Prediction of Fetal Lung Maturity in Diabetic Women by Pulmonary Artery Doppler study (Controlled Clinical Trial)

Original Article

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ABSTRACT

Objective: The goal of this controlled clinical experiment was to use pulmonary artery Doppler to predict foetal lung maturity in diabetic pregnant women having elective uncomplicated caesarean sections.

Materials and Methods: From September 2017 to March 2018, the study was carried out at the Ain Shams University Maternity Hospital's Faculty of Medicine. This research, which included 80 patients who were ready to undergo foetal pulmonary artery Doppler ultrasonography, was divided into two groups as follows: 40 pregnant women with managed diabetes mellitus made up the case group. A total of 40 pregnant women without diabetes mellitus complications made up the (control group). The proximal part of the main pulmonary artery is where the measurements of the foetal pulmonary artery flow waveform (FPAF) were made. The FPAF waveform (average values of 3 waves) was used to quantify the systolic/diastolic ratio, pulsatility index (PI), resistance index (RI), and acceleration time/ejection time ratio (At/Et). With the same U/S equipment, a senior single sonographer completed all measurements. Senior neonatologists performed infant resuscitation and evaluation after birth.

Results: Regarding the PA At/Et ratio, there were statistically significant differences between infants born to mothers with managed diabetes and children delivered without RDS; however, there were no statistically significant changes with regard to the other PA Doppler parameters. The Receiver-operating characteristic (ROC) curve for predicting RDS in patients with controlled DM using PA At/Et ratio had excellent predictive value (AUC=0.740, *p-value 0.012*), and the mean PA At/Et ratio was significantly higher in infants born with RDS than infants born without RDS in women with controlled DM (0.34 vs 0.21, respectively). A cutoff criterion of PA At/Et ratio >0.25 exhibited an 88.9% specificity and a 75% sensitivity.

Conclusion: PA Further research should focus on individuals with difficult and uncontrolled diabetes mellitus and a bigger sample size in order to predict the foetal lung maturity in managed DM patients using the At/Et ratio.

Key Words: Diabetes mellitus, fetal lung maturity, pulmonary artery doppler.

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INTRODUCTION

Three to five percent of all pregnancies are complicated by diabetes mellitus, which is also a substantial contributor to maternal morbidity and neonatal morbidity and death'.

A lack of pulmonary surfactant, a naturally occurring phospholipid necessary to reduce surface tension inside the alveoli to avoid alveolar collapse, results in neonatal respiratory distress syndrome (RDS), which is respiratory impairment that manifests at or soon after birth[2].

Because the lungs are the last foetal organs to properly develop, the risk of newborn RDS declines with gestational age. Despite the fact that neonatal RDS does not just occur following preterm births, it is frequently thought of as a disorder of premature babies[3].

Preterm births can occur naturally after the start of labour, whether or not there has been a preterm rupture of the membranes. Preterm births can also occasionally be doctor-initiated. Births can be accidentally premature due to gestational age (GA) mistake, which is frequently observed in women who give birth by elective CS[4]. Obstetricians sometimes choose to end pregnancies before they spontaneously begin to give birth in certain circumstances. Finding those foetuses that are at risk for RDS is one of the biggest concerns when deciding whether in high-risk pregnancies to terminate the pregnancy. Several techniques are described to assess foetal lung maturity (FLM), including amniocentesis, an invasive procedure associated with a small but real risk to pregnancy,

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including preterm labour, premature rupture of the membranes, abruption plancenta, and measurement of the lecithin / sphingomyelin (L/S) ratio, presence or absence of phosphatidyl glycerol (PG), fluorescent polarisation test, foam stability or shake[5].

These factors have led to a long-standing search for noninvasive ultrasound techniques to evaluate foetal lung maturity, but efforts to date (including measurements of lung volumes, gestational age, epiphysis centres, placental grading, and estimated foetal weight) have been ineffective in clinical settings. As the lungs grow throughout pregnancy, so does the pulmonary vasculature, where the total quantity of smooth muscle tissue increases, the number of pulmonary arteries increases, and the pulmonary artery vascular resistance somewhat lowers. This results in a steady rise in pulmonary blood flow[6].

Previous research has demonstrated that foetal pulmonary artery Doppler waveforms in hypoplastic foetal lungs and predictable changes in foetal lung echogenicity during pregnancy and a progressive increase in ratio correlate with increasing gestational age[7].

Previous research 210 has shown that the ratio of acceleration to ejection time in the foetal main pulmonary artery can predict the foetal lung maturity as determined by amniocentesis biochemical tests or by comparing the clinical outcome of delivered fetuses[6.11].

The purpose of the study is to evaluate the reliability of foetal pulmonary artery Doppler in predicting the maturity of the fetus's lungs in diabetic pregnant mothers

PATIENTS AND METHODS

This study was a controlled clinical trial (prospective study) during the period from September 2017 till July 2018. 80 pregnant women planned to undergo elective uncomplicated cesarean section, in the Faculty of Medicine, Ain Shams University Maternity Hospital, were enrolled in this study. Women were prepared to do fetal pulmonary artery Doppler ultrasound and designed as the following 2 groups:

(Case group): included 40 pregnant women with controlled diabetes mellitus.

(Control group): included 40 pregnant women not complicated with diabetes mellitus.

Inclusion Criteria:

Gestational age is above 37 weeks and Singleton pregnancy.

Exclusion Criteria:

Pregnant females less than 37 weeks of gestational age, Multiple pregnancy, Uncertain gestational age, History of cardiac or hypertension disease, Obstetric hemorrhage as antepartum hemorrhage. Intrauterine growth retardation, Congenital anomalies, Amniotic fluid index less than 10 or more than 20 and pregnant women complicated with uncontrolled diabetes mellitus.

Women included in this study were subjected to the following: Informed written consent approved by ethical committee of the department obtained from the patient after explaining the aim of the research. Full history taking, General examination. Abdominal examination and Investigations [Fasting blood sugar, 2h-postprandial blood sugar and Glycosylated Hemoglobin (HBA1C)]. Abdominal U/S: by two-dimensional abdominal ultrasound in real time. The identical equipment was used by Dr. Mohammed El Sherbiny to do all measurements (Samsung H60, Convex probe 2-8 MHz, made in South Korea). To get a 4 chamber image of the heart, women were positioned in a semi-recumbent position with an axial plane through the foetal thorax. Rotating the transducer from the 4 chamber view to the short axis image of the heart allowed one to trace the major pulmonary artery all the way to where it splits into right and left branches. We employed both pulsed and coloured Doppler. The proximal part of the main pulmonary artery is where the measurements of the foetal pulmonary artery flow waveform (FPAF) were made. The FPAF waveform (average values of 3 waves) was used to quantify the systolic/diastolic ratio, pulsatility index (PI), resistance index (RI), and acceleration time/ejection time ratio (At/Et). (At) denotes the period of time between the onset of ventricular systole and the attainment of peak velocity. The period of time between the start and finish of ventricular systole is referred to as (Et). Measurements were made of foetal biometry, amniotic fluid index, and umbilical artery Doppler RI. Neonatal resuscitation and assessment was done by senior neonatologist: Apgar score at 5 and 10 minutes, need for admission to neonatal ICU and the development of RDS (Diagnosed by the presence of at least 2 of the following 3 criteria):

a- Evidence of respiratory compromise (tachypnea, retractions, and/or nasal flaring) shortly after delivery and a persistent oxygen requirement for longer than 24 hours.

b- Administration of exogenous pulmonary surfactant.

c- Radiographic evidence of hyaline membrane disease.

Consent procedure:

Every patient provided informed consent. The researcher ensured that potential research subjects, or their

authorised representatives, were fully informed about the nature and goal of the clinical study, the possible risks and benefits of study participation, and their rights as research subjects by putting in place an appropriate informed consent process. Before executing any study-specific procedures on the subject, the investigator first obtained the written, signed informed consent of each subject, or the subject's authorised representative. The original, duly-signed informed consent form was kept by the investigator.

Subject confidentiality:

All evaluation forms, reports and other records not included unique personal data to maintain subject confidentially.

Sample size justification:

The effect size from the previous study was found to be 0, 327, and setting a (two-sided) test at 0,05 and 0,3 at 0,1 the sample size was found to be 80 patients to be divided into 2 groups in accordance with the null hypothesis that there is no correlation between pulmonary artery peak systolic velocity (PSV)and Respiratory Distress Syndrome (RDS) (GAFA Moety *et al*., 2015).

Statistical methods:

Data were analyzed using NCSS© 12 Statistical Software 2018 (NCSS, LLC. Kaysville, Utah, USA). Continuous numerical data were presented as mean and standard deviation and intergroup differences were compared using the unpaired t test. Categorical data were presented as number and percentage and intergroup differences were compared using Fisher's exact test. Ordinal data were compared using the chi-squared test for trend. Correlations were tested using the Pearson product-moment.

The correlation coefficient (Pearson r) is interpreted as in Table 1:

Correlation coefficient	Strength of correlation
<0.2	Very weak
0.2-0.39	Weak
0.4-0.59	Moderate
0.6-0.79	Strong
0.8-1.0	Very strong

The predictive value of echocardiographic measures was examined using receiver-operating characteristic (ROC) curve analysis. The area under the ROC curve (AUC) is interpreted as in Table 2:

teasntae Area under ROC curve (AUC)	Diagnostic value
0.9-1.0	Excellent
0.8-0.89	Good
0.7-0.79	Fair
0.6-0.69	Poor
<0.6	Fail

P-values <0.05 were considered statistically significant.

ROC curve was used to evaluate the performance of different tests differentiate between certain groups.

Diagnostic characteristics were calculated as follows:

- Sensitivity = (True positive test/Total positive golden) x 100.

- Specificity = (True negative test/Total negative golden) x 100.

RESULTS

Table 3: Comparison of patients with or without DM: Numerical variables

Variable	Non-diabetic (n=40)		Controlled DM (n=40)			95%CI	*p-value*	S
	Mean	SD	Mean	SD	Difference			
Age(yr)	28.0	3.9	27.4	2.7	-0.60	-2.09 to 0.89	*0.425*	NS
GA(wk)	37.4	0.8	37.2	0.7	-0.14	-0.47 to 0.20	*0.421*	NS
AFI	11.1	1.1	12.0	1.6	0.95	0.35 to 1.55	*0.002*	NS
BMI(kg/m^2)	26.6	2.0	27.7	1.5	1.03	0.24 to 1.81	*0.011*	S
FBS(mg/dl)	86.5	12.9	96.4	14.7	9.95	3.79 to 16.11	*0.002*	S
PBS(mg/dl)	143.6	11.0	150.9	7.7	7.30	3.07 to 11.53	*0.001*	S
HbA1c(%)	5.4	0.6	6.0	0.4	0.68	0.45 to 0.90	*<0.0001*	S
EFW(g)	3050.0	171.0	3282.5	164.7	232.5	157.8 to 307.2	*<0.0001*	S
NBW(g)	3136.3	158.5	3652.5	159.3	516.3	445.5 to 587.0	*<0.0001*	S

Data are mean and standard deviation (SD), 95% CI = 95% confidence interval, *Unpaired t test, s = Significant, NS= non-significant.

Table 3. shows that there were statistical significant differences between women in the Non-diabetic group and Controlled DM group as regard BMI, FBS, PPBS, HbA1C, EFW, NBW but there were no statistical significant differences between the two groups as regard mean age, GA, AFI.

Table 4: Comparison of patients with or without DM in Doppler indices and Apgar score

Variable	Non-diabetic (n=40)		Controlled DM (n=40)			95% CI	*p-value*	S
	Mean	SD	Mean	SD	Difference			
PA PSV(cm/s)	62.90	13.78	72.63	10.37	9.73	4.30 to 15.16	0.001	S
PA EDV(cm/s)	6.72	2.13	6.62	2.13	-0.10	-1.05 to 0.85	0.835	S
PA S/D ratio	10.20	13.68	8.01	8.62	-2.20	-7.29 to 2.89	0.393	NS
PA PI	2.10	0.44	1.97	0.29	-0.14	-0.30 to 0.030	0.108	NS
PA RI	0.89	0.10	0.91	0.04	0.02	-0.011 to 0.06	0.190	NS
PA At/Et ratio	0.22	0.04	0.22	0.05	0.01	-0.013 to 0.03	0.515	NS
Apgar 1	6.9	0.9	6.7	1.0	-0.18	-0.6109 to 0.26	0.427	NS
Apgar 5	9.3	0.9	8.9	1.7	-0.35	-0.96 to 0.26	0.261	NS

Data are mean and standard deviation (SD),95% CI = 95% confidence interval,*Unpaired t test, s= Significant, NS= non-significant.

Table 4. shows that there were statistical significant differences between women in the Non-diabetic group and Controlled DM group as regard PA PSV but there were no statistical significant differences between the two groups as regard PA EDV, PA S/D ratio, PA PI, PA At/Et ratio, Apgar score 1min and Apgar score 5 min.

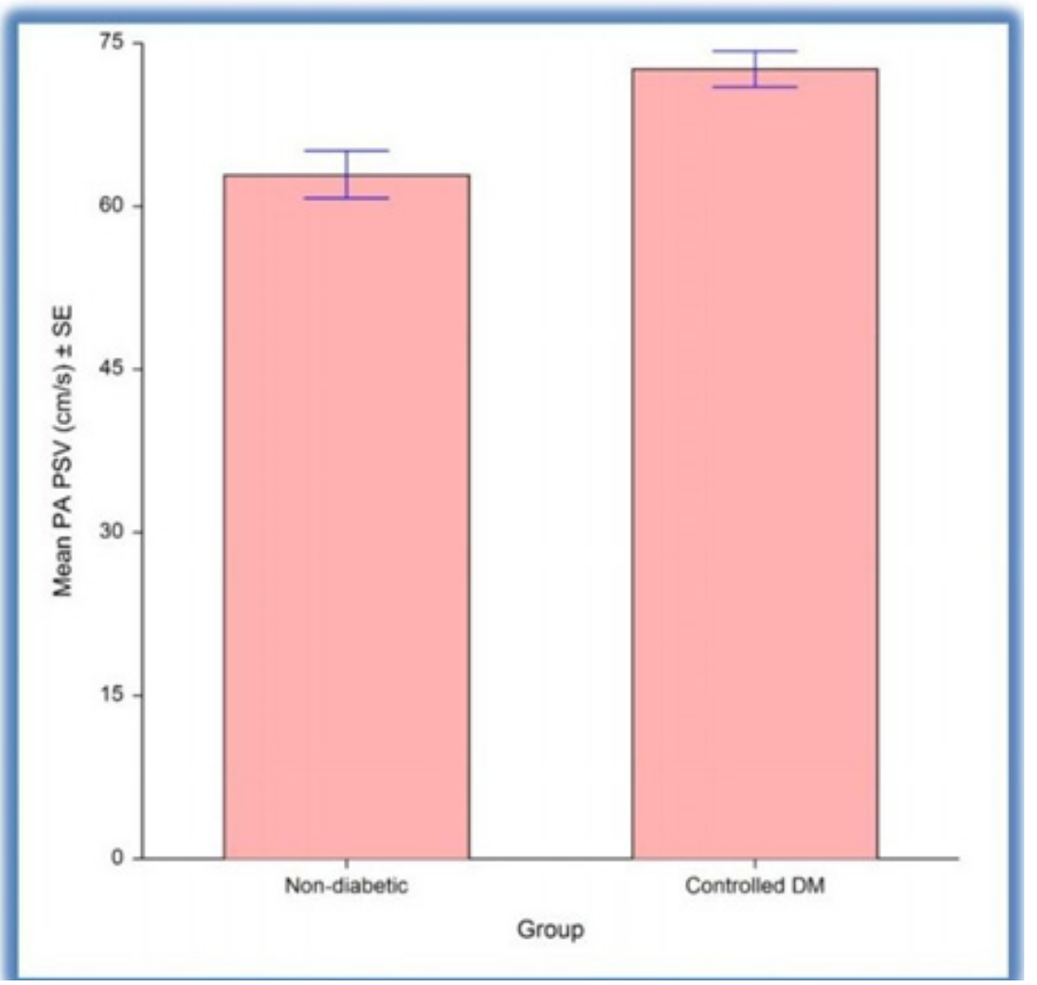

Fig. 1: Mean PA PSV in patients with or without DM. Error bars represent the standard error of the mean (SE).

Figure 1. Shows the Mean PA PSV was significantly higher in women with controlled DM group than Non DM group (72.63 vs 62.90 respectively), (*p<0.05 = 0.001*).

Table 5: Comparison of patients with or without DM: Categorical variables

Variable		Non-diabetic (n=40)		Controlled DM (n=40)		
		n	Column%	N	Column %	*p-value**
Parity	PO	3	7.5%	1	2.5%	*0.594#*
	P1	11	27.5%	12	30.0%	
	P2	19	47.5%	18	45.0%	
	P3	6	15.0%	9	22.5%	
	P4	1	2.5%	0	0.0%	
Neonate's gender	M	15	37.5%	16	40.0%	*1.000*
	F	25	62.5%	24	60.0%	
Persistent respiratory compromise>24h	-	38	95.0%	36	90.0%	*0.675*
	+	2	5.0%	4	10.0%	
Need for exogenous surfactant	-	40	100.0%	39	97.5%	*1.000*
	+	0	0.0%	1	2.5%	
X-ray evidence of HMD	-	38	95.0%	37	92.5%	*1.000*
	+	2	5.0%	3	7.5%	
Number of RDS criteria	Nil	38	95.0%	36	90.0%	*0.675*
	Two	2	5.0%	4	10.0%	
RDS	No RDS	38	95.0%	36	90.0%	*0.675*
	RDS	2	5.0%	4	10.0%	

Data are number (n) and column percentage (%), *Fisher's exact test unless otherwise indicated, #Chi-squared test for trend.

Table 5. shows that there were no statistical significant differences between women in the Non-diabetic group and Controlled DM group as regard Parity, Neonate's gender, criteria for diagnosis of infant with RDS as regards: Persistent respiratory compromise >24 h, Need for exogenous surfactant, X-ray evidence of HMD.

Table 6: Comparison of PA Doppler parameters in patients with controlled DM who had babies with or without RDS

Variable	Controlled DM group (n=40)				Difference	95% CI	*P-value**
	No RDS (n=36)		RDS (n=4)				
	Mean	SD	Mean	SD			
PA EDV(cm/s)	6.4	2.0	8.3	3.01	1.81	-0.41 to 4.04	*0.108*
PA PSV(cm/s)	72.7	10.7	71.8	6.97	-0.90	-12.10 to 10.30	*0.872*
PA S/D ratio	8.11	9.09	7.11	1.32	-1.00	-10.31 to 8.31	*0.830*
PA PI	1.95	0.29	2.14	0.28	0.19	-0.12 to 0.50	*0.225*
PA RI	0.91	0.03	0.94	0.06	0.04	-0.003 to 0.08	*0.068*
PA At/Et ratio	0.21	0.03	0.34	0.03	0.13	0.10 to 0.17	*<0.0001*

Data are mean and standard deviation (SD),95% CI =95% confidence interval, *Unpaired t test

Table 6. Shows that there were statistical significant differences between infants born with RDS and infants without RDS in women with controlled DM as regard PA At/Et ratio but there is no statistical significant differences as regard other PA Doppler parameters.

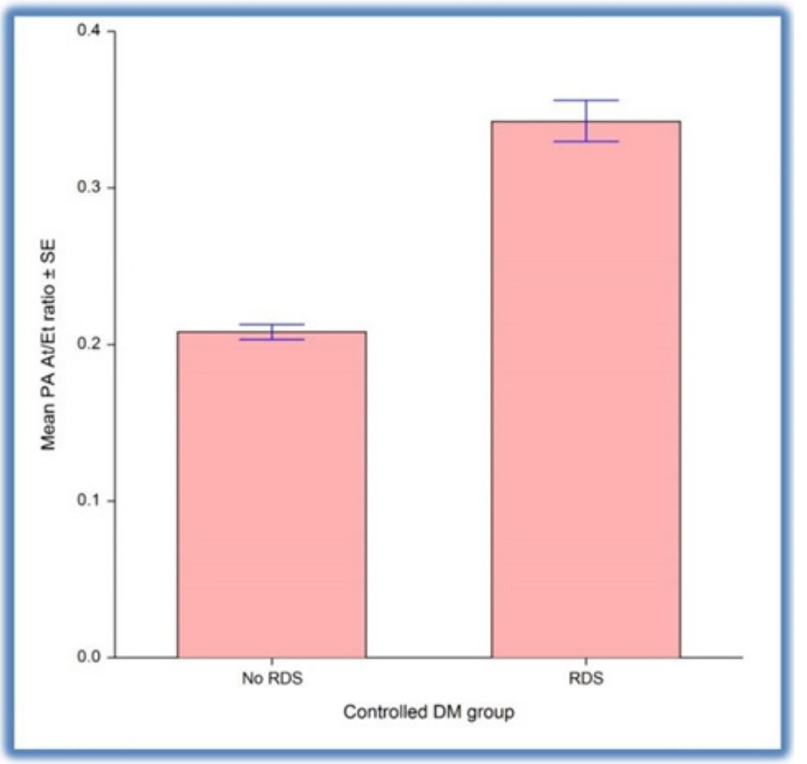

Fig. 2: Mean PA At/Et ratio in patients with controlled DM who had babies with or without RDS. Error bars represent the standard error of the mean (SE).

Figure 2. Shows the Mean PA At/Et ratio was significantly higher in infants born with RDS than infants born without RDS in women with controlled DM (0.34 vs 0.21 respectively), (*p<0.05=<0.0001*).

Table 7: Comparison of PA Doppler parameters in patients with non-diabetic group

	Non diabetic group				Difference	95%CI		*P-value*
	No RDS (n=38)		RDS (n=2)					
	Mean	SD	Mean	SD				
PA EDV	6.39	2.55	6.80	1.83	-0.41	-4.13	3.32	*0.825*
PA PSV	62.20	13.79	76.20	2.26	-14.00	-33.99	5.99	*0.164*
PA S/D ratio	10.29	14.04	8.17	0.11	2.12	-18.23	22.46	*0.834*
PA PI	2.04	0.26	3.26	1.47	-1.22	-1.74	-0.70	*<0.001*
PA RI	0.88	0.10	0.99	0.00	-0.11	-0.25	0.03	*0.130*
PA AT/ET ratio	0.21	0.02	0.35	0.00	-0.14	-0.17	-0.11	*<0.001*

Table 7. Shows that there were statistical significant differences between infants born with RDS and infants without RDS in women with non-diabetic group as regard PA At/Et ratio and PA PI but there is no statistical significant differences as regard other PA Doppler parameters.

Table 8: Receiver-operating characteristic (ROC) curve analysis for prediction of

ROC parameter	Predictor:PA At/Et ratio
AUC	0.740
SE	0.149
95%CI	0.577 to 0.865
p-value	0.012*
Youden index J	0.819
Associated criterion	>0.25
Sensitivity	75.0
95%CI	20.3-95.9
Specificity	88.9
95%CI	73.9-96.8
+LR	6.8
95% CI	4.39-9.11
-LR	0.28
95% CI	0.18-0.38
+PV	42.9
95% CI	27.89-57.92
-PV	97.0
95% CI	63.05-99.8

ROC = receiver-operating characteristic curve, SE = standard error, 95% CI = 95% confidence interval, Youden J index = ([sensitivity + specificity] -1), +LR = positive likelihood ratio, -LR = negative likelihood ratio, +PV = positive predictive value,-PV =negative predictive value.

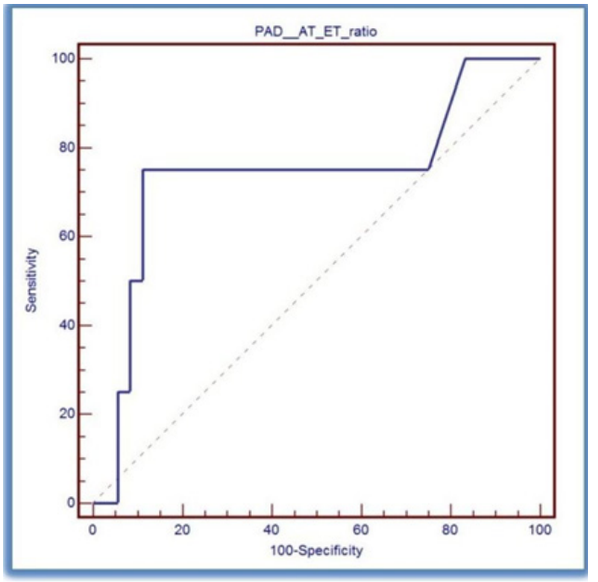

Fig. 3: Receiver-operating characteristic (ROC) curve for prediction of RDS in patients with controlled DM using PA At/Et ratio.PA At/Et ratio had excellent predictive value (AUC=0.740, *p-value 0.012*). A cutoff criterion of PA At/Et ratio >0.25 had a sensitivity of 75% and specificity of 88.9%.

Table 9: Secondary outcome measures in both study groups

Outcome		Non-diabetic		Controlled DM		
		n	%	n	%	*P-value**
NICU admission	-	38	95.0%	36	90.0%	*0.675*
	+	2	5.0%	4	10.0%	
Need for CPAP	-	40	100.0%	39	97.5%	*1.000*
	+	0	0.0%	1	2.5%	
Need for nasal CPAP	-	38	95.0%	40	100.0%	*0.494*
	+	2	5.0%	0	0.0%	
External surfactant administration	-	40	100.0%	39	97.5%	*1.000*
	+	0	0.0%	1	2.5%	
ETT insertion	-	40	100.0%	37	92.5%	*0.241*
	+	0	0.0%	3	7.5%	

Data are number (n) and percentage.
*Fisher's exact test.

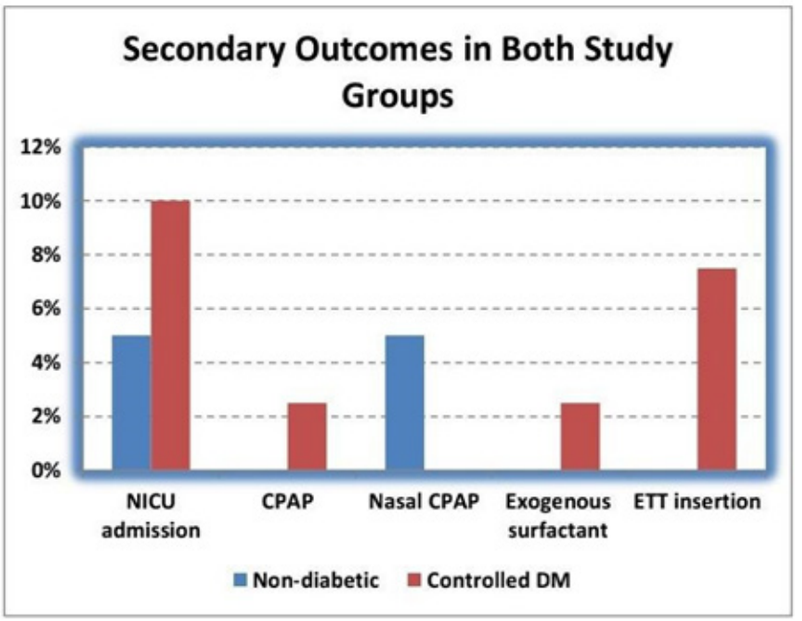

Fig. 4: Secondary outcome measures in both study groups.

There is no statistically significant difference between the two study groups as regards fetuses which need Neonatal Intensive Care Unit (NICU) admission, application of Continuous Positive Airway pressure (CPAP), Nasal CPAP, administration of exogenous surfactant therapy or endotracheal tube insertion (mechanical ventilation).

Table 10: Comparison of infants born with or without RDS: Numerical variables

	No RDS (n=74)		RDS (n=6)		Difference	95%CI	*P-value**
Variable	Mean	SD	Mean	SD			
Age(yr)	27.6	3.3	28.8	3.7	1.25	-1.57 to 4.08	*0.380*
BMI(kg/m²)	27.1	1.8	27.7	2.7	0.57	-0.97 to 2.11	*0.462*
FBS(mg/dl)	91.1	14.7	95.5	14.5	4.41	-8.00 to 16.81	*0.482*
PPBS(mg/dl)	146.3	9.8	159.8	3.7	13.58	5.52 to 21.64	*0.001*
HbA1c(%)	5.7	0.6	6.1	0.6	0.45	-0.05 to 0.96	*0.079*
GA(wk)	37.3	0.8	37.6	0.6	0.32	-0.32 to 0.96	*0.319*
AFI	11.5	1.5	12.3	0.5	0.87	-0.32 to 2.07	*0.149*
EFW(g)	3152.7	202.9	3333.3	136.6	180.63	12.22 to 349.04	*0.036*
PA EDV(cm/s)	6.58	2.07	7.77	2.58	1.18	-0.60 to 2.97	*0.190*
PA PSV(cm/s)	67.32	13.41	73.28	5.94	5.96	-5.07 to 17.00	*0.285*
PA S/D ratio	9.23	11.86	7.60	1.29	-1.63	-11.33 to 8.07	*0.739*
PA PI	2.00	0.28	2.51	0.90	0.51	0.22 to 0.81	*0.001*
PA RI	0.89	0.07	0.96	0.05	0.06	0.003 to 0.13	*0.041*
PA At/Et ratio	0.21	0.03	0.35	0.02	0.14	0.12 to 0.16	*<0.0001*
NBW(g)	3375.0	297.0	3633.3	312.5	258.33	6.45 to 510.22	*0.045*
Apgar 1	7.0	0.8	4.7	0.5	-2.29	-2.94 to-1.64	*<0.0001*
Apgar 5	9.3	1.2	6.7	0.5	-2.63	-3.65 to-1.61	*<0.0001*

Data are mean and standard deviation (SD),95% CI = 95% confidence interval,
*Unpaired t test.

Table 10. shows that there were statistical significant differences between infants born with RDS and infants born without RDS as regard PBS, EFW, NBW,PA PI, PA At/Et ratio, Apgar score1 min and Apgar score 5 min.

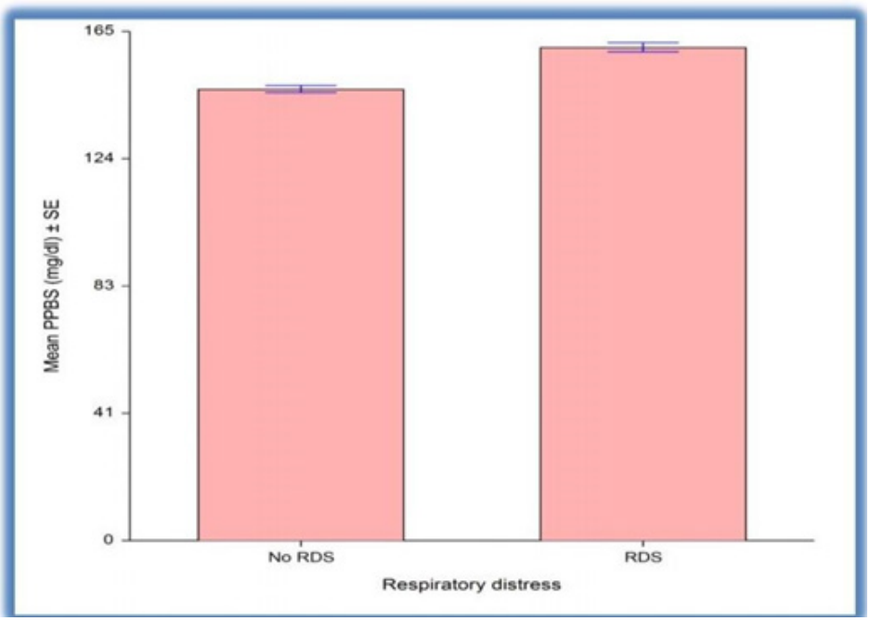

Fig. 5: Mean PBS in patients who had babies with or without RDS. Error bars represent the standard error of the mean (SE).

Figure 5. Shows the Mean PBS was significantly higher in infants born with RDS than infants born without RDS (159.8 vs 146.3 respectively), (*p<0.05=0.001*).

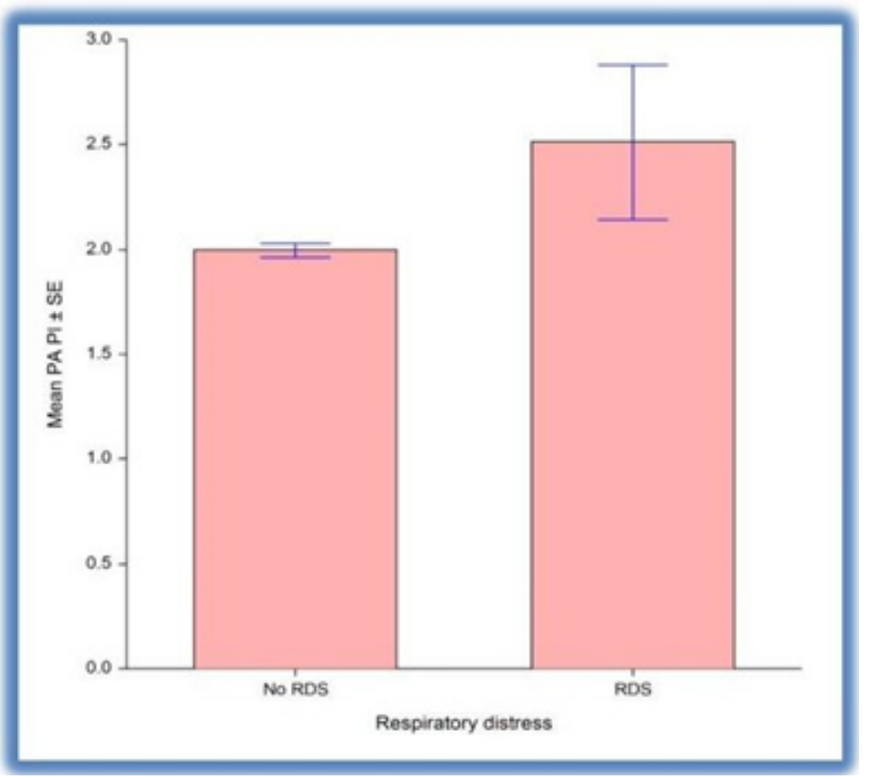

Fig. 6: Mean PA PI in babies with or without RDS. Error bars represent the standard error of the mean(SE).

Figure 6. Shows the Mean PA PI was significantly higher in infants born with RDS than infants born without RDS (2.51 vs.2.00 respectively), (*p<0.05=0.001*).

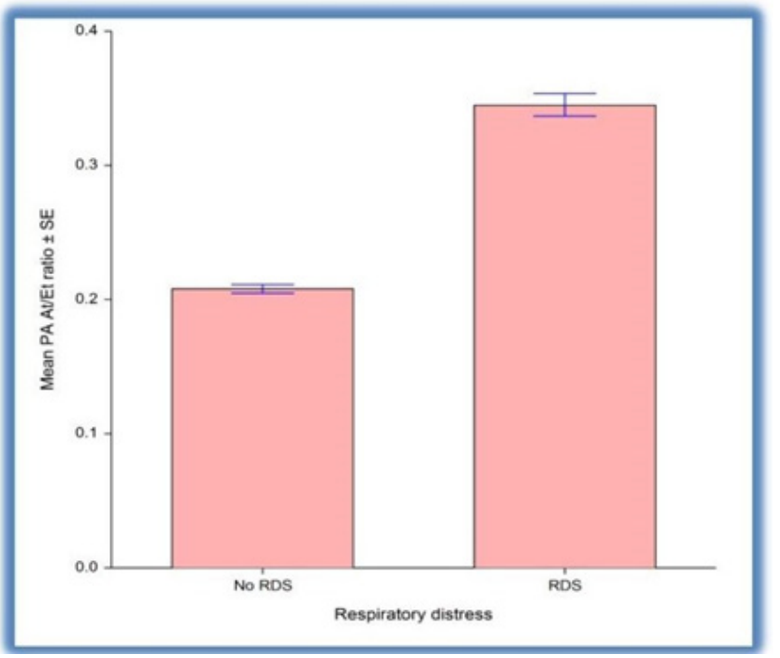

Fig. 7: Mean PA At/Et ratio in babies with or without RDS. Error bars represent the standard error of the mean (SE).

Figure 7.Shows the Mean PA At/Et ratio was significantly higher in infants born with RDS than infants born without RDS (0.35 vs. 0.21 respectively), (*p<0.05=0.001*).

Table 11: Receiver-operating characteristic (ROC) curve analysis for prediction of RDS using PBS, PA PI or PA At/Et ratio

ROC parameter	Predictor		
	PPBS	PA PI	PA At/Et
AUC	0.889	0.768	0.740
SE	0.041	0.097	0.149
95%CI	0.798 to 0.948	0.660 to 0.855	0.577 to 0.865
z statistic	9.443	2.776	7.294
p-value	<0.0001	0.006	0.012*
Youden index J	0.8108	0.4775	0.819
Associated criterion	>155 mg/dl	>2.21	>0.25
Sensitivity	100	66.7	75.0
95%CI	54.1-100.0	22.3-95.7	20.3-95.9
Specificity	81.1	81.1	88.9
95% CI	70.3-89.3	70.3-89.3	73.9-96.8
+LR	5.29	3.52	6.8
95% CI	3.3-8.5	1.7-7.4	4.39-9.11
-LR	0	0.41	0.28
95% CI	*	0.1-1.3	0.18-0.38
+PV	30	22.2	42.9
95% CI	21.1-40.7	12.0-37.4	27.89-57.92
-PV	100	96.8	97.0
95% CI	*	90.6-98.9	63.05-99.8

ROC= receiver-operating characteristic curve, SE = standard error, 95% CI=95% confidence interval, Youden J index = ([sensitivity + specificity] -1), +LR = positive likelihood ratio, -LR = negative likelihood ratio, +PV = positive predictive value, -PV = negative predictive value, *Could not be estimated.

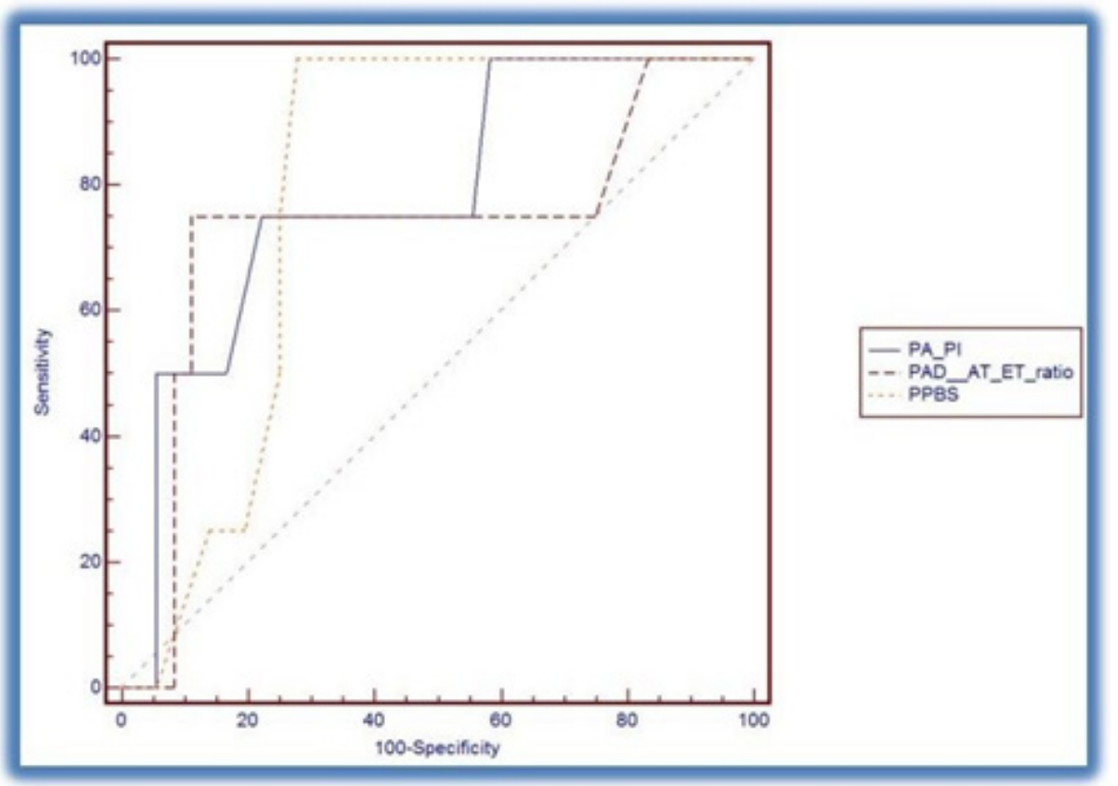

Fig. 8: Receiver-operating characteristic (ROC) curve for prediction of RDS using PPBS,PA PI or PA At/Et ratio.PPBS had excellent predictive value (AUC=0.889, *p-value <0.0001*). A cutoff criterion of PBS >155mg/dl had a sensitivity of 100% and specificity of 81.1%. PA PI had fair predictive value (AUC = 0.768, *p-value =0.006*). A cutoff criterion of PA PI>2.21 had a sensitivity of 66.7% and specificity of 81.1%.PA At/Et ratio had excellent predictive value (AUC=0.74, *p-value 0.012*).A cutoff criterion of PA At/Et ratio >0.25 had a sensitivity of 75% and specificity of 88.9%.

Table 12: Comparison of patients with or without RDS: Categorical variables

Variable		No RDS(n=74)		RDS (n=6)		
		N	Row%	n	Row%	*p-value**
Glycemic status	No DM	38	95.0%	2	5.0%	*0.299*
	DM	36	90.0%	4	10.0%	
Parity	PO	4	100.0%	0	0.0%	*0.200#*
	P1	22	95.7%	1	4.3%	
	P2	34	91.9%	3	8.1%	
	P3	13	86.7%	2	13.3%	
	P4	1	100.0%	0	0.0%	
Neonate's gender	M	27	87.1%	4	12.9%	*<0.001*
	F	47	95.9%	2	4.1%	

Data are number (n) and row percentage (%),*Fisher's exact test unless otherwise indicated, #Chi-squared test for trend.

Table 12. shows that there were no statistical significant differences between infants born with RDS and infants born without RDS as regard glycemic status and parity but there were statistically significant differences as regard neonate's gender being more in males than females.

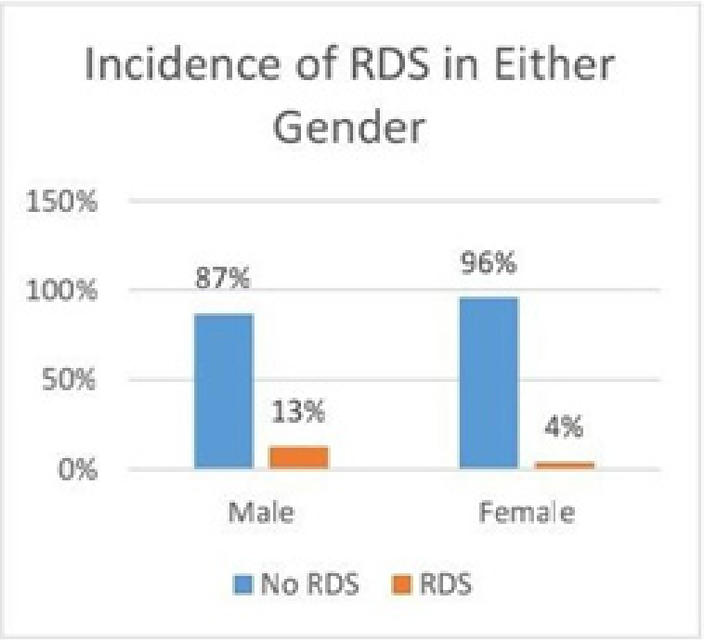

Fig. 9: Incidence of RDS in either gender.

DISCUSSION

One of the most frequent causes of infant respiratory failure and neonatal mortality is respiratory distress syndrome (RDS). RDS was once thought to be mostly present in preterm newborns. RDS is now more frequently diagnosed in term infants due to widespread knowledge of the condition'. Therefore, one of the most crucial objectives of obstetrical care is the evaluation of foetal lung maturity. Traditionally, amniocentesis and the analysis of component proteins and lipid in the amniotic fluid have been used to determine the maturity of embryonic lungs. However, amniocentesis is an invasive operation that is only advised under certain circumstances.

About 0.7% of amniocentesis cases result in risks and problems, including preterm labour and delivery, early rupture of the membranes, placental abruption, and fetomaternal bleeding[10]. A noninvasive test is preferred to prevent the dangers of amniocentesis. Based on prior research showing a relationship between foetal pulmonary artery Doppler waveform acceleration/ejection time and growing gestational age, as well as between the latter and foetal lung maturity tests in amniotic fluid[5].

The goal of the current study was to use foetal pulmonary artery Doppler to predict foetal lung maturity in diabetic pregnant women.

The goal of this study is to predict the development of respiratory distress syndrome in diabetic pregnant women and foetuses who will require admission to the Neonatal Intensive Care Unit (NICU), use of Continuous Positive Airway Pressure (CPAP), Nasal CPAP, administration of exogenous surfactant therapy, or insertion of an endotracheal tube (mechanical ventilation).

From September 2017 to March 2018, this clinical controlled trial (prospective study) was carried out at the Ain Shams University Maternity Hospital's Faculty of Medicine. 80 patients who were scheduled to have an elective, straightforward caesarean section were included. They were also ready to do foetal pulmonary artery Doppler ultrasonography, and they were divided into the following two groups. 40 pregnant women without complex diabetes mellitus made up the control group, whereas 40 pregnant women with managed diabetic mellitus made up the case group. These expectant ladies provided informed permission and had their complete medical histories, examinations, and investigations obtained.

At least two of the following three criteria must be present in order to diagnose the development of RDS: Exogenous pulmonary surfactant administration, radiographic evidence of hyaline membrane disease, and signs of respiratory compromise (tachypnea, retractions, and/or nasal flaring) early after birth with a persistent oxygen demand for more than 24 hours.

The current study's findings showed that, when comparing infants born to mothers with managed diabetes mellitus with children born without RDS, there were statistically significant differences in the PA At/Et ratio, but not in the other PA Doppler parameters.

The Receiver-operating characteristic (ROC) curve for predicting RDS in patients with controlled DM using PA At/Et ratio had excellent predictive value (AUC = 0.740, *p-value 0.012*), and the mean PA At/Et ratio was significantly higher in infants born with RDS than infants born without RDS in women with controlled DM (0.34 vs 0.21, respectively). A cutoff criterion of PA At/Et ratio >0.25 exhibited an 88.9% specificity and a 75% sensitivity.

In terms of BMI, FBS, PPBS, HbA1C, EFW, NBW, and PA PSV, there were statistically significant differences between women in the Non-diabetic group and the Controlled DM group. However, there were no statistically significant differences between the two groups in terms of mean age, GA, AFI, PA EDV, PA S/D ratio, PA PI, PA At/Et ratio, Apgar score 1min, or Apgar score 5

Women in the controlled DM group had a mean PA PSV that was substantially greater than women in the non-DM group (72.63 vs. 62.90, respectively; *p 0.05= 0.001*).

There were no statistically significant differences between the women in the non-diabetic group and the controlled DM group in terms of parity, the gender of the newborn, or the criteria for diagnosing a baby with RDS, including the need for exogenous surfactant and the presence of HMD on X-rays.

Newborns with RDS and infants without RDS had statistically significant variations in PPBS, EFW, NBW, PA PI, PA At/Et ratio, Apgar score 1 min and Apgar score 5 min.

Infants born with RDS had a substantially greater mean PA PI (2.51 vs.2.00, respectively) than infants born without RDS (*p 0.05 = 0.001*).

Regarding foetuses who require admission to the Neonatal Intensive Care Unit (NICU), use of Continuous Positive Airway pressure (CPAP), nasal CPAP, administration of exogenous surfactant therapy, or placement of an endotracheal tube, there were no statistically significant differences between the two study groups (mechanical ventilation).

The current study's findings were in agreement with those of Bahaa Eldin *et al*., who discovered that a high At/Et ratio in the foetal pulmonary artery is "associated with the subsequent development of RDS in neonates of diabetic mothers." However, the current study's cutoff value for the PA At/Et ratio was greater than 0.25, and their sample size was very small.

They assessed the primary foetal pulmonary artery's Doppler indices and its contribution to the diagnosis of respiratory distress syndrome (RDS) in diabetic pregnancies. A prospective cohort study was created, and 40 pregnant diabetes women were chosen for it. The development of newborn RDS and the At/Et ratio in the foetal pulmonary artery velocimetry waveform were directly correlated. With a cutoff value of 0.31, sensitivity is 76.4%, specificity is 82.5%, and positive and negative predictive values are 76.2% and 79.3%, respectively[12].

Also This study concurs with Schenone *et al*. in that foetal pulmonary artery Doppler may offer a noninvasive method of assessing foetal lung maturity with acceptable levels of sensitivity, specificity,and predictive values; however, they compare their findings with surfactant/albumin ratio using an invasive method (amniocentesis), and the authors did not correlate At/Et with clinical RDS.

In their study, 43 patients were included. For predicting immature surfactant/albumin ratio findings, the cutoff value of 0.3149 had a specificity of 93% (95% CI 77-98%), a sensitivity of 73% (95% CI 48-89%), a negative predictive value of 87% (95% CI 70-95%), and a positive predictive value of 85% (95% CI 58-96%)[10].

In regards to mean foetal pulmonary artery, the findings of the present study were in accordance with those of Guan *et al*. Although their patients used prenatal corticosteroids, Doppler may be able to predict foetal lung maturity.

In 52 pregnant women who were due to give delivery prematurely, Doppler indices of MPA were done. With a gestational age-specific threshold of less than or equal to the fifth percentile, AT by alone was able to predict RDS with a sensitivity of 78.6% and a specificity of 89.7%. The AT/ET ratio has a 71.4% sensitivity and a 93.1% specificity for RDS prediction[6].

Additionally, Moety *et al*. found that the MPA At/Et might be used to predict the onset of newborn RDS with excellent sensitivity and specificity. At/Et showed the highest association (r = 0.602, *P0.001*). In foetuses who had RDS, PI and RI were considerably greater, although At/Et and PSV were significantly lower. RDS development was predicted by a cutoff value of 0.305 for At/Et (sensitivity:76.4%; specificity:91.6%)[4].

The findings of the present investigation concurred with those of Kim *et al*. with relation to the embryonic pulmonary artery. Although they conducted their investigation on preterm complex pregnant women with preterm premature rupture of membranes and maternal hypertensive disorders of pregnancy, Doppler velocimetry may offer a valid noninvasive tool to assess foetal lung development (including preeclampsia, superimposed preeclampsia, and chronic hypertension).

In the final analysis, neonates with RDS (n = 11) had substantially shorter gestational ages at delivery than those without RDS (n =42 foetuses; 37 moms). When compared

to foetuses who did not develop RDS, the pulmonary artery At/Et ratio was much greater in those that did. After correcting for gestational age using logistic regression analysis, RDS prediction score (=a hundredfold At/Et ratio) is substantially correlated with the later development of RDS (odds ratio = 1.31, 95% confidence range 1.05 to 1.63, *p=0.017*)[11].

In addition to stating that At/Et was inversely correlated with the lecithin/sphingomyelin ratio discovered through amniocentesis, Azpurua *et al*. also reported that ultrasound evaluation of foetal pulmonary artery blood flow may be a promising new non-invasive technique to evaluate foetal lung maturity. However, due to a small sample size (29 foetuses) and a single newborn with RDS, their study was unable to examine the relationship between At/Et and the emergence of clinical RDS.

They looked at women who had singletons and had clinically necessary amniocentesis to check the embryonic lung development. The ratio of lecithin to sphingomyelin in the amniotic fluid inversely correlated with the acceleration-time/ejection-time in the foetal pulmonary artery[2].

According to Güngör *et al*., there were no statistically significant differences in the PA Doppler results between foetuses who developed RDS and those who did not, and there were also no significant differences between the PA Doppler results for both groups before and after steroid administration. The findings of the current study contradict these findings.

They prospectively enrolled 40 singleton pregnancies between 24 and 34 gestational weeks with a diagnosis of premature delivery. To increase foetal lung maturation, they were given corticosteroids. Before and 48 to 72 hours after steroid treatment, foetal PA and UA Doppler measurements were assessed[13].

Further refuting this study's findings is Lindsley *et al.* observation's that there was no change in pulmonary blood flow between foetuses with and without respiratory distress syndrome (RDS).

Pregnant women at risk for PTB who were being treated with corticosteroids (betamethasone) had their major foetal pulmonary artery (MPA) blood flow prospectively assessed and compared to an uncomplicated group without steroid medication[14].

CONCOLUSION

This treatment is less expensive than amniocentesis, safe, simple, and without problems. In terms of the PA At/Et ratio, there were statistically significant differences between babies born with RDS and babies born without RDS in women with managed DM. In terms of the PA At/Et ratio and PA PI, there were statistically significant differences in non-diabetic women.

Between the two groups, there were statistically significant differences in terms of BMI, FBS, PBS, HbA1C, EFW, NBW and PA PSV.

There were statistically significant variations in the proportionof male neonates compared to female neonates.

CONFLICT OF INTEREST

There are no conflicts of interests.

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