Ultrasound parameters including proximal tibial epiphysis (PTE) followed by distal femoral epiphysis (DFE) then amniotic fluid free floating particles (FFP) are precise predictors in the assessment of RDS with varying degrees of performance.

Conflict of interest : none

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