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Role of fetal main pulmonary artery doppler indices in the prediction of fetal lung maturity

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ABSTRACT

Background: In terms of pregnancy termination, an accurate and precise assessment of fetal lung maturity is considered as the most importance factor for determining the ideal time. A non-invasive way to do so is amniocentesis, however it is invasive way which can lead to little but real hazard to the pregnancy. So, noninvasive sonographic procedures to assess lung development is most required.
Aim of the study: To study the role of fetal main pulmonary artery Doppler (MPA) indices in expectation of Fetal Lung Maturity (FLM) and determine a highly sensitive and specific cut point of Doppler indices.
Patients and Methods: Our prospective cohort study included 200 pregnant women 38 weeks fulfilling the inclusion and exclusion criteria, A number of distinctive parameters where measured from the fetal pulmonary artery flow (FPAF) waveform (At/Et, S/D, PSV, PI and RI) for determination of neonatal Respiratory Distress Disorder (RDS) and compare the findings found in Doppler with clinical the resultant outcome.
Results: About 46 (23%) fetuses who were RDS (+ve) and 154 (77%) fetuses without RDS (-ve). There was a positive correlation between At/Et and PSV, and an inversely correlation between PI and RI with RDS. There was no significant change in the S/D ratio. Strongest correlation was found with At/Et. AT/ET was significantly lower in the RDS +ve group and the development of neonatal RDS was anticipated with a cutoff point of 0.32, with a high sensitivity specificity, and accuracy (98.0%, 92.0%, and 95.0%) respectively.
Conclusion: By using MPA At/Et FLM and Neonatal RDS can be anticipated with both high sensitivity and specificity.

Keywords: *Fetal Lung Maturity; Neonatal Respiratory Distress Syndrome; Fetal Main Pulmonary Artery Doppler Indices*

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INTRODUCTION

Neonatal respiratory distress syndrome (RDS) is the respiratory impairment at or shortly once birth and remains as significant reason behind neonatal mortality and morbidity. [1] RDS can lead to neonatal morbidity and mortality in both early term and late preterm periods[1,2] , where elective delivery before 39 weeks is associated with a preventable increase in neonatal morbidity and admissions to the neonatal intensive care unit (NICU) leading to more costs.[3] Taking into consideration in several conditions of high risk pregnancies, obstetric care providers, decide to terminate pregnancy before spontaneous delivery is begun. In terms of detremaning the optimal time for pregnancy termination , one of the most concerns is detecting those fetuses whom are at risk for RDS. As RDS risk diminishes with the increase of the gestational age, since the last fetal organs to practically develop are lungs.[4]

Before labor, it appears rationale to survey fetal lung maturity (FLM). Biochemical tests have been developed as lecithin/sphingomyelin ratio, absence or presence of phosphatidyl glycerol and amniotic liquid, fluorescent polarization, foam stability or shake test lamellar body count have been utilized; in any case, all rely on amniocentesis, which is an invasive method to determine foetal lung maturity and the risk of neonatal RDS and offer obstetricians help in choosing the delivery date.[5]

The biological, chemical and physical properties of the amniotic liquid are considered as the primary standard tests of foetal lung maturity by an invasive technique that presents potential pregnancy's problems, such as rupture of membranes

prematurely, preterm labour, , fetomaternal hemorrhage, placental abruption, fetal injury, and even death for the mother or the fetus[6-9]. Therefore, Historically, amniocentesis for foetal lung maturity has been done for these purposes. Nevertheless risks that are linked to amniocentesis in final trimester are comparatively low, there have been documented complications.[2,10]

Therefore, there is a need for noninvasive test. The sonographic echogenicity of fetal lung changes in an anticipated way during pregnancy.[4] Latest results have shown that the percentage of foetal main pulmonary arteries can anticipate foetal lung maturity in relation to the clinical outcomes of the delivered foetuses or to biochemical tests of amniocentesis[6,] Dooppler velocimetry offers a simple non-invasive method to evaluate the foetal pulmonary circulation. Doppler velocimetry has been used for measuring fetal pulmonary blood flow in right or left pulmonary arteries plus peripheral branches of them, however, the rate of satisfactory Doppler records is average and disparate.[11]

Regarding all the points discussed before, we assume that “using foetal pulmonary artery Doppler indices can aid in determining FLM”. This study is going to determine, whether foetal main pulmonary artery Doppler indices could predict fetal lung maturity in term fetuses in third trimester of gestational age more than 38 weeks or not, and if so, is there a cut point of Doppler indices with high sensitivity and specificity for this reason. Our aim is to study the reliability of using foetal main pulmonary artery Doppler indices in foetal lung maturity prediction.

PATIENTS AND METHODS

This prospective cohort study was done at Gynecology and Obstetrics Department at Sayed Galal university Hospital. During the period from January 1st, 2020 till November 30st, 2020. Patients were selected from outpatient clinic, and patients admitted in Sayed Galal Obstetrics-Gynecology department. This study included 200 pregnant women who attended outpatient clinics in Sayed Galal Hospital with the following criteria: Age: 18-40, gestational age 38 weeks with living fetus, Intact fetal membranes and Expected delivery within 48 hours of admission before elective cesarean section. We excluded cases who were pregnant less than 38 weeks of gestation, multiple gestation, uncertain gestational age, diabetic or cardiac women, IUGR or congenital fetal anomalies, accidental hemorrhage associated with moderate or severe bleeding and cases suffering from polyhydramnios and oligohydramnios. for prevention of sonography false results, severe medical condition leading to misleading results.

The study was approved by the ethics committee after proper counseling. Female participants who applied for enrolment and provided informed written consent. All patients selected to take place in this study were exposed to the following: Full history taking including age, history of any medical disorders, history of any previous operations, menstrual history (last menstrual period, regularity of the cycle). Women have been scanned in supine posture. Prenatal sonographic test was done involves foetal biometry (BPD, FL and HC) for measuring the gestational age of the fetus and estimated foetal weight and to exclude retardation of the intrauterine growth or macrosomia. Amniotic fluid index was also measured. The amniotic fluid index was also calculated. The axial portion of the foetal thoracic at level of the 4-chamber cardiac view was magnified by modifying the depth, not by zooming, until most of the display is occupied by the thoracic section, eliminating visible acoustic shadows from foetal ribs or spine. After that, the foetal main pulmonary artery (MPA) was showed in order to obtain the three-vessel view by slightly translating the transducer superiorly (3VV) (Figur 1).

Inclusion criteria: Comminuted patellar fractures

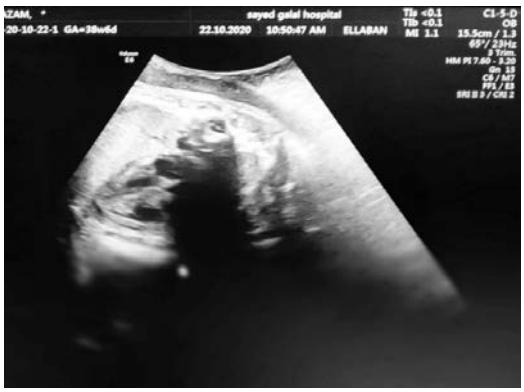

Fig 1: The 4-chamber view of the foetal heart

Pulsed Doopler sample gate is situated in the middle of foetal MPA (between pulmonary valves and pulmonary artery bifurcation). After enhancing the image as possible, we set sample gate to 3 mm. Sample gate was calibrated to 3 mm while the image was improved as much as possible. Foetal MPA Waveforms create a certain pattern "spike and dome," and small notch at the end of systole. That particular form of the MPA wave form is important to distinguish between the rounded, complete and triangular shaped ductus arteriosus waveform after the ideal foetal MPA waveform has been collected, the related Doppler velocity Parameters are measured by a manual trace three times with average measurements. Doppler Parameters contain the acceleration time (AT; time period from base to top of the PSV), ejection time (ET; from the start to the end of the ventricular systole), from these measurements AT/ET ratio was estimated (Figur. 2). Other Doppler parameters were measured using automated traces such as the peak blood flow velocity reached during systole (PSV), the pulsatility index (PI) and the resistance index (RI). After birth,

the measurement of each newborn included APGAR 1, 5minutes, the incidence of RDS and the need for NICU admissions. Respiratory distress caused by reasons differ from RDS and disorders such: Neonatal sepsis, haemodynamic collapse, symptomatic anaemia and meconium Aspiration as these conditions may particularly predispose to unreliable outcomes, Regardless of the maturity of the lung.

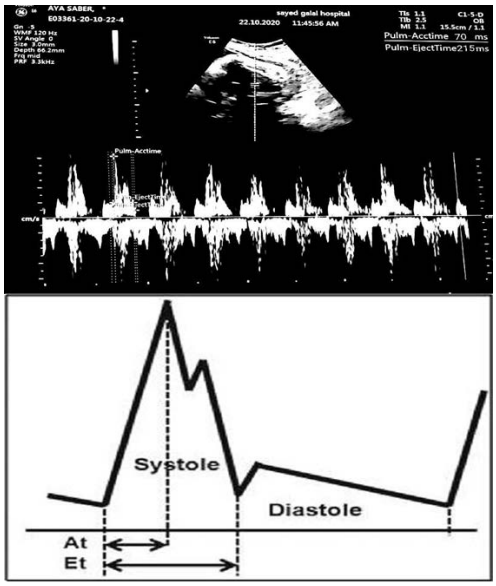

Fig 2: It shows the acceleration and ejection time. Spike and Dome Pattern.

Statistical analysis:

Data were analyzed using SPSS version 21.0. The qualitative data were presented using number and percent. In order to compare the various classes of categorical variables, Chi-square test was used. While quantitative results were represented by mean and standard deviations. Regarding normally distributed data, independent population was compared using independent t-test if they are two, while more than that were analyzed using ANOVA (F-test). Results is considered significant if two-tailed P-value was equal to or less than 0.05.

RESULTS

Therehwere no statistically significant differences in demographic data between neonatal without and with RDS (Table 1).

Regarding neonatal clinical data, there was statistically significant difference between neonates without and with RDS ($P < 0.05$). APGAR 1 min in group I ranged from 6-9 with mean value 8.05 ± 0.86 and in group II ranged from 5-8 with mean value 6.91 ± 0.87. APGAR 5m in group I ranged from 8-10 with mean value 8.92 ± 0.76 and in group II ranged from 5-8 with mean value 6.98 ± 0.84. All cases in group II need incubation (Table 2).

	Without RDS Group I		With RDS Group II		Test p
Age Range Mean SD	 19-38 28.78 6.05		 20-38 29.24 5.89		 T=0.962 0.3090
	No	%	No	%	
Parity PG MG	 72 82	 46.75 53.25	 24 22	 52.17 47.83	 X^2 =0.821 0.2604
BMI Range Mean SD	 21-31 26.45 2.99		 21.2-30 25.19 2.57		 T=1.65 0.064 N.S.

Table 1: Comparison between the studied groups regarding demographic and clinical characteristics.

	Without RDS GroupI		With RDS Group II		Test p
APGAR 1 min Range Mean SD	 6-9 8.05 0.86		 5-8 6.91 0.87		 T=3.25 0.001*
APGAR 5 m Range Mean SD	 8-10 8.92 0.76		 5-8 6.98 0.84		 T=2.98 0.001*
	No	%	No	%	
Incubation No Yes	 147 7	 95.45 4.55	 0 46	 0.0 100.0	 X^2 = 5.58 0.001*

Table 2: Comparison between neonates without and with RDS regarding neonatal clinical data.

Regarding neonatal weight, there was statistically significant difference between neonates without and with RDS ($P < 0.05$). Weight in group I ranged from 2.7-4.2 with mean value 3.20 ± 0.28 and in group II ranged from 3.07 ± 0.36. but also, there was no statistically significant difference between two groups regarding gender ($P > 0.05$) (Table 3).

According Pulmonary artery indices, the MPA At/Et was significantly lower in fetuses diagnosed with RDS compared with those without (0.29 ± 0.03 versus 0.4± 0.00,). MPA PI and RI were significantly higher mean value (3.28 ± 1.02 and 1.07 ± 0.20 cm s − 1 versus 2.6 ± 0.9 and 0.9 ± 0.2cm s – 1) whereas PSV was significantly lower in fetuses with RDS (40.39 ± 6.19 versus 50.3±10.3 cm s − 1). No statistically significant difference regarding S/D ($P > 0.05$) between the two groups (Table 4).

According to sensitivity, specificity and accuracy of PSV and AT/ET in prediction of fetal lung maturity, the PSV sensitivity was 81.0%, specificity was 84.0% and accuracy 83.0% at cut off value 45.0, while AT/ET sensitivity was 98.0, specificity was 92.0% and accuracy was 95.0% at cut off value 0.32 (Table 5 & figure 3).

	Without RDS Group I		With RDS Group II		Test p
Weight(kg) Range Mean SD	 2.7-4.2 3.20 0.28		 2.4-3.9 3.07 0.36		 T=2.66 0.0041*
	No	%	No	%	
Gender Male Female	 73 81	 47.40 52.60	 26 20	 56.52 43.48	 X^2 =0.925 0.3208 N.S.

Table 3: Comparison between neonates without and with RDS regarding neonatal weight and gender.

	Without RDS Group I	With RDS Group II	T p
PSV Range Mean SD	 35.0-69.9 50.3 10.3	 30.2-54 40.39 6.19	 5.26 0.001*
S/D Range Mean SD	 0.9-9.5 5.4 2.5	 2-9 5.44 2.08	 0.587 0.4813
PI Range Mean SD	 1-4.1 2.6 0.9	 1.6-4.9 3.28 1.02	 5.14 0.001*
RI Range Mean SD	 0.5-1.5 0.9 0.2	 0.7-1.5 1.07 0.20	 3.02 0.0285*
AT/ET Range Mean SD	 0.32-0.46 0.4 0.0	 0.23-0.33 0.29 0.03	 6.14 0.001*

Table 4: Comparison between neonates without and with RDS regarding MPA Doppler findings.

Test Result Variable(s)	Area Under the curve	Cut off value	P value	Sensitivity	Specificity	Accuracy	Asymptotic 95% C.I	
							Lower Bound	Upper Bound
PSV	.870	45.0	.0012	81.0	84.0	83.0	.803	.971
AT/ET	.992	0.32	.0001	98.0	92.0	95.0	.983	1.000

Table 5: Sensitivity, Specificity and accuracy of PSV and AT/ET in prediction of fetal lung maturity.

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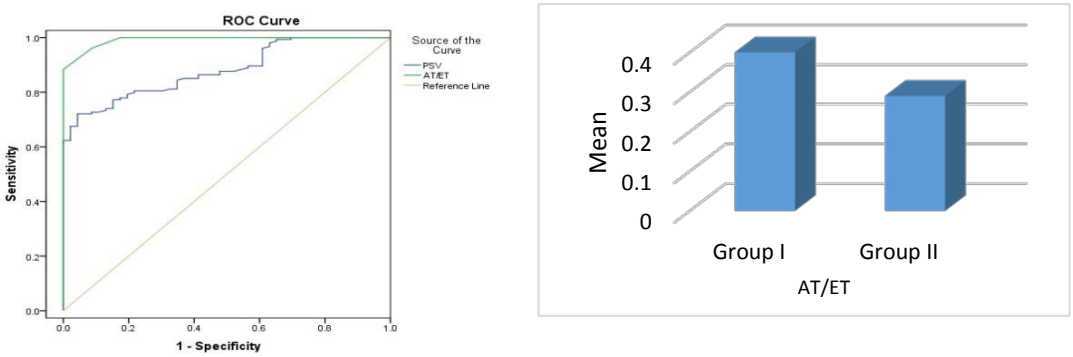

Fig 3: ROC curve for Predicition value of PSV and AT/ET in predicting the fetal lung maturity.

DISCUSSION

Respiratory distress syndrome (RDS) appears to be a significant cause of neonatal morbidity and mortality, as well as RDS incidence and severity which has an inverse proportion with the gestational age in time of birth. Precisely, the deficiency in pulmonary surfactant results in neonatal RDS specifically. As a result, several interventions have been introduced trying to prevent it.[12]

Over the past 30 years, a variety of non-invasive sonographic studies have been proposed to predict foetal pulmonary maturity, including foetal biometry, placental maturation, umbilical artery Doppler velocimetry, foetal breathing patterns and nasal fluid flow velocity waveforms, and foetal intestine and ossification centres of long foetal bones. However, none of them proved to be appropriately reproducible or reliable.[13, 14]

To predict the probability of foetal lung maturity, several antenatal tests have been introduced. Nevertheless being used commonly in the obstetric practice, they still do not have an accurate predictive value, specifically in the late periods of gestation, and requires performing amniocentesis which is invsive.[15]

Recent studies have shown that to predict fetal lung maturity, ratio in fetal main pulmonary artery can be used by biochemical studies of amniocentesis or by evaluating with the clinical outcome of the foetuses delivered.[6]

Here in this study, Fetal MPA Doppler indices were examined in (200) term feti about 38 weeks for predicting lung maturity. this gestational age (38 weeks.) was chosen as before that GA, where there is a high risk of fetal lung immaturity, and so testing of FLM in this gestational age is not useful useful to detect the cut point at which we can predict FLM. About 46 feti were RDS (+ve) and 154 feti without RDS. Neonatal RDS was diagnosed with foetal blinded MPA Doppler waveform findings when there is at least two out of three of these parameters, Clinically: respiratory failure signs (retraction, tachypnea, and, or nasal flairing) soon after birth and an intensified need for oxygen (fractional concentration of inspired oxygen > 0/4) for more than 24 hours. Radiographic: hyaline membrane disease evidences such as: reticulo-nodular sequence, air bronchogram and ground glass presentation in the absence of other respiratory diseases. Reacts to exogenous pulmonary surfactants. This research revealed that in compare to foetuses who have not develop neonatal RDS, fetuses that developed RDS had significantly lower At/Et and PSV and higher PI and RI. This means that foetuses who develop RDS have higher pulmonary vascular resistance and pressure and lower pulmonary blood flow compared with fetuses that do not develop RDS. A cut of point of 0.32 in the AT/ ET ration anticipated the development of neonatal RDS with a high sensitivity, specificity, and accuracy (98.0%, 92.0%, and 95.0% respectively).

Our findings have been in agreement with Schenone et al study who compared the AT/ET to albumin/surfactant ratio. Schenone and his colleagues found a positive correlation between ratio in fetal MPA and TDx-FLM-II in the amniotic fluid. This means that an increasing in the At/Et ration has association with more mature lung and less risk to develop RDS, and that supports our findings, They proved that a PATET cutoff of 0.3149 has a sensitivity of 73%, specificity of 93% predicting TDx-FLM II results, with no study of clinical end points of feti and development of RDS.[14]

Guan and his colleagues explain differences in foetal main pulmonary artery (MPA) waveforms in the Doppler during the gestation from 22 to 42 weeks, as well as their neonatal respiratory distress syndrome (RDS) predictive values and important and positive linear correlation between AT, AT/ET ratio and the gestational age, peak systolic velocity and average velocity were identified. Fetal MPA Doppler velocimetry could be accurately done during pregnancy. AT and AT/ET ratios of the foetal MPA Doppler waveform can aid in recognizing the foetuses who have the risk to develop neonatal RDS, these results match with our study, but here our study shows that also pulmonary RI, PSV show statically significant correlation. MPA At/Et and PS were

positively correlated, whereas RI has inverse correlation in the development of RDS, strongest correlation was regarding At/Et ratio, In the second phase of Guan study, the study was limited and didn't determine a cut point of MPA doppler indices.[5]

Azpurua et al.[6] showed that the acceleration time/ejection time ratio in the FPA and the amniotic fluid lecithin/sphingomyelin ratio has an inverse correlation. Which means the Ultrasound measurement of foetal pulmonary artery blood flow can promise a new non-invasive procedure to assess the foetal lung maturity, but their study had limitations of being small sample size (29 feti) with only one infant with RDS, also using an invasive procedure with little but serious risk to pregnancy, but here the study depends on non-invasive safe widely accepted available method. [6]

However, our results contradicted Kim et al.[7] as he found that Pulmonary artery AT/ET ratio has an inverse correlation to the maturity of the fetal lung.

Kim et al.[7] compared fetal MPA Doppler indicies results with the clinical outcome of feti after birth as developing RDS. They described a cut point of ratio (0.326) for predicting RDS, and claimed that more than 0.326, means subsequent development of RDS.

CONCLUSION

Evaluation of Fetal Mean Pulmonary Artery Doppler by ultrasound can be used as a rapid noninvasive accurate method for prediction of Fetal Lung Maturity and neonatal RDS. MPA Doppler indices, as At/Et, RI, PSV, and PI indices can be used for prediction of FLM. The strongest correlation was found as regarding At/Et and the cut point of 0.32 is achieved by a high sensitivity and specificity.

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