PRENATAL PREDICTION OF FETAL LUNG MATURITY BY MEASURING FETAL PULMONARY ARTERY DOPPLER INDICES

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Abstract

Objective: This study aimed to assess FLM before labour to minimize the incidence of neonatal RDS in cesarean section deliveries by measuring fetal pulmonary artery doppler indices.

Methods: This observational cross sectional study was performed on 100 women undergoing cesarean sections from August 2017 till October 2020 at Obstetrics & Gynecology Department, Faculty of Medicine, Zagazig University. Detailed history, physical examination, detailed obstetric ultrasound examination were done. By using 2D voluson pro-730 ultrasound equipped with a 3 to 5 MHz convex array sector transducer with comment on placental location and maturity, fetal biometry (BBD, HC, FL, AC), estimated fetal weight and amniotic fluid index. fetal MPA waveform was obtained, relevant Doppler velocity variables were manually traced three times and the average was taken. The variables included the systolic/diastolic (S/D) ratio, pulsatility index (PI), resistance index (RI), PSV and the At/Et ratio. Neonates are assessed by a pediatrician to diagnose presence of respiratory distress. For statistical analysis, we used the Statistical Packages for Software Sciences (SPSS) version 21.

Results: Mean age of patients was 28.28 years old, mean gestional age was 38.354 weeks. Mean amniotic fluid index was 7.37. mean neonatal birth weight was 3078 gram. Seventeen percent has developed RDS while, Fourteen percent was admitted to NICU. All patients had delivered by CS. Seventy-eight percent of them had elective CS. there is significant relation between development of RDS and gestational age at delivery. mean S/D ratio 6.866. mean PI 2.17 cm/S. mean RI 0.768 cm/S. mean PSV 68.255 cm/S. mean AT/ET ratio 0.312. There is statistically significant relation between RDS development and each of S/D ratio, PI, RI, and AT/ET ratio. (S/D ratio, PI and RI were significantly higher in neonates had RDS while those patients had significantly lower AT/ET ratio). There is statistically non-significant relation between RDS development and PSV. The best cutoff of AT/ET ratio in diagnosis of respiratory distress among our studied neonates was<0.283 with area under curve 0.868 with sensitivity 82.4%, specificity 97.6%, positive predictive value (PPV) 87.5%, negative predictive value (NPV) 96.4% and accuracy 95% (p<0.05)

.The ability of S/D ratio, PI, RI and PSV to predict RDS development had the same sensitivity but lower specificity compared with that of At/Et .

Conclusions: The Pulmonary artery AT/ET measurement may provide a noninvasive means of determining FLM with relatively acceptable levels of sensitivity, specificity, and predictive values.

Keywords: Amniotic fluid (AF); FLM, RDS, Acceleration time /Ejection time (AT/ET) ratio.

INTRODUCTION

Respiratory distress syndrome (RDS) is acommon problem in the first few days of neonatal life which is diagnosed with the presence of one or more symptoms of tachypnea, intercostal muscle retraction, grunting, nasal flaring and cyanosis **(1) .**Introduced antenatal steroids and exogenous surfactant improving results of RDS; which remains a major cause of neonatal morbidity and mortality. It is responsible for 30% - 40% of newborns' hospital admission. It also accounts for approximately 20% of neonatal deaths **(2)** .Management strategies for reducing RDS risk's, fetal lung maturity (FLM) evaluation in amniotic fluid could assist in determining delivery time in pregnancy having maternal and/or fetal complication might require preterm delivery **(3).** Methods for testing FLM as lamellar body counting, lecithin-sphingomyelin,PG %, or TDx FLM assay II were done in amniotic fluid, and required invasivly procedures **(4).** A lot of efforts were done to predict FLM for determination when fetus is likely to develop neonatal complications (as RDS of newborn or death). Many methods for evaluating FLM were described, and most of them were involves doing amniocentesis **(3).** Amniocenteses have high risks and complications in around 0.7%of patients **(5)**. At first ultrasound use for gestational age calculations, there are a lot of evidents on ultrasound dating which is less accurate three to four weeks. Substitute to improved ultrasound dating late in 3th trimester and to decided fetal maturity **(6).** Ultrasound consider as gold standard for fetus antenatal screening **(7)**. Associaing ultrasonically detectable placental changes with increase in gestational age firstly by Weinsberg et al, but Grannum et al who introduced grading system depending on placentas ultrasonographic appearance. Where placental grading system used as method for predicting FLM. strong correlation reported among Grade III placenta and mature Lecithin/Sphingomyelin % **(8) (9).** Amniotic fluid turbidity assayed by OD at 650 nm have been correlated with the respiratory surfactants in amniotic fluid. There was surge in sebaceous gland activities, size and number, sebum produced, as primary constituent of vernix caseosa, pre term labor onset's **(10)** .Free floating particles (FFPs) had correlated with congenital malformations , bleeding , and anencephaly in second trimester. Amniotic fluid particles in third trimester were nothing but vernix and less due to meconium **(11**). FFPs exhibiting snow storm and blizzard appearance in amniotic fluid could use for evaluation FLM using real time ultrasound. Parulekar et al found largest echogenic amniotic fluid size particles at several gestational ages **(12, 13)**. Fetal skeletal bones become more visible by using ultrasound only if it were calcified. While primary ossification center developed early in pregnancies, secondary ossification center form at later pregnancies and early neonatal life and also were hypo echogenic structure throughout intrauterine life while Only secondary ossification centers within epiphyseal cartilage in proximal tibia, distal femur, and occasionally, the proximal humerus appeared prenatally **(14) (15).** Ultrasonographic detecting lower and upper limb EOC allow to gestational ages prediction's during third pregnancy trimester with certainty of high degrees. Mostly, cartilage central cell's in distal femur epiphyses and proximal tibia beginning to ossify throughout third trimester **(16) (17)**. Doppler effects allowed to measure several variables which were associated with fetal hemodynamics. **(18).** Pervious investigation

reported their values for many variables. Where some of those were used for practical purposes, as predicting FLM method's **(19).** Doppler importance as non-invasive method to estimate pulmonary artery pressure in neonates and adults were illustrated in pervious investigation **(20)**. Doppler evaluations of main pulmonary artery was useful in analysis of vascular system impedance and changing in variables demonstrated to had correlation with GA, FLM and neonatal results **(21).** Fetal pulmonary artery Doppler velocimetry might be very useful for predicting FLM depending on sonographic echogenicity of fetal lung change in predictable pattern **(22)** , pulmonary artery Doppler velocimetry had used in attempts to identify fetuses at pulmonary hypoplasia risks and neonates with RDS had increasing pressure in pulmonary vasculature, and decreased post treatement by artificial surfactant (**23)**. Recently investigation showed the ratio in fetal main pulmonary artery could predict FLM as compared to biochemical tests for amniocenteses or compared with clinical results for delivered fetuses **(24).** Many formulas used for estimating pulmonary artery pressure by Doppler wave acceleration times. Dabestani et al. said the excellent correlation (R = 0.98) among formula [pulmonary artery pressure = 90 – (0.62 × fetal main pulmonary artery acceleration time)] and actual pulmonary artery pressure **(25, 26)**. Characteristic shortening of pulsed Doppler pulmonary acceleration time in adult cases having chronic pulmonary hypertension has noted and shortening of AT/ET % of pulmonary arteries was independent of heart rates and correlated with pulmonary arterial pressure elevation's **(27).** Doppler velocimetry of main pulmonary artery, provided characteristics waveform, and allow to distinguish from signal emanating from ductus arteriosus. Ductus arteriosus waveform characterized by rounded, full, and triangular-shaped systolic blood flow as “dome-like.” and had greater diastolic flow and peak velocity than pulmonary artery (**28)**. Signals emanating from pulmonary arteries , were characterize throughout sharp systolic peak blood flow with needle-like appearance, as “spike and dome” pattern. Small “notch” of reverse flow was seen at systole end **(29).** spike components for systolic blood flow was made up of rapidly acceleration and deceleration phase. Diastolic phase begining with brief reversal from blood flow caused by pulmonary valves closure's. And, blood flow continues in forward direction through ventricular diastoles, albeit at lower velocity **(29).** Accelerating time defined as time among onset of mechanic right ventricular systole and peak systolic velocity; ejection time represent by time among begin and mechanic right ventricular systole end. For calculating PATET, acceleration time divided by ejection time average's **(30).**

METHODS

Our investgation performed in compliance with recommendation from Helsinki's declaration **(31)** and approved by ethics committee of Zagazig University (IRB approval no. ZU-IRB #705-3-3-2013).

Study Design, Setting, and Eligibility Criteria

We conducted observational cross sectional study at Zagazig University Hospitals, Egypt, between August 2017 and October 2020.We included one hundred women aged between 20-39 years old undergoing cesearean sections .We excluded patients who had delivered vaginally, those with either oligo or polyhydraminos, those with medical diseases , fetuses with congenital fetal malformation

Study procedures

After assessing the eligibility criteria, all patients signed informed consent & were subjected to a

complete history taking as well as physical examinations. Ultrasound examination either on the day of delivery or within one week before delivery by using 2D voluson pro-730 ultrasound equipped with a 3 to 5 MHz convex array sector transducer with comment on: (placental location and maturity, fetal biometry (BBD, HC, FL, AC), estimated fetal weight and amniotic fluid index . The fetal heart is examined in a systematic manner (the four-chamber view, the outflow tracts and the three-vessel view). At the axial view of the thorax, with the fetus at rest without fetal breathing movements, the examiner followed the MPA until midway between the pulmonary valve and the bifurcation of the right and left branches (Image 1). The pulsed Doppler sample gate was adjusted to 3mm and the angle of insonation was maintained at < 15°. Doppler gain and scale were adjusted for optimal velocity waveform display clearly showing the peak systolic velocity (PSV) and early diastolic notch. The MPA Doppler waveform appeared with its characteristic shape. Characteristic shapes for MPA waveform was very important for differentiating it from wave of ductus arteriosus, which was rounded, fuller and triangular in shape with greater diastolic flow. Post optimal fetal MPA waveform obtained, relevant Doppler velocity variables are manually trace 3 times and averages taken. Variables include systolic/diastolic %, pulsatility index, resistance index, PSV and At/Et %. For obtaining At/Et, time interval from ventricular systole begin to peak velocity (At) divided by time interval started from begin to ventricular systole end (Figure 1).

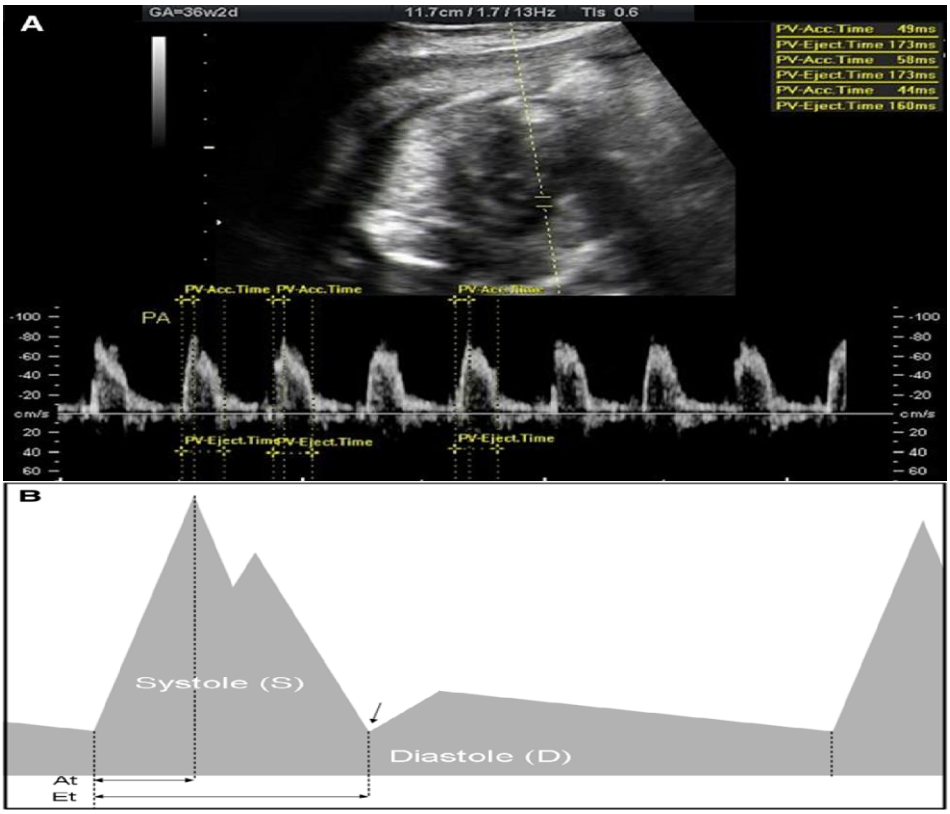

Figure 1: A, Blood flow velocity waveform measurement during main pulmonary artery in normal fetus was show. B, A different parameters are measure and/or calculate from FPAF waveform of single cardiac cycle, include S/D %, PI _ [S-D]/A, RI _ [S-D]/S, At, and Et.

Clinical assessment of the neonate

Upon delivery, the neonatal sex was recorded. A pediatrician, handled neonate. Neonatal birth weight and Apgar scores (1 and 5 min) were reported. RDS diagnosis is based on clinical signs of respiratory distress, supplemental oxygen and typical chest X-ray, air bronchograms and ground glass appearance. Need &

duration of neonatal intensive care stay were regestired.

Primary Fetal Outcome Measures:

RDS diagnosed if at least 2 of 3 from these criterias presented:

1) Respiratory failure Evidences shortly post birth and increase oxygen required for more than 24 hours.

2) Radiographic evidence of hyaline membrane diseases as: reticulonodular pattern appearance.

3) Response to exogenous pulmonary surfactant.

Secondary Outcome Measures:

Incubation Need was recorded, if pediatrician decided to incubate neonate. Incubation reason as ventilation, was registered .

Statistical Analysis

For statistical analysis, we used the Statistical Packages for Software Sciences (SPSS) version 21. Descriptive analysis was performed to describe the patients' characteristics. We reported the qualitative data as frequencies and percentages, while the quantitative data were reported as mean and standard deviation (SD). We used the Fisher test to compare the categorical variables. $P \leq 0.05$ consider significantly value.

RESULTS

population Characteristic's

We included 100 patients in our study.

Table (1) Distribution of the studied patients according to demographic and obstetric data:

N=100	Parameter
28.28 ± 4.472 20 – 39	Age (year): M ± SD Range
2.98 ± 1.22 1 – 6	Gravidity: M ± SD Range
1.82 ± 1.173 0 – 5	Parity: Mean ± SD Range
38.354 ± 1.344 36 – 39	Gestational age at delivery: Mean ± SD Range

Table (2) Relation between development of RDS and maternal baseline data:

Test		Development of RDS		Parameter
p	**t/Z**	**No**	**Yes**	
		N=83 (%)	**N=17 (%)**	
0.167	1.409	28.33 ± 4.53 20 – 39	27.65 ± 3.89 20 – 32	Age Mean ± SD Range
0.943	-0.072	3.04 ± 1.194 1 – 6	2.65 ± 1.272 1 – 5	Gravidity: Mean ± SD Range
0.934	-0.083	1.87 ± 1.135 0 – 5	1.53 ± 1.281 0 – 4	Parity: Mean ± SD Range
<0.001**	-12.141	38.647 ± 1.037 37 – 41	36.956 ± 1.75 36 – 41	GA at delivery Mean ± SD Range

Z Mann Whitney test t Independent sample t test **p≤0.01 is statistically highly significant

No significantly relation among developing RDS and either maternal age, parity or gravidity. On the other hand, there is significant relation between development of RDS and gestational age at delivery (lower in those who had developed RDS).

Table (3) Distribution of the studied patients according to mode of delivery:

N=100	Parameter
100 (100%)	Mode of delivery: CS
78 (78%) 22 (22%)	Type of CS: Elective Urgent

All patients had delivered by CS. Seventy-eight percent of them had elective CS.

Table (4) Relation between RDS development and mode of delivery:

Test		RDS		
p	χ^2	**No**	**Yes**	
		N=86 (%)	**N=17 (%)**	
<0.001**	Fisher	7 (8.4) 76 (91.6)	15 (88.2) 2 (11.8)	Mode of delivery: Urgent CS Elective CS

χ^2Chi square test t Independent sample t test **p≤0.01 is statistically highly significant

There is statistically significant relation between development of RDS and mode of delivery (larger percentage of those had developed RDS delivered by urgent CS mode).

Ultrasound examination

Table (5) Distribution of the studied patients according to result of ultrasonographic examination:

N=100	Parameter
7.37 ± 1.502 5 – 10	Amniotic fluid index: Mean ± SD Range
3122.0 ± 428.665 2200 – 3800	Expected fetal weight (g): Mean ± SD Range
38.365 ± 1.372 35 weeks and 3 days – 41 weeks and 2 days	Gestational age (week): Mean ± SD Range

Table (6) Relation between development of RDS and ultrasonographic data:

Test		RDS		Parameter
p	**t**	**No**	**Yes**	
		N=83 (%)	**N=17 (%)**	
<0.001**	-6.183	7.593 ± 1.442 5 – 10	6 ± 1.109 5 – 8	Amniotic fluid index: Mean ± SD Range
<0.001**	-11.272	3257.83 ± 315.12 2700 – 3800	2458.82 ± 255.1 2200 – 3000	Expected fetal weight(g): Mean ± SD Range
0.001**	-3.834	38.66 ± 1.055 37 , 41+2day	36.92 ± 1.809 35+3 d, 41 week	Gestational age (week): Mean ± SD Range

t Independent sample t test **p≤0.01 is statistically highly significant

There is statistically significant relation between development of RDS and amniotic fluid index, expected fetal weight and estimated gestational age. (All were significantly lower in those who had developed RDS).

Pulmonary artery Doppler indices

Table (7) Relation between development of RDS and Doppler parameters of the studied patients:

Test		RDS development		Doppler parameters
p	**t**	**No**	**Yes**	
		N=83 (%)	**N=17 (%)**	
0.015*	2.688	6.864 ± 0.121 6.68 – 7.32	6.994 ± 0.121 6.76 – 7.31	S/D ratio Mean ± SD Range
<0.001**	5.864	2.155 ± 0.024 2.1 – 2.21	2.243 ± 0.06 2.11 – 2.29	PI (cm/S) Mean ± SD Range
<0.001**	7.005	0.757 ± 0.02 0.71 – 0.79	0.822 ± 0.038 0.75 – 0.88	RI (cm/S) Mean ± SD Range
0.143	-1.475	68.489 ± 3.309 65.78 – 76.5	67.11 ± 4.41 64.45 – 76.35	PSV (cm/S): Mean ± SD Range
<0.001**	-6.127	0.327 ± 0.021 0.28 – 0.392	0.242 ± 0.055 0.206 – 0.392	AT/ET ratio: Mean ± SD Range

t Independent sample t test *p<0.05 is statistically significant **p≤0.001 is statistically highly significant

There is statistically significant relation between RDS development and each of S/D ratio, PI, RI, and AT/ET ratio (S/D ratio, PI and RI were significantly higher in neonates had RDS while those patients had significantly lower AT/ET ratio). There is statistically non-significant relation between RDS development and PSV.

Table (8) Performance of AT/ET ratio in diagnosis of RDS among the studied neonates:

p	Accuracy	NPV	PPV	Specificity	Sensitivity	AUC	Cutoff
<0.001**	95%	96.4%	87.5%	97.6%	82.4%	0.868	<0.283

**p≤0.001 is statistically highly significant

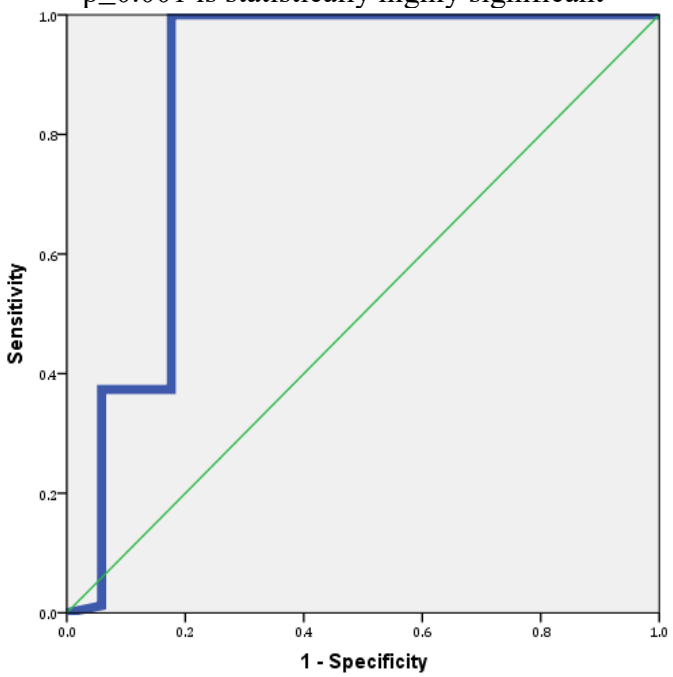

Figure (2) ROC curve showing performance of AT/ET in diagnosis of RDS among the studied neonates

The best cutoff of AT/ET ratio in diagnosis of respiratory distress among the studied neonates was<0.283 with area under curve 0.868 with sensitivity 82.4%, specificity 97.6%, positive predictive value (PPV) 87.5%, negative predictive value (NPV) 96.4% and accuracy 95% (p<0.05)

Table (9) Performance of Doppler parameters in diagnosis of respiratory distress among neonates:

Total	RDS		Doppler parameter
	No	**Yes**	
15	1	14	Positive
85	82	3	Negative
100	83	17	Total

Positive if cutoff of 3 out of the 5 markers fulfill suggestion of RDS

p	Kappa	Accuracy	NPV	PPV	Specificity	Sensitivity
<0.001**	0.851	96%	96.5%	93.3%	98.8%	82.4%

Doppler parameter (if cutoff of 3 out of the 5 markers fulfill suggestion of RDS development) can diagnose RDS in 14 out of 17 neonates that had been actually had RDS and can rule out RDS in all those who had never developed RDS) with sensitivity 82.4%, specificity 98.8%, PPV 93.3%, NPV 96.5% and accuracy 96%. There is strong agreement between both parameters

Neonatal assessment

Table (10) Distribution of the studied patients according to neonatal parameters

N=100	Parameter
3078.0 ± 451.641 2000 – 4000	Neonatal birth weight (g): Mean ± SD Range
45 (45%) 55 (55%)	Sex: Female Male
17 (17%) 83 (83%)	APGAR at 1 minute: <7 ≥7
14 (14%) 86 (86%)	APGAR at 5 minutes: <7 ≥7
86 (86%) 14 (14%)	NICU admission: No Yes
83 (83%) 17 (17%)	RDS: No Yes
20 (20%) 80 (80%)	Dexa administration: No Yes

Female represented 45% of them. Seventeen and fourteen percent of them had APGAR scores<7 at 1 and 5 minutes respectively. Seventeen percent has developed RDS while, Fourteen percent was admitted to NICU.

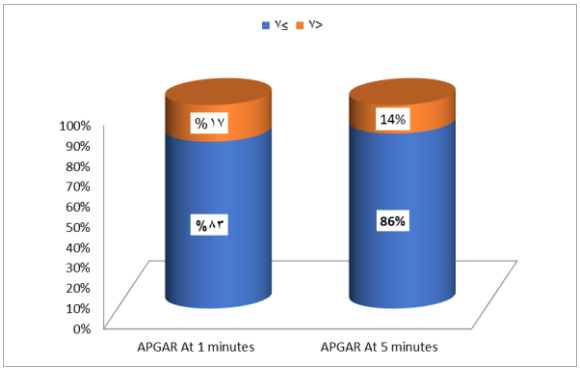

Figure (3) Compound bar chart showing distribution of the studied patents according to APGAR score at 1 and 5 minutes.

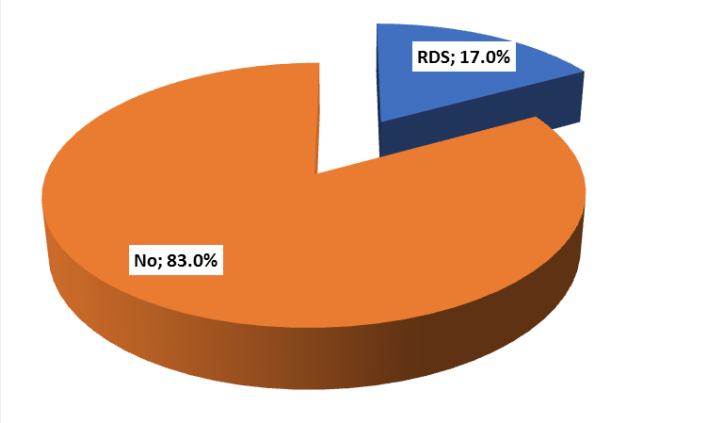

Figure (4) Pie chart showing distribution of the studied patients according to RDS development

Table (11) Relation between development of RDS and neonatal data:

Test		RDS development		Parameter
p	**t/χ^2**	**No**	**Yes**	
		N=83 (%)	**N=17 (%)**	
<0.001**	-13.167	3227.71 ± 319.42 2600 – 4000	2347.06 ± 234.83 2000 – 2800	Actual birth weight (g): Mean ± SD Range
0.003*	Fisher	43 (51.8) 40 (48.2)	2 (88.2) 15 (11.8)	Sex: Female Male
<0.001**	Fisher	1 (1.2) 82 (98.8)	17 (100) 0 (0)	APGAR at 1 minute <7 ≥7
<0.001**	Fisher	0 (0) 83 (100)	14 (82.4) 3 (17.6)	APGAR at 5 minute <7 ≥7
<0.001**	Fisher	5 (6) 78 (94)	15 (88.2) 2 (11.8)	Dexa administration: No Yes

χ^2Chi square test t Independent sample t test **p≤0.01 is statistically highly significant

There is statistically significant relation between development of RDS and actual birth weight (it was significantly lower in those who had developed RDS). There is also statistically significant relation between RDS development and neonatal sex, APGAR at 1 and 5 minute and maternal antenatal dexa administration.

DISCUSSION

fetal MPA Doppler value examination helped in predicting neonatal RDS development in late preterm and early term fetuses. Late preterm are premature newborns delivered between 34 and 36+6 weeks, early term infants were delivered in 37 and 38+6 weeks **(32).**

Before 34 weeks, fetal lung immaturity risk's was very high, and FLM examination was not useful. Fetuses delivered post 39 weeks had low RDS risk's (**33**, **34)**.

Between 34 and 38+6 weeks gestation is area of possibility of RDS developing, where obstetrician need to test for FLM before trying to deliver the baby **(35).**

ACOG and SMFM guidelines advise clinicians against use FLM test outcome in decisions to deliver for different pregnancy scenarios: well-dated pregnancies **(36)**, suboptimally dated pregnancies **(37)**, non-medically indicated early pregnancies **(36, 32)**, and medically indicated early pregnancies **(32)**.

Results revealed that continuous positive airway pressure and hyperbilirubinemia requiring phototherapy increased in non-medically indicated early term births with FLM results suggestive of mature lungs (**35)**.

Neonates delivered at 36–38 weeks have increased RDS risk's, hyperbilirubinemia, and hypoglycemia despite mature FLM **(38).**

Society of Obstetrics and Gynecologists of Canada updated guidelines regarded to using antenatal corticosteroid therapy and emphasized that, balance between steroids benefits in reduced perinatal morbidities against its different complications must be weighted (**39)**.

European consensus guidelines on managing respiratory distress had updated every 3 years since 2007 **(40)**. Single sentence in European guidelines (2019) regarding to FLM testing. (In many cases establishment of FLM might be better than giving steroids to women **(40).**
Among all proposed US parameters for GA, none is very precise particularly when taken for first time throughout third trimester. US is +3-4 weeks less accurate in third trimester , which creates problem for Obstetrician in deciding fetal maturity (**41).**

In this study, fetal MPA Doppler indices for predicting FLM were examined in fetuses in the third trimester. The results of this study have shown a decreased impedance in the pulmonary vasculature as the fetus approaches term. Compared with fetuses that did not develop neonatal RDS, fetuses that developed RDS had significantly lower At/Et and higher PI , RI and S/D ratio.
Chaoui et al. reported the use of numerical variables to apply over the pulmonary Doppler wave including the acceleration / ejection time ratio to evaluate the pulmonary vascular resistance. This ratio correlates inversely with the arterial pressure of the vessel being evaluated (**29. 42)** and acceleration time <100 ms indicate a high pulmonary hypertension probabilities (**25)**.

Pulmonary flow analysis was reliable tool for evaluating pulmonary pressure when evaluated total pulmonary resistance (**43).**

Pulmonary artery pressure in neonates with RDS was increased and it decreased as RDS resolved . In contrast, when condition was evolves into chronic lung diseases (**44)** (**45)**.

We have observed the MPA At/Et was positively correlated, and S/D ratio, PI and RI inverse correlated with GA. These results are totally consistent with those of **23**, **29** and **46**.

Inverse corrlation between GA and RI might be caused by increased lumen of pulmonary vessels, vascular elasticity and continued pulmonary angiogenesis with advancing GA (**22** and **47)**.

The best cutoff of AT/ET ratio in diagnosis of respiratory distress among our studied neonates was<0.283 with area under curve 0.868 with sensitivity 82.4%, specificity 97.6%, positive predictive value (PPV) 87.5%, negative predictive value (NPV) 96.4% and accuracy 95% ($p<0.05$) .The ability of S/D ratio , PI , RI and PSV to predict RDS development had the same sensitivity but lower specificity compared with that of At/Et .These results are consistent with prior studies at similar GAs . **(29, 46, 30, 48).**

It was concluded from our results that if cutoff of 3 out of the 5 markers (AT/ET , S/D ratio , PI , RI ,PSV) fulfill suggestion of RDS development) , RDS can be diagnosed with sensitivity 82.4%, specificity 98.8%, PPV 93.3%, NPV 96.5% and accuracy 96%.

A study which is consistent with our results showed the MPA At/Et and the TDx- FLM-II are positively correlated (**18),** and one study not coping with our results is that At/Et inversely correlated with lecithin/sphingomyelin ratio obtained by amniocentesis **(30)** . However, the association of At/Et with the development of clinical RDS could not be studied as their study sample size (29 fetuses) was low with only one infant diagnosed with RDS. our results coincide with the established physiologic principles of fetal lung maturation.

CONCLUSION

PATET measuring might provide noninvasive means of determination of FLM with acceptable sensitivity level, and predictive values. More studies should involve broader gestational ages range and using bigger samples size. Broader gestational age might illustrate better correlation coefficient and predictive value. This method had potentiality to be applied clinically, thereby avoid several invasive amniocenteses complications in future.

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Ethics approval and consent to participate:
Our investigation protocol approve by Institutional Review Board (IRB) of Faculty of Medicine, Zagazig University, Egypt (IRB approval no. ZU-IRB #705-3-3-2013).

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List of Abbreviations
RDS Respiratory distress syndrome
FLM Fetal lung maturation
AT/ET Aacceleration time /ejection time
S/D Systolic/diastolic ratio
PSV Peaks ystolic velocity

RI Resistance index
PI Pulsatility index

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