Journal of Perinatology (2015) 35, 1015–1019

www.nature.com/jp

ORIGINAL ARTICLE

# Can fetal pulmonary artery Doppler indices predict neonatal respiratory distress syndrome?

GAFA Moety[1], HM Gaafar[1] and NM El Rifai[2]

**OBJECTIVE:** To study whether fetal main pulmonary artery (MPA) Doppler indices can predict the development of neonatal respiratory distress syndrome (RDS).

**STUDY DESIGN:** This prospective cross-sectional study included pregnant women between 34 and 38+6 weeks gestation. The diagnostic accuracy of MPA Doppler measurements (systolic/diastolic (S/D) ratio, peak systolic velocity (PSV), pulsatility index (PI), resistance index (RI) and acceleration time/ejection time (At/Et)) for diagnosis of neonatal RDS was tested.

**RESULT:** Of the 698 eligible fetuses, 55 (7.87%) developed neonatal RDS. PSV, PI, RI and At/Et were positively correlated with gestational age. The strongest correlation was found with At/Et ($r = 0.602$, $P < 0.001$). PI and RI were significantly higher, whereas At/Et and PSV were significantly lower in fetuses that developed RDS. A cutoff value of 0.305 for At/Et predicted the development of RDS (sensitivity: 76.4%; specificity: 91.6%).

**CONCLUSION:** Development of neonatal RDS can be predicted using the MPA At/Et with high sensitivity and specificity.

*Journal of Perinatology* (2015) **35,** 1015–1019; doi:10.1038/jp.2015.128; published online 22 October 2015

## INTRODUCTION

Respiratory distress syndrome (RDS) is one of the most common causes of neonatal respiratory failure and neonatal death.[1] It was believed that RDS is mainly found in premature infants;[2] however, great awareness of RDS has led to its more frequent diagnosis in term neonates.[3]

Preterm deliveries can follow spontaneous onset of labor with or without preterm rupture of membranes; however, preterm deliveries are, sometimes, provider-initiated.[4] Deliveries can be unintentionally preterm because of gestational age (GA) error as commonly seen in women delivered by elective Cesarean section (CS).[5]

Given the importance of RDS as a cause of neonatal morbidity and mortality in late preterm deliveries[6] and early term period,[7] it seems logic to assess fetal lung maturity (FLM) before labor.

A number of tests as lecithin/sphingomyelin ratio, the presence or absence of phosphatidylglycerol and the amniotic fluid lamellar body count have been used to determine FLM; however, all depend on amniocentesis, which is an invasive procedure that carries risks and complications in ~0.7% of cases, including preterm labor, preterm rupture of membranes, placental abruption and fetomaternal hemorrhage.[8]

Hence, a noninvasive test is desirable. The sonographic echogenicity of the fetal lung changes in a predictable pattern throughout pregnancy.[9] Also, previous studies have addressed the relationship between fetal pulmonary artery Doppler waveforms and fetal pulmonary hypoplasia.[10,11] Moreover, as the lung develops throughout gestations, so does the pulmonary vasculature, where both the absolute number of pulmonary arteries rises and the pulmonary arterial vascular resistance decreases slightly.[12]

With the aid of these facts, we hypothesized that the use of fetal pulmonary artery Doppler indices may help in the determination of FLM.

Fetal pulmonary artery acceleration time/ejection time (At/Et) ratio has been shown to be correlated with advancing fetal GA[13] and FLM testing in amniotic fluid.[14,15] Two previous studies[13,16] have demonstrated that At/Et can predict RDS development in preterm infants. However, whether this is also true for late preterm and early term period was not studied.

In this study, we tried to examine whether fetal main pulmonary artery (MPA) Doppler indices can predict the subsequent development of neonatal RDS in late preterm (34 to 36+6 weeks) and early term (37 to 38+6 weeks) fetuses.

## METHODS

### Participants

This prospective cross-sectional study was conducted at Cairo University Teaching Hospital, Egypt from October 2013 to February 2015 and was approved by the hospital research ethics committee.

Women attending the delivery unit between 34 and 38+6 gestational weeks, either in active labor or indicated for selective CS, were consecutively enrolled in the study.

Women were included in the study if they had a singleton pregnancy with an accurate GA (defined as dating by a certain last menstrual period or by first-trimester ultrasound). Only fetuses delivered within 24 h of admission were included.

Exclusion criteria were a known fetal chromosomal or major structural abnormality and the prior antenatal corticosteroid administration. Fetuses discovered to have structural anomalies after delivery were also excluded.

After obtaining an informed consent, maternal age and parity were recorded, and an ultrasound examination was performed.

### Doppler examination of the fetal pulmonary artery

A single examiner (from the authors' team) performed all ultrasound examinations using the Voluson 730 ultrasound machine (GE Healthcare Austria GmbH, Seoul, South Korea) equipped with a 3 to 5 MHz convex array sector transducer.

[1]Obstetrics and Gynecology Department, Cairo University, Cairo, Egypt and [2]Department of Pediatrics, Faculty of Medicine, Cairo University, Cairo, Egypt. Correspondence: Dr NM El Rifai, Department of Pediatrics, Faculty of Medicine, 4 Gamal Salem Street, Dokki, Cairo 02, Egypt.
E-mail: nihal-r@hotmail.com
Received 6 August 2015; accepted 1 September 2015; published online 22 October 2015

After a routine ultrasound examination, including fetal biometry, estimated fetal weight and amniotic fluid index, the examiner examined the fetal heart 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. The pulsed Doppler sample gate was adjusted to 3 mm 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 (sharp systolic peak blood flow with a needle-like appearance, commonly referred to as a 'spike and dome' pattern). A small notch of reversed flow is also seen at the end of the systole.[17] The characteristic shape of MPA waveform is important to differentiate it from the wave of the ductus arteriosus, which is rounded, fuller and triangular in shape with greater diastolic flow.[18]

After the optimal 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.

To obtain the At/Et, the time interval from the beginning of the ventricular systole to the achievement of peak velocity (At) was divided by the time interval from the beginning to the end of ventricular systole (Et) (Figure 1).

### Diagnosis of neonatal RDS

Upon delivery, the route of delivery was recorded as well as the neonatal sex. A single pediatrician, from the authors' team, who was blinded to the fetal MPA Doppler measurements, handled the neonate. Neonatal birth weight (NBW) and Apgar score (at 1 and 5 min) were recorded.

The diagnosis of RDS was based on clinical signs of respiratory distress (tachypnea, retractions and/or nasal flaring), supplemental oxygen requirement of 0.4 or greater for at least 24 h and typical chest X-ray findings with reticulogranular patterns, air bronchograms and ground glass appearance.[19] The duration of neonatal intensive care admission was also recorded.

### Statistical analysis

Data were statistically described in terms of mean ± s.d., median and range or frequencies and percentages when appropriate. Comparison of numerical variables between the study groups was carried out using Student's *t*-test for independent samples. For comparing categorical data, $\chi^2$ test was performed. Exact test was used instead when the expected frequency is $< 5$. Correlation between various variables was carried out using Pearson's moment correlation equation for linear relation in normally distributed variables and Spearman's rank correlation equation for non-normal variables/nonlinear monotonic relation. Accuracy was represented using the terms sensitivity and specificity. Receiver operator characteristic analysis was used to determine the optimum cutoff value for pulmonary At/Et ratio, PI and RI in predicting neonatal RDS. Multivariate logistic regression analysis was carried out to test the association between changes in Doppler parameters and the occurrence of RDS after adjustment for GA. *P*-values $< 0.05$ was considered statistically significant. All statistical calculations were carried out using computer program SPSS 15 for Microsoft Windows (2006) (Chicago, IL, USA).

## RESULTS

A total of 756 fetuses were examined, 28 (3.7%) fetuses were not delivered within 24 h; these were excluded leaving 728 fetuses, of which 14 fetuses (1.92%) proved to have structural abnormalities on ultrasound examination; these were also excluded. Technically accepted Doppler waveforms were obtained in 698 of 714 (97.7%) eligible fetuses. This is because in 16 women, the MPA Doppler waveforms could not be obtained properly either because the fetal spine was directed anteriorly (6 fetuses) or because the woman was unable to lie at rest because of labor pains (10 women). Thus, a total of 698 fetuses were eligible for final analysis. Of these, 55 (7.87%) were diagnosed with RDS according to the neonatal criteria.

Table 1 presents maternal and fetal data in addition to ultrasound findings in fetuses diagnosed with RDS and those without RDS. Fetuses that developed RDS had a significantly lower GA at delivery, higher amniotic fluid index, lower estimated fetal weight on ultrasound and lower NBW. Fetuses with RDS had also a significantly lower Apgar scores and were more commonly admitted to neonatal intensive care. Interestingly, RDS was more commonly encountered in male fetuses.

The MPA At/Et was significantly lower in fetuses diagnosed with RDS compared with those without ($0.209 \pm 0.054$ versus $0.332 \pm 0.066$, $P < 0.001$). MPA PI and RI were significantly higher ($2.27 \pm 0.23$ and $0.8 \pm 0.11$ cm s$^{-1}$ versus $2.18 \pm 0.23$ and

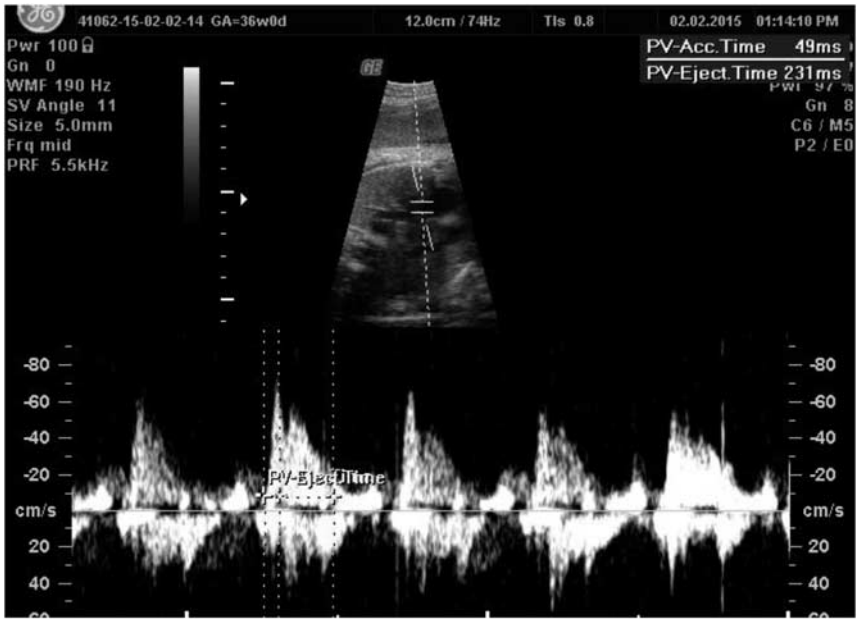


**Figure 1.** Measurement of the main pulmonary artery (MPA) acceleration time and ejection time. The acceleration time/ejection time (At/Et) ratio can then be calculated.

**Table 1.** Comparison between fetuses with and without neonatal RDS[a]

| | *Fetuses with RDS (n = 55)* | *Fetuses without RDS (n = 643)* | P-*value* |
|---|---|---|---|
| Maternal age (years) | 27.71 ± 4.7 | 28.31 ± 5.29 | 0.418 |
| Nullipara (no. (%)) | 15 (27.3%) | 192 (29.9%) | 0.687 |
| GA at delivery (weeks) | 35.83 ± 1.51 | 37.43 ± 1.64 | < 0.001 |
| *Mode of delivery* | | | |
| VD (no. (%)) | 33 (60%) | 364 (56.6%) | 0.626 |
| CS (no. (%)) | 22 (40%) | 279 (43.4%) | 0.626 |
| *Ultrasound measurements* | | | |
| AFI (cm) | 13.31 ± 5.71 | 10.66 ± 2.19 | < 0.001 |
| EFW (g) | 2704.02 ± 635.95 | 2991.73 ± 413.67 | < 0.001 |
| *MPA indices* | | | |
| S/D | 6.92 ± 0.29 | 6.86 ± 0.29 | 0.183 |
| PI (cm/s) | 2.27 ± 0.23 | 2.18 ± 0.23 | 0.003 |
| RI (cm/s) | 0.8 ± 0.11 | 0.76 ± 0.09 | 0.002 |
| PSV (cm/s) | 65.05 ± 5.33 | 67.21 ± 4.8 | 0.002 |
| At/Et ratio | 0.209 ± 0.054 | 0.332 ± 0.066 | < 0.001 |
| *Neonatal data* | | | |
| NBW (g) | 2707.75 ± 652.89 | 3031.27 ± 1196 | 0.048 |
| Male sex (no. (%)) | 35 (63.6%) | 311 (48.4%) | 0.03 |
| Apgar 1 min | 4.15 ± 0.67 | 6.97 ± 0.69 | < 0.001 |
| Apgar 5 min | 5.98 ± 0.59 | 9.09 ± 0.55 | < 0.001 |
| Apgar < 7 at 5 min (no. (%)) | 48 (87.3%) | 4 (0.6%) | < 0.001 |
| NICU (no. (%)) | 55 (100%) | 36 (5.6%) | < 0.001 |

Abbreviations: AFI, amniotic fluid index; At/Et, acceleration time/ejection time; CS, Cesarean section; EFW, estimated fetal weight; GA, gestational age; MPA, main pulmonary artery; NBW, neonatal birth weight; NICU, neonatal intensive care; PI, pulsatility index; PSV, peak systolic velocity; RDS, respiratory distress syndrome; RI, resistance index; S/D, systolic/diastolic ratio; VD, vaginal delivery. [a]As regards maternal, clinical and ultrasound data.

**Table 2.** Multivariate logistic regression analysis for RDS prediction of the MPA Doppler indices

| | *OR* | *95% CI* | P-*value* |
|---|---|---|---|
| At/Et ratio | 2.079 | 24.924–173.539 | < 0.001 |
| PI | 6.242 | 2.553–15.264 | < 0.001 |
| RI | 86.856 | 8.425–895.394 | < 0.001 |
| PSV | 1.038 | 0.973–1.107 | 0.263 |

Abbreviations: At/Et, acceleration time/ejection time; CI, confidence interval; MPA, main pulmonary artery; OR, odds ratio; PI, pulsatility index; PSV, peak systolic velocity; RDS, respiratory distress syndrome; RI, resistance index.

$0.76 \pm 0.09\ cm\ s^{-1}$; *P*: 0.003 and 0.002, respectively), whereas PSV was significantly lower in fetuses with RDS ($65.05 \pm 5.33$ versus $67.21 \pm 4.8\ cm\ s^{-1}$; *p*: 0.002). S/D ratio was not significantly different between the two groups (Table 1).

Multivariate logistic regression analysis for RDS development revealed that the association between fetal MPA Doppler indices (At/Et, PI and RI) and the postnatal development of RDS remained significant after controlling for GA at delivery (Table 2). However, PSV showed nonsignificant difference after controlling for GA (*P*: 0.263).

**Table 3.** Sensitivity and specificity of At/Et ratio, PI and RI for predicting neonatal RDS

| | *Cutoff value* | *Sensitivity (%)* | *Specificity (%)* | *AUC* |
|---|---|---|---|---|
| At/Et ratio | 0.305 | 76.4 | 91.6 | 0.899 |
| PI | 2.15 | 69.1 | 44.5 | 0.609 |
| RI | 0.77 | 67.3 | 43.5 | 0.635 |

Abbreviations: At/Et, acceleration time/ejection time; AUC, area under the curve; PI, pulsatility index; RDS, respiratory distress syndrome; RI, resistance index.

Spearman's correlation coefficient showed that GA was significantly ($P < 0.001$) correlated with At/Et ($r = 0.602$), PSV ($r = 0.327$), PI ($r = -0.339$) and RI ($r = -0.567$). The strongest correlation was seen with At/Et. However, S/D ratio was not correlated with GA ($r = -0.03$, p: 0.433).

The receiver operating characteristic curve revealed that the cutoff value of 0.305 for At/Et yielded a sensitivity of 76.4% and a specificity of 91.6% for prediction of neonatal RDS with an area under the curve of 0.899.

The PI and RI, however, showed lower sensitivity and specificity for predicting RDS (Table 3 and Figure 2).

## DISCUSSION

In this study, we examined the value of fetal MPA Doppler indices in predicting neonatal RDS development in late preterm and early term fetuses.

Late preterm are premature newborns delivered between 34 and 36+6 weeks of gestation, whereas early term infants are those delivered between 37 and 38+6 weeks of gestation.[20]

This GA (34 to 38+6 weeks) was chosen because before 34 weeks, the risk of fetal lung immaturity is high, and thus testing of FLM is not useful in this GA. A fetus delivered after 39 weeks, on the other hand, has a very low risk of developing RDS, as many studies have suggested 39 weeks gestation as the optimum for planned CS.[21,22]

Between 34 and 38+6 weeks gestation is an area of a possibility of developing RDS, hence an obstetrician should test for FLM before attempting to deliver a fetus in this GA range.

The results of this study have shown that compared with fetuses that did not develop neonatal RDS, fetuses that developed RDS had significantly lower At/Et and PSV and higher PI and RI. This means that fetuses that develop RDS have higher pulmonary vascular resistance and pressure and lower pulmonary blood flow compared with fetuses that do not develop RDS. In concordance with our results, MPA At/Et was reported to be significantly lower in preterm fetuses that developed RDS in two previous studies.[13,16]

The difference between the two groups for At/Et, PI and RI in this study remained significant after controlling for GA. This means that these three indices can be used as independent predictors for RDS development.

This study has shown that MPA At/Et and PSV were positively correlated, whereas PI and RI were inversely correlated with GA. The strongest correlation was found between GA and At/Et. S/D ratio did not change significantly through the studied period of gestation. These results are totally consistent with those of Chaoui *et al.*[17] who described the Doppler echocardiography of the main stems of the pulmonary arteries in the normal human fetus. The authors suggested that pulmonary vascular compliance increases and mean pulmonary artery pressure decreases as pregnancy advances, resulting in a gradual increase in pulmonary blood flow.[17] Also, Rasanen *et al.*[23] have stated that the pulmonary artery impedance decreases as the GA advances. The inverse relation

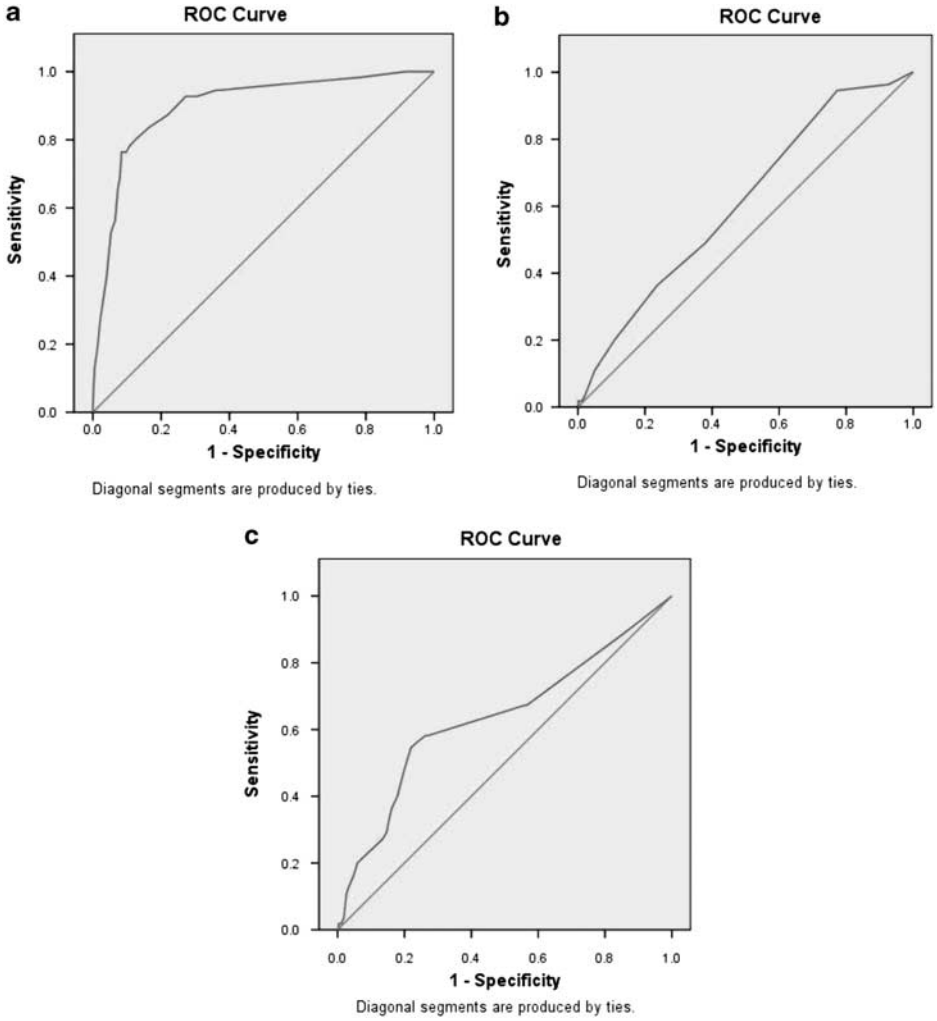


**Figure 2.** Receiver operating curve (ROC) of the (**a**) At/Et ratio, (**b**) PI and (**c**) RI for predicting neonatal respiratory distress syndrome (RDS) development.

between GA and RI is probably caused by the increasing lumen of the pulmonary vessels, increased vascular elasticity and continued pulmonary angiogenesis that occur with advancing GA.[24] Similarly, Guan *et al.*[13] reported a significant correlation of GA with At, At/Et, PSV, end-diastolic velocity and mean velocity in 288 healthy fetuses from 22 to 42 weeks gestation.

Schenone *et al.*[15] have reported that MPA At/Et and the TDx-FLM-II (measured in the amniotic fluid) were positively correlated, which means that an increased At/Et is associated with a more mature lung and a less risk of developing RDS, which supports our findings.

On the contrary, Azpurua *et al.*[14] have reported that At/Et was inversely correlated with lecithin/sphingomyelin ratio obtained by amniocentesis. Their study, however, could not study the association of At/Et with the development of clinical RDS as their study sample size (29 fetuses) was low with only one infant diagnosed with RDS.

MPA At/Et was reported to be inversely related to pulmonary artery pressure measured directly at cardiac catheterization.[25] Also, pulmonary artery pressure is known to be raised in infants with RDS.[26] This makes it possible that MPA At/Et may be useful in prediction of the development of neonatal RDS.

In this study, a cutoff value for At/Et of 0.305 could predict the development of neonatal RDS in a fetus delivered between 34 and 38+6 weeks with a sensitivity of 76.4% and a specificity of 91.6%, with an area under the curve/receiver operator characteristic of 0.899. The ability of PI and RI to predict RDS development had lower sensitivity and specificity compared with that of At/Et.

Hence, beside being easy and noninvasive, MPA At/Et provides a high sensitivity and specificity, as compared with amniocentesis-based tests of FLM that were reported to have high sensitivity but low specificity.[27]

Guan *et al.*[13] reported that At/Et could predict RDS development in preterm fetuses with a sensitivity of 71.4% and a specificity of 93.1%. Similarly, Schenone *et al.*[15] found that a cutoff value for At/Et of 0.314 provided a sensitivity of 73% and a specificity of 93% for predicting immature surfactant/albumin ratio results in 43 fetuses with a mean GA of 36 weeks. However, the authors did not correlate At/Et with clinical RDS.

To our knowledge, two previous studies have correlated At/Et of the fetal pulmonary artery with chemical markers of FLM obtained through amniocentesis namely lecithin/sphingomyelin ratio[14] and the surfactant/albumin ratio TDx-FLM-II[15]. Two other studies have examined fetal pulmonary artery Doppler indices to predict the development of neonatal RDS in preterm births only.[13,16] The above studies were limited by the small sample sizes; also, none had studied the development of RDS in early term fetuses.

To our knowledge, this is the first large study (698 fetuses) that studied the prediction of RDS development in both late preterm

(34 to 36+7 weeks gestation) and early term (37 to 38+6 weeks gestation) fetuses.

This study is also strengthened by its prospective design and that it examined the association of fetal MPA Doppler indices with the clinical end point of interest, namely RDS. Moreover, the Doppler measurements were taken on the same day of delivery, thus avoiding the changes that may occur in Doppler measurements. This study was conducted on a large population with diverse comorbidities, which increases its clinical applicability.

Although this study has revealed that MPA At/Et can predict neonatal RDS development in women in labor and those indicated for selective CS, yet whether this is also true for women not in labor and those scheduled for elective CS needs to be further studied.

In conclusion, and based on our results, we can introduce fetal MPA At/Et as noninvasive accurate method for neonatal RDS prediction in a critical range of GA (34 to 38+6 weeks) in which the risk of development of RDS warrants FLM testing.

We recommend that a fetus with At/Et below 0.305 should be delivered in a well-equipped hospital with facilities of respiratory support, as it carries the risk of developing neonatal RDS.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## REFERENCES

1 Liu J. Respiratory distress syndrome in full-term neonates. *J Neonatal Biol* 2012; **S1**: e001.
2 Koivisto M, Marttila R, Kurkinen-Raty M, Saarela T, Pokela ML, Jouppila P *et al.* Changing incidence and outcome of infants with respiratory distress syndrome in the 1990s: a population-based survey. *Acta Paediatr* 2004; **93**: 177–184.
3 Bouziri A, Ben Slima S, Hamdi A, Menif K, Belhadj S, Khaldi A *et al.* Acute respiratory distress syndrome in infants at term and near term about 23 cases. *Tunis Med* 2007; **85**: 874–879.
4 Menon R. Spontaneous preterm birth, a clinical dilemma: etiologic, pathophysiologic and genetic heterogeneities and racial disparity. *Acta Obstet Gynecol Scand* 2008; **87**: 590–600.
5 March of Dimes, PMNCH, Save the Children, WHO. *Born Too Soon: The Global Action Report on Preterm Birth*. World Health Organization: Geneva, Switzerland, 2012.
6 McIntire DD, Leveno KJ. Neonatal mortality and morbidity rates in late preterm births compared with births at term. *Obstet Gynecol* 2008; **111**: 35–41.
7 Tita AT, Landon MB, Spong CY, Lai Y, Leveno KJ, Varner MW *et al.* Eunice Kennedy Shriver NICHD Maternal-Fetal Medicine Units Network. Timing of elective repeat cesarean delivery at term and neonatal outcomes. *N Engl J Med* 2009; **360**(2): 111–120.
8 Gordon MC, Narula K, O'Shaughnessy R, Barth WH Jr. Complications of third-trimester amniocentesis using continuous ultrasound guidance. *Obstet Gynecol* 2002; **99**: 255–259.
9 Tekesin I, Anderer G, Hellmeyer L, Stein W, Kuhnert M, Schmidt S. Assessment of fetal lung development by quantitative ultrasonic tissue characterization: a methodical study. *Prenat Diagn* 2004; **24**: 671–676.
10 Chaoui R, Kalache K, Tennstedt C, Lenz F, Vogel M. Pulmonary arterial Doppler velocimetry in fetuses with lung hypoplasia. *Eur J Obstet Gynecol Reprod Biol* 1999; **84**: 179–185.
11 Fuke S, Kanzaki T, Mu J, Wasada K, Takemura M, Mitsuda N *et al.* Antenatal prediction of pulmonary hypoplasia by acceleration time/ ejection time ratio of fetal pulmonary arteries by Doppler blood flow velocimetry. *Am J Obstet Gynecol* 2003; **188**: 228.
12 Laudy JA, de Ridder MA, Wladimiroff JW. Human fetal pulmonary artery velocimetry: repeatability and normal values with emphasis on middle and distal pulmonary vessels. *Ultrasound Obstet Gynecol* 2000; **15**: 479.
13 Guan Y, Li S, Luo G, Wang C, Norwitz ER, Fu Q *et al.* The role of Doppler waveforms in the fetal main pulmonary artery in the prediction of neonatal respiratory distress syndrome. *J Clin Ultrasound* 2014; **43**: 375–383; published online in Wiley Online Library (wileyonlinelibrary.com).
14 Azpurua H, Norwitz ER, Campbell KH, Funai EF, Pettker CM, Kleine M *et al.* Acceleration/ejection time ratio in the fetal pulmonary artery predicts fetal lung maturity. *Am J Obstet Gynecol* 2010; **203**(40): e1–e8.
15 Schenone MH, Samson JE, Jenkins L, Suhag A, Mari G. Predicting fetal lung maturity using the fetal pulmonary artery Doppler wave acceleration/ejection time ratio. *Fetal Diagn Ther* 2014; **36**: 208–214.
16 Kim SM, Park JS, Norwitz ER, Hwang EJ, Kang HS, Park C *et al.* Acceleration time-to-ejection time ratio in fetal pulmonary artery predicts the development of neonatal respiratory distress syndrome: a prospective cohort study. *Am J Perinatol* 2013; **30**: 805–811.
17 Chaoui R, Taddei F, Rizzo G, Bast C, Bollmann R. Doppler echocardiography of the main stems of the pulmonary arteries in the normal human fetus. *Ultrasound Obstet Gynecol* 1998; **11**: 173–179.
18 Mitchell JM, Roberts AB, Lee A. Doppler waveforms from the pulmonary arterial system in normal fetuses and those with pulmonary hypoplasia. *Ultrasound Obstet Gynecol* 1998; **11**: 167–172.
19 Hamvas A. Pathophysiology and management of respiratory distress syndrome. In: Martin RJ, Fanaroff AA, Walsh MC (eds). *Fanaroff and Martin's Neonatal–Perinatal Medicine*, 9th edn, Vol. 1. Elsevier Mosby: St Louis, MO, USA, 2011, pp 1106–1116.
20 Raju TN, Higgins RD, Stark AR, Leveno KJ. Optimizing care and outcome for late-preterm (near-term) infants: a summary of the workshop sponsored by the National Institute of Child Health and Human Development. *Pediatrics* 2006; **118** (3): 1207–1214.
21 Hourani M, Ziade F, Rajab M. Timing of planned caesarean section and the morbidities of the newborn. N. *Am J Med Sci* 2011; **3**(10): 465–468.
22 Gawlik S, Müller M, Kuon RJ, Szabo AZ, Keller D, Sohn C. Timing of elective repeat caesarean does matter: Importance of avoiding early-term delivery especially in diabetic patients. *J Obstet Gynaecol* 2014; **30**: 1–6 (e-pub ahead of print).
23 Rasanen J, Huhta JC, Weiner S, Wood DC, Ludomirski A. Fetal branch pulmonary arterial vascular impedance during the second half of pregnancy. *Am J Obstet Gynecol* 1996; **174**: 1441–1449.
24 Grenache DG, Gronowski AM. Fetal lung maturity. *Clin Biochem* 2006; **39**: 1–10.
25 Kosturakis D, Goldberg SJ, Allen HD, Loeber C. Doppler echocardiographic prediction of pulmonary arterial hypertension in congenital heart disease. *Am J Cardiol* 1984; **53**: 1110–1115.
26 Evans NJ, Archer LN. Doppler assessment of pulmonary artery pressure during recovery from hyaline membrane disease. *Arch Dis Child* 1991; **66**: 802–804.
27 Luo G, Norwitz ER. Revisiting amniocentesis for fetal lung maturity after 36 weeks' gestation. *Rev Obstet Gynecol* 2008; **1**: 61.