

## Role of 3D Ultrasound for Assessment of Fetal Lungs

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### Abstract

**Background:** Fetal lung maturity is vital to the survival rate of neonates, and is a determinant of extra uterine life. Neonatal respiratory distress syndrome and associated complications account for 28% of neonatal deaths. Although the wide use of glucocorticoids has decreased the incidence of Neonatal respiratory distress syndrome, approximately 10% of neonates still develop the syndrome.

**Aim of Study:** To study the role of 3D ultrasound for assessment of fetal lungs.

**Patients and Methods:** A total of 50 pregnant women 34-40 weeks gestation after a complication-free normal course of pregnancy were enrolled in the study. They were classified into 2 groups as follows: 1. Group A: (n=25) women 34-37 weeks gestation. 2. Group B: (n=25) women 37-40 weeks gestation. All the included women were subjected to: Full history taken. Ultrasound examination to confirm GA, assess Amniotic Fluid Index (AFI) and to exclude fetal anomalies. 3D ultrasound was carried out to assess fetal lung volume. After child birth, APGAR score at (1, 5 and 10min) was assessed together with occurrence of RDS and the further need for neonatal ICU admission and respiratory support measurements.

**Results:** The mean value of fetal lung volume was significantly increased in term group ( $52.96 \pm 4.91$ ) when compared to preterm group ( $44.08 \pm 6.43$ ) ( $p=0.001$ ). In the term group the percentage of neonates which did not experience Respiratory Distress Syndrome (RDS) was 60% compared to 24% in the preterm group ( $p=0.001$ ). In the preterm group the percentage of admitted neonates in the Intensive Care Unit (ICU) was statistically increased (68%) when compared to the term group (54%) ( $p=0.047$ ). The percentage of women in the preterm group received prenatal steroids 36% was statistically higher than those in the term group 24% ( $p=0.047$ ). In the present study, fetal lung volume was positively correlating with gestational age ( $r=0.531$ ;  $p$ -value=0.001). In the present study, in the preterm group RDS was negatively correlated with steroids ( $r=-0.304$ ;  $p$ -value=0.032).

**Conclusion:** Ultrasound indices, including fetal lung volume may serve as useful alternatives to amniotic fluid phospholipids in analyzing fetal lung maturity. Fetal lung volume might be an accurate non-invasive predictor for the occurrence of neonatal RDS among preterm fetuses in whom

the risk of RDS development deserve fetal lung maturity testing.

**Key Words:** 3D ultrasound – Fetal lungs.

### Introduction

**THE** maturation of fetal pulmonary system is a complex process entailing cellular, physiological, and biological interactions that usually occurs late in gestation being one of the last maturing fetal systems [1].

Therefore, respiratory distress is commonly encountered among premature babies immediately after birth resulting in significant neonatal morbidity or mortality. It has been established to correlate with structural and functional lung immaturity. It is described as respiratory distress in infants that sets in within a few hours of parturition. The incidence of RDS is inversely proportional to gestational length and has been estimated to range from 30% below gestational week 28 to 5% in neonates born in a gestational week above 34 [2].

Three types of tests are traditionally used to assess the degree of Fetal Lung Maturity (FLM) namely; the biochemical testing for surfactant components (e.g. Lecithin/sphingomyelin ratio), biophysical testing for surfactant functionality (e.g. Foam stability index) or physical testing of the amniotic fluid opacity (e.g. lamellar body counts [3]).

All these tests involve the use of amniotic fluid (as it communicates directly with lung fluid), therefore, invasively and indirectly evaluate the probability of lung maturity. Moreover, they predict lung maturity more accurately than immaturity. Tests that directly assess fetal lung function are yet not available [4].

Ultrasound cannot measure biochemical changes in the growing lung or histological changes but

it is reasonable to assume that both morphological and biochemical changes alter the propagation properties in the fetal lung. The possibilities of using ultrasound as a non-invasive method for assessment of fetal lung maturity have been greatly explored over the last 30 years [5].

Three-dimensional sonographic measurements are shown to be helpful in assessing the fetal lung volume. Fetal lung volumetry with 3D sonography can be regarded as a good alternative to MRI [6].

#### *Aim of the work:*

The purpose of this study is to correlate lung parameters using three dimensional ultrasound (3D US) with lung maturity assessed by postnatal outcome, and to develop reference cutoff value for these parameters (mean FLV) as measure that could be used to predict the development of neonatal RDS.

### **Patients and Methods**

This study cross section study was conducted on fifty pregnant females aged 18 years up to 40 years between 34 to 40 weeks gestational age of pregnancy at Ain Shams University Hospitals, Egypt, between March 2019 and August 2019.

The study included female participants from 18 years up to 40 years old, with singleton pregnancy with no history of chronic hypertension or diabetes (type I or type II) before pregnancy. While patients who refused to participate in the study and fetal malformation were excluded from the study.

The participants were divided into two groups; Group A (women pregnant 34-37 weeks gestation) and Group B (women pregnant 37 to 40-week gestation. Gestational Age (GA) was established by menstrual dates, which was confirmed by obstetric ultrasound.

For both groups, full history was taken. Ultrasound was done to confirm GA, assess Amniotic Fluid Index (AFI) and to exclude fetal anomalies. GE Voluson S6 ultrasound machine, equipped with 3D probe RAB2-6-RS 2-5MHz was carried out to assess fetal lung volume.

All participants signed an informed consent after explaining the objective of the study to them.

The methods and procedures of the present study are in agreement with the Heliniski Declaratin for Ethical Medical research.

The protocol was revised by the Ethical committee of Obstetrics and Gynecology Department and/or the Ethical Committee of Faculty of Medicine, Ain Shams University.

Women had adequate time to consider enrollment and discuss options with their physician prior to cesarean section. All eligible patients who present to labor and delivery for cesarean section were examined upon presentation. After inclusion criteria have been met, the patient was approached for consent to participate in the study. Patients were given study information and the consent form to review. Consent was documented by the patient's signature indicating understanding and agreement to participate in the study.

The participating women have the right to withdraw from the study without being adversely impacted regarding the medical service she should receive.

Statistical analysis comparisons among patients underwent cleaning uterine cavities with a dry laparotomy sponge after delivery of the placenta and patients who didn't undergo cleaning uterine cavities were done using the Student's *t*-test for continuous variables and Pearson's chi square test for categorical variables.

*Statistical package:* Data entry and statistical analysis were done using Statistical Package for Social Science (SPSS) version 21.0.

#### *Statistical analysis:*

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. The data collected were tabulated and analyzed by SPSS (statistical package for social science) version 25 (Armonk, NY: IBM Corp) on IBM compatible computer. The data was tested for normality using Kolmogorov-Smirnov test, Shapiro-Wilk tests. Two types of statistics were done:

#### *Descriptive statistics:*

According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean  $\pm$  SD (for parametric data) median and inter-quartile range (for non-parametric data).

#### *Analytic statistics:*

Chi-square test ( $\chi^2$ ): Was used to study comparison and association between two qualitative variables. Student *t*-test: Was used for comparison between two groups having quantitative variables

with normal distribution (for parametric data). Mann-Whitney U-Test: Is a test of significance used for comparison between two groups having quantitative variables without normal distribution (for non-parametric data), correlation by Spearman's correlation. A *p*-value of <0.05 was considered statistically significant.

**Results**

Table (1): Demographic data of the two studied groups.

	Groups		<i>p</i> -value
	Group A (n=25) (Preterm Group)	Group B (n=25) (Term Group)	
<i>Age (years):</i>			
Range	18-33	18-33	0.974
Mean ± SD	23.96±4.21	23.92±4.415	
<i>GA (weeks):</i>			
Range	34-37	38-40	0.001**
Mean ± SD	34.88±0.781	38.92±0.759	

The (Table 1) shows preterm group (n=25) where the pregnant women at 34-37 weeks of gestation, their age ranged from 18 to 33 years with mean age was equal to 23.96 years (± SD =4.21) and term group (n=25) where the pregnant women at 37-40 weeks gestation, their age ranged from 18 to 33 years with mean age was equal to 23.92 years (± SD=4.41), There was no statistical significant difference between the mean age in the two studied groups.

Table (2): Comparison between mode of delivery in the two studied groups.

Mode of delivery	Groups				Total		<i>p</i> -value
	Group A (n=25) (Preterm Group)		Group B (n=25) (Term Group)		N	%	
	N	%	N	%			
Normal	10	40	13	52	23	46	0.395
CS	15	60	12	48	27	54	
Total	25	100	25	100	50	100	

Table (3): Comparison between fetal lung volume in the two studied groups.

Fetal lung volume	Groups		<i>p</i> -value
	Group A (n=25) (Preterm Group)	Group B (n=25) (Term Group)	
Range	35-55	44-61	0.001**
Mean ± SD	44.08±6.43	52.96±4.91	

The (Table 2) shows that in preterm group, 15 women out of 25 had a cesarean delivery 60%, while in term group 12 women out of 25 had a cesarean delivery 48% with no statistically significant difference (*p*=0.395).

This (Table 3) shows that, the mean value of fetal lung volume had statistically significant increase in term group (52.96±4.91) when compared to preterm group (44.08±6.43) (*p*<0.001).

Table (4): APGR score measured at different time of measurements in the two studied groups.

APGR score	Groups				<i>p</i> -value
	Group A (n=25) (Preterm Group)		Group B (n=25) (Term Group)		
	N	%	N	%	
<i>APGR 1 minute:</i>					
Normal foal	1	4.0	23	92.0	0.001**
Intervention	15	60.0	2	8.0	
Life threatening	9	36.0	0	0.0	
<i>APGR 5 minutes:</i>					
Normal foal	5	20.0	23	92.0	0.001**
Intervention	20	80.0	2	8.0	
<i>APGR 10 minutes:</i>					
Normal foal	7	28.0	23	92.0	0.001**
Intervention	18	72.0	2	8.0	

This table shows that the percentage of neonates who had life threatening APGR score measured at 1 minute in preterm group was 36%, while in term group was zero which statistically significant increase in preterm group (*p*=0.001). APGR score measured at both 5 and 10 minutes recorded that the percentage of neonates who needed intervention in preterm group was 80% & 72% and in term group 8.0% & 8.0% respectively indicating statistically significant increase in preterm group (*p*=0.001 & 0.001, respectively).

Table (5): Respiratory distress syndrome in the two studied groups.

RDS	Groups				Total		<i>p</i> -value
	Group A (n=25) (Preterm Group)		Group B (n=25) (Term Group)		N	%	
	N	%	N	%			
No RDS	10	40	23	92	33	66	0.001*
RDS	15	60	2	8	17	34	
Total	25	100	25	100	50	100	

This table shows that in the term group the percentage of neonates which did not experience Respiratory Distress Syndrome (RDS) was 92% which was significantly higher than the 40% in the preterm group ( $p=0.001$ ).

Table (6): Neonatal Intensive Care Unit (ICU) admission in the two studied groups.

ICU admission	Groups						p-value
	Group A (n=25) (Preterm Group)		Group B (n=25) (Term Group)		Total		
	N	%	N	%	N	%	
No admission	10	32	25	100	23	46	0.047*
Admission	15	68	0	0	27	54	
<b>Total</b>	<b>25</b>	<b>100</b>	<b>25</b>	<b>100</b>	<b>50</b>	<b>100</b>	

This table shows that in the preterm group the percentage of admitted neonates in the Intensive Care Unit (ICU) was statistically higher (68%) when compared to the term group (0%) ( $p=0.047$ ).

Table (7): Prenatal steroids administration in the two studied groups.

Prenatal Steroids administration	Groups						p-value
	Group A (n=25) (Preterm Group)		Group B (n=25) (Term Group)		Total		
	N	%	N	%	N	%	
No	16	64	22	88	38	76	0.047*
Yes	9	36	3	12	12	24	
<b>Total</b>	<b>25</b>	<b>100</b>	<b>25</b>	<b>100</b>	<b>50</b>	<b>100</b>	

This table shows that, the percentage of women who were administered prenatal steroids in the preterm group 36%, was statistically higher than those in the term group 12%, whereas ( $p=0.047$ ).

Table (8): Correlation between fetal lung volume and different studied parameters in both groups.

Parameters	Fetal Lung Volume (FLV)	
	r	p-value
Gestational age	0.531	0.001*
APGR 1 minute	-0.687	0.001*
APGR 5 minutes	-0.692	0.010**
APGR 10 minutes	-0.693	0.001**
RDS	-0.768	0.001**
NICU admission	-0.766	0.001**
Steroids	0.244	0.088

Fetal Lung Volume (FLV) was positively correlated with gestational age ( $r=0.531$ ;  $p$ -value=0.001).

At the same time, fetal lung volume was negatively correlated with APGR score at 1 minute ( $r=0.687$ ;  $p$ -value=0.001), 5 minutes ( $r=0.692$ ;  $p$ -value=0.001), and 10 minutes ( $r=-0.693$ ;  $p$ -value=0.001), RDS ( $r=-0.768$ ;  $p$ -value=0.001) and NICU admission ( $r=0.766$ ;  $p$ -value=0.001).

On the other hand, the fetal lung volume was no statistically correlated with prenatal administration of steroids ( $r=0.244$ ;  $p=0.088$ ).

Table (9): Correlation between RDS and steroids in both groups.

Parameters	Respiratory distress syndrome (RDS)	
	r	p-value
Steroids	-0.304	0.032*

This table shows that RDS was negatively correlated with steroids ( $r=-0.304$ ;  $p$ -value=0.032).

Table (10): The diagnostic indices (sensitivity, specificity, positive predictive and negative predictive values) of FLV in the studied patients.

Cutoff	Sensitivity	Specificity	PPV	NPV
>49.50*	87.80	88.20	92.90	68.2

Receiver Operating Curve (ROC) was used to determine the cutoff value of FLV in determining neonatal respiratory function outcome. Our ROC results revealed that the FLV cutoff value is greater than 49.50 and the area under the ROC curve is equal to 0.936 which indicating that it is an excellent predictor for neonatal respiratory function outcome. The sensitivity, specificity, positive predictive and negative predictive values of FLV were 87.80%, 88.20%, 92.90% and 68.2%.

#### • Clinical background:

Female patient 28 years old (pregnant  $\pm 35$  weeks).



Fig. (1): 3D ultrasound using VOCAL method shows fetal right lung volume measuring 45.29cm (group A - a case pregnant  $\pm 35$  weeks).



In the present study, fetal lung volume was positively correlating with gestational age ( $r=0.531$ ;  $p$ -value=0.001). As the image quality more influenced by the shadowing of the spine and ribs especially after 34 weeks with inaccurate measurement of the lung volume [18] and this is in agreement with the study of Osada and his colleagues which included one hundred twenty-five healthy neonates with birth weights.

In the present study, in the preterm group RDS was negatively correlated with steroids ( $r=-0.304$ ;  $p$ -value=0.032).

In the present study, Receiver Operating Curve (ROC) was used to determine the cutoff value of FLV in determining neonatal respiratory function outcome. Our ROC results revealed that the FLV cutoff value is greater than 49.50 and the area under the ROC curve is equal to 0.936 which indicating that it is an excellent predictor for neonatal respiratory function outcome. The sensitivity, specificity, positive predictive and negative predictive values of FLV were 87.80%, 88.20%, 92.90% and 68.2% respectively.

Laban and his colleagues found that neonatal RDS is less likely with FLV of at least 32cm<sup>3</sup> [11].

Prendergast and his colleagues reported that 3D FLVs might be useful in predicting neonatal respiratory outcome among fetuses with abnormal lung growth (with congenital diaphragmatic hernia & with anterior wall defects) [19].

Wang and his colleagues reported that; based on comparison with the amniotic fluid phospholipids analysis, FLV >50mL was considered to indicate fetal lung maturity with high sensitivity and specificity [9].

#### Conclusion:

To date, no unified sonographic standard of fetal lung maturity exists, due to the variability of fetal lung echoes during pregnancy and complications associated with the fetal position, pregnant mother, or equipment. Ultrasound indices, including fetal lung volume may serve as useful alternatives to amniotic fluid phospholipids in analyzing fetal lung maturity. Fetal lung volume might be an accurate non-invasive predictor for the occurrence of neonatal RDS among preterm fetuses in whom the risk of RDS development deserve fetal lung maturity testing.

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## دور الموجات فوق الصوتية ثلاثية الأبعاد في تقييم رئتي الجنين

خلفية: يعتبر نضج رئتي الجنين أمراً حيوياً لمعدل بقاء الأطفال حديثي الولادة، وهو محدد لحياة الرحم الإضافية. متلازمة الضائقة التنفسية الوليدية والمضاعفات المرتبطة بها مسؤولة عن ٢٨٪ من الوفيات بين الأطفال حديثي الولادة. على الرغم من أن الإستخدام الواسع للجلوكونيكورتيكويد قد قلل من حدوث متلازمة الضائقة التنفسية الوليدية، إلا أن ما يقرب من ١٠٪ من الأطفال حديثي الولادة ما زالوا يصابون بالمتلازمة.

الهدف من البحث: دراسة دور الموجات فوق الصوتية ثلاثية الأبعاد في تقييم رئتي الجنين.

المرضى وطرق البحث: تم تسجيل إجمالي ٥٠ سيدة حامل ٣٤-٤٠ إسبوعاً من الحمل بعد مسار الحمل الطبيعي الخالي من المضاعفات في الدراسة. تم تصنيفهم إلى مجموعتين على النحو التالي: ١- المجموعة أ: (عدد ٢٥ سيدة) من ٣٤ إلى ٣٧ إسبوعاً من الحمل. ٢- المجموعة ب: (عدد ٢٥ سيدة) ٣٧-٤٠ إسبوعاً من الحمل. تم إخضاع جميع النساء المشمولات إلى: تم أخذ التاريخ الكامل. الفحص بالموجات فوق الصوتية لتأكيد العمر الحمل، وتقييم مؤشر السائل الأمنيوسي وإستبعاد التشوهات الجنينية. تم إجراء الموجات فوق الصوتية ثلاثية الأبعاد لتقدير حجم رئتي الجنين. بعد ولادة الطفل، تم تقييم درجة APGAR عند (١ و ١٠ دقائق) مع حدوث متلازمة ضيق التنفس والحاجة الإضافية لدخول وحدة العناية المركزة للولدان وقياسات الدعم التنفسي.

النتائج: تمت زيادة القيمة المتوسطة لحجم رئتي الجنين بشكل كبير في مجموعة المدى (٤.٩١±٥٢.٩٦) بالمقارنة مع مجموعة الخدج (٦.٤٣±٤٤.٠٨) (ع=٠.٠٠١). في مجموعة المصطلح كانت النسبة المئوية للولدان الذين لم يتعرضوا لمتلازمة الضائقة التنفسية (متلازمة ضيق التنفس) ٦٠٪ مقارنة ب ٢٤٪ في مجموعة الخدج (p=0.001). في مجموعة الخدج، زادت النسبة المئوية للولدان المقبولين في وحدة العناية المركزة (ICU) إحصائياً (٦٨٪) مقارنة بمجموعة المصطلح (٥٤٪) (p=0.047). كانت النسبة المئوية للنساء في مجموعة الخدج اللاتي تلقين المنشطات قبل الولادة ٣٦٪ أعلى إحصائياً من تلك في مجموعة المصطلح ٢٤٪ (p=0.047). في هذه الدراسة، كان حجم رئتي الجنين مرتبطاً بشكل إيجابي مع عمر الحمل (r=0.531، قيمة p=0.001). في هذه الدراسة، في مجموعة الخدج إرتبطت متلازمة ضيق التنفس سلباً بالاستيرويدات (r=-0.304، قيمة p=0.032).

الخلاصة: مؤشرات الموجات فوق الصوتية، بما في ذلك حجم رئتي الجنين قد تكون بمثابة بدائل مفيدة للفوسفوليبيدات السائلة في تحليل نضج رئتي الجنين. قد يكون حجم رئتي الجنين مؤشراً دقيقاً غير جراحي لحدوث متلازمة ضيق التنفس الوليدي بين الأجنة الخدج الذين يستحق لديهم خطر الإصابة بمتلازمة ضيق التنفس إختبار نضج رئتي الجنين.