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Acceleration/Ejection Time Ratio in the Fetal Pulmonary Artery Predicts Fetal Lung Maturity in Diabetic Pregnancies

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Abstract

To study the Doppler indices of the main fetal pulmonary artery, namely pulsatility index(PI), resistance index(RI), and the acceleration-time/ejection-time ratio(At/Et) and their role in predicting respiratory distress syndrome(RDS) in diabetic pregnancy.A prospective cohort study was developed, in which 40 diabetic pregnant women were selected, underwent fetal pulmonary artery flow velocity measurements, including systolic/diastolic ratio, pulsatility index, resistance index, and acceleration-time/ejection-time ratio were obtained using spectral Doppler ultrasound and correlated with the development of neonatal RDS. There was a direct correlation between the At/Et ratio in the fetal pulmonary artery velocimetry waveform and development of neonatal RDS. A cut off value of 0.31 provides Sensitivity=76.4% and Specificity=82.5% (positive predictive value=76.2% and negative predictive value=79.3%). An elevated At/Et ratio in the fetal pulmonary artery is associated with the subsequent development of RDS in neonates of diabetic mothers.

Keywords

Respiratory distress syndrome. fetal pulmonary artery lung velocity. doppler ultrasound. diabetes mellitus. apgar score

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I. Introduction

Diabetes mellitus complicates 3–5% of all pregnancies and is a major cause of perinatal morbidity and mortality, as well as maternal morbidity [1].

Respiratory distress syndrome (RDS) of the newborn, also called hyaline membrane disease, is the most common cause of respiratory distress in premature infants, correlating with structural and functional lung immaturity. It occurs in 24,000 infants born in the United States annually. It is most common in infants born at fewer than 28 weeks' gestation and affects one third of infants born at 28 to 34 weeks' gestation, but occurs in less than 5 percent of those born after 34 weeks' gestation [2].

A number of biochemical tests have been developed to predict the risk of RDS and assist obstetric care providers in delivery timing. These tests, including, among others, the lecithin/sphingomyelin (L/S) ratio and the presence or absence of phosphatidylglycerol (PG), require amniocentesis, followed by direct or indirect measurement of the surface active properties of surfactant phospholipids secreted by the fetal lungs into the amniotic fluid. Amniocentesis is an invasive procedure and is associated with a small but real risk to the pregnancy, including preterm premature rupture of membranes, preterm labor, placental abruption, fetomaternal hemorrhage, fetal injury, and rarely fetal or even maternal death [3].

II. Materials and Methods

This study was conducted in Kasr Alainy Maternity hospital from January 2013 to september 2014 and it included 40 pregnant women complicated with diabetes mellitus class (B-C) according to White classification:

- Class B: onset at age 20 or older or with duration of less than 10 years.
- Class C: onset at age 10-19 or duration of 10–19 years.

All the patients had the following:

Inclusion Criteria:

1- Gestational age is 36-40 weeks.
2- Singleton pregnancy.
3-Time of termination after completed 36 weeks by elective uncomplicated cesarean section (average blood loss, no meconium and with average time of easy fetal extraction). It was done by senior obstetrician and anaesthetist.

Exclusion Criteria:

1- Pregnant females less than 36 weeks of gestational age or more than 40 weeks.
2- Multiple pregnancy.
3- Uncertain gestational age.
4- History of cardiac or hypertension disease.
5- Obstetric hemorrhage as antepartum hemorrhage.
6- Intrauterine growth retardation.
7- Congenital anomalies.
8- Amniotic fluid index less than 10 or more than 20.

Women included in this study were subjected to the following:

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1. Informed written consent approved by ethical committee of the department must be obtained from the patient after explaining the aim of the research for every patient.

2. Full history taking:
• Personal history
• Past history (medical history of diabetes)
• Family history
• Obstetric history (stillbirth, abortion, preterm birth, macrosomic neonate, congenital malformations and previous gestational diabetes)
• Menstrual history
• Contraceptive history

3. General examination

4. Abdominal examination

5. Investigation:
• FBS
• 2hPP
•Glycosylated Hemoglobin (HBA1C)

6. Abdominal U/S: by real time two dimensional abdominal U/S. All measurements were performed by senior single sonographer with same machine (Voluson prov GE united states). Women were placed in semirecumbent position and an axial plane through the fetal thorax to achieve 4 chamber view of the heart. The main pulmonary artery was followed to the point where it divides into right and left branches by rotating the transducer from the 4 chamber view to the short axis view of the heart. Pulsed and colour Doppler was used. The fetal pulmonary artery flow waveform (FPAF) measurements was taken within the proximal portion of the main pulmonary artery.

A number of different parameters were measured from the FPAF waveform (average values of 3 waves), including the systolic/diastolic ratio, pulsatility index(PI), resistance index(RI), and the acceleration-time/ejection-time ratio(At/Et). At refers to the time interval from the beginning of ventricular systole to the achievement of peak velocity. Et refers to the time interval from the beginning to the end of ventricular systole.

Fetal biometry, Amniotic fluid index, and Doppler RI of of umbilical artery was measured.

7. Neonatal resuscitation and assessment by senior neonatologist
- Apgar score at 5 and 10 minutes.
- Need for admission to neonatal ICU.
- The development of RDS as follows ***(European Consensus Guidelines):***
Diagnosed by the presence of at least 2 of the following 3 criteria:
1-Evidence of respiratory compromise (tachypnea, retractions, and/or nasal flaring) shortly after delivery and a persistent oxygen requirement for longer than 24 hours.
2-Adminstration of exogenous pulmonary surfactant.
3-Radiographic evidence of hyaline membrane disease.

Statistical Analysis
Data were statistically described in terms of mean □ standard deviation (□ SD), and range, or frequencies (number of cases) and

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percentages when appropriate. Comparison between the study groups was done using paired t test. Agreement across sides of measurements within the individuals was analyzed as 95% limits of agreement, i.e. the mean of the difference between two locations ±2SD. The consistency in the ranking of the subjects across sites and sides of measurements was analyzed using Spearman's correlation coefficient. The intraobserver variation was analyzed as the intraclass correlation coefficient (ICC) by means of random-effects regression. p values less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows.

III. Results

This is a discriptive study correlating the Doppler indices of the main fetal pulmonary artery, namely pulsatility index(PI), resistance index(RI), and the acceleration-time/ejection-time ratio(At/Et) and their role in predicting respiratory distress syndrome(RDS) in diabetic pregnancy.

A total of 40 diabetic patients consented to participate in the study. The data was collected and analysed revealing the following results:

Demographic Data

The mean maternal age for study group was 27.5 ± 5.7 (class B 26.4± 5.4 and class C 31.4± 5.5).

Neonatal Data

Regarding neonatal data, 6 neonates were diagnosed as having RDS with NICU admission. There were no cases of intraventricular hemorrhage, pneumothorax, and other neonatal complications including retinopathy of prematurity, necrotizing enterocolitis, bronchopulmonary dysplasia, or death.

As required by our study inclusion/exclusion criteria, a complete ultrasound evaluation was achieved in all 40 study subjects included in the final analysis.The amniotic fluid volume was normal, with a mean amniotic fluid index of 11.6± 1.6. The mean At/Et ratio was 0.25 ± 0.05 for study group(p value = 0.6).

Comparing those who developed RDS with normal neonates in study group, we found that there was no correlation between any of the age,pulmonary S/D , RI or PI ratios. Only AT/ET ratio (Diabetic 0.3 ± 0.6) correlated with RDS development (Diabetic group p=0.005).

CUT OFF value for the AT/ET for RDS in study group = 0.31 with Sensitivity=76.4% and Specificity=82.5% (positive predictive value=76.2% and negative predictive value=79.3%).

IV. Discussion

A number of noninvasive sonographic tests to predict fetal pulmonary maturity have been proposed over the past 30 years, including fetal biometry, placental maturation, umbilical artery Doppler velocimetry, fetal breathing movements and nasal fluid flow velocity waveforms, and examination of the fetal

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intestine and ossification centers of the fetal long bones. However, none has proven to be sufficiently reproducible or accurate for use in clinical practice [4].

We studied the value of fetal pulmonary artery Doppler indices in prediction of neonatal respiratory distress syndrome in diabetic pregnancies.

We choosed the maternal age between 18 and 35 years. This is by far the commonest maternal age during pregnancies and by that our results would be applied on the largest number of pregnant ladies in the general population.

We also included in our study the fetal biometry measurements and estimated fetal weights of the studied fetuses to prove that all cases have sizes between 5th and 95th percentiles and that none had intrauterine growth restriction or macrosomia.

We also measured the amniotic fluid indices of our subjects and made sure that they lie within the normal ranges.

All cases must have done a 2nd trimesteric anomaly scan . History was taken from the mother and general examination was done to exclude common medical disorders such as hypertension to make sure that our values are authentic and external factors will not alter our results.

RDS were commoner among class C than class B.

We found that an elevated acceleration-time/ejection-time ratio (At/Et ratio) in the fetal pulmonary artery is associated with the subsequent development of Respiratory distress syndrome (RDS) in the neonates of diabetic mothers.

V. Conclusion

Comparing those who developed RDS with normal infants in control group and diabetic group, we found that AT/ET ratio correlated with RDS (Diabetic group p=0.005).

The net result from this study that Doppler ultrasound may be a useful tool in the diagnosis of fetal lung maturity; if the AT/ET ratio is below the cutoff value (0.31 with Sensitivity=76.4% and Specificity=82.5%) there is fetal lung maturity and an amniocentesis may be avoided.

Many authors studied the value of fetal pulmonary indices to predict fetal lung maturity but this is the first study on diabetic patients. This is a small scale study which opens the way for multicenteric large scale studies inorder to verify our results.

Larger prospective studies are needed to assess the sensitivity and specificity for At/Et ratios to predict FLM and to further assess whether the At/Et ratio can replace amniocentesis for FLM testing with a view to preventing neonatal RDS.

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VI. References

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Table I: Mean age, parity, BMI, Gestational age for study group.

	Mean	Std. Deviation
Maternal Age	27.55	5.77
Parity	2.33	2.2
BMI	28.2	5.6
Gestational Age	37.4	2.1

Table II: Mean FBS, 2hpp and HBA1C for study group.

	Mean	Std. Deviation
FBS	119	24.6
2hpp	130	14.5
HBA1C	5.7	2.4

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Table III: Mean fetal weight and Apgar score at 1 & 5 min.

	Mean	Std. Deviation
Fetal Weight (kg)	3.6	0.6
Apgar 5 min	6.1	2.6
Apgar 10 min	6.8	2.8

Table IV: Comparison between Diabetic group class B and C as regarding development of RDS.

		RDS		
		NO	YES	Total
CLASS	B	29	2	31
	C	5	4	9
	Total	34	6	40

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Table V: Comparing study group as regarding age, S/D , RI, PI, AT/ET, umbilical RI ratios and AFI in relation to development of RDS.

GROUP		RDS	N	Mean	Std. Deviation	P value
CASES	Maternal AGE	NO	34	26.7059	5.35146	.26
		YES	6	32.3333	6.21825	
	Pulmonary S/D	NO	34	6.5353	.40293	.98
		YES	6	6.8283	.28639	
	Pulmonary RI	NO	34	.7368	.13389	.13
		YES	6	.8417	.24983	
	Pulmonary PI	NO	34	1.9682	.13277	.18
		YES	6	2.0667	.30111	
	Pulmonary AT/ET	NO	34	.2374	.03527	**.005**
		YES	6	.3250	.06124	
	UMBILICAL. RI	NO	34	.6971	.08943	.87
		YES	6	.7033	.08892	
	AFI	NO	34	11.7647	1.55814	.28
		YES	6	11.0000	1.67332	

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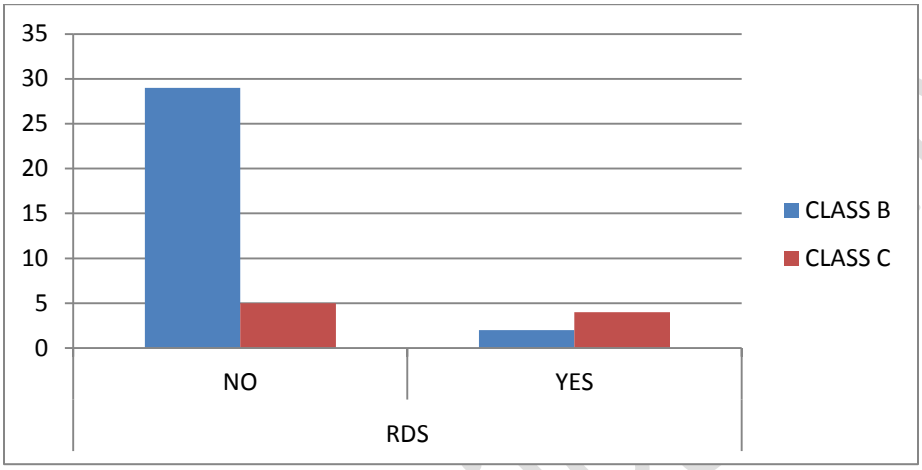

Figure (1): Comparison between Diabetic group class B and C as regarding development of RDS.

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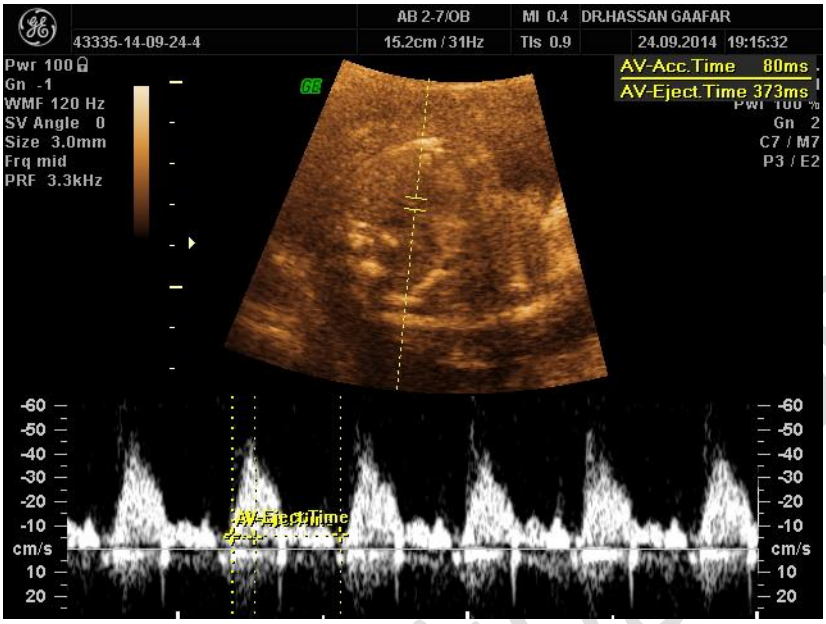

Figure (2): AT/ET ratio (0.21) of fetal pulmonary artery of a patient with good neonatal outcome (No RDS).

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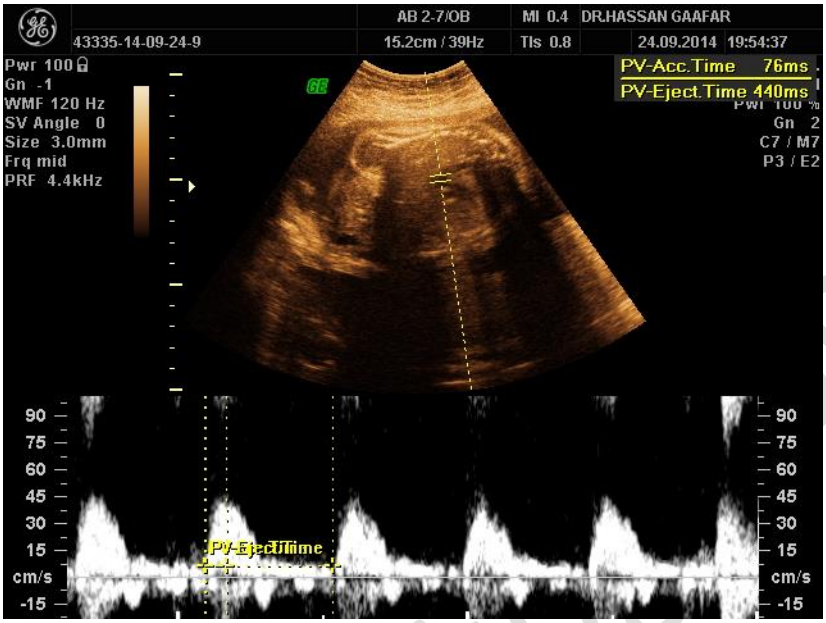

Figure (3): AT/ET ratio (0.17) of fetal pulmonary artery of a patient with good neonatal outcome (No RDS).

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