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CLINICAL ARTICLE

Prediction of neonatal respiratory distress syndrome in term pregnancies by assessment of fetal lung volume and pulmonary artery resistance index

Mohamed Laban [a,*], Ghada M. Mansour [a], Mohammed S.E. Elsafty [a], Alaa S. Hassanin [a], Sahar S. EzzElarab [b]

[a] Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, Cairo, Egypt
[b] Early Cancer Detection Unit, Ain Shams Maternity Hospital, Cairo, Egypt

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ABSTRACT

Objective: To develop reference cutoff values for mean fetal lung volume (FLV) and pulmonary artery resistance index (PA-RI) for prediction of neonatal respiratory distress syndrome (RDS) in low-risk term pregnancies. *Methods:* As part of a cross-sectional study, women aged 20–35 years were enrolled and admitted to a tertiary hospital in Cairo, Egypt, for elective repeat cesarean at 37–40 weeks of pregnancy between January 1, 2012, and July 31, 2013. FLV was calculated by virtual organ computer-aided analysis, and PA-RI was measured by Doppler ultrasonography before delivery. *Results:* A total of 80 women were enrolled. Neonatal RDS developed in 11 (13.8%) of the 80 newborns. Compared with neonates with RDS, healthy neonates had significantly higher FLVs ($P < 0.001$) and lower PA-RIs ($P < 0.001$). Neonatal RDS is less likely with FLV of at least 32 cm^3 or PA-RI less than or equal to 0.74. Combining these two measures improved the accuracy of prediction. *Conclusion:* The use of either FLV or PA-RI predicted neonatal RDS. The predictive value increased when these two measures were combined.

1. Introduction

Neonatal respiratory distress syndrome (RDS) is defined as respiratory failure that occurs after birth due to absence of lung surfactant, a substance that is required to prevent alveolar collapse and for inflation of the lungs [1]. This condition is a leading cause of neonatal morbidity and mortality: estimates suggest that 80 000 cases of neonatal RDS occur every year in the USA alone, with 8500 neonatal deaths [1].

Risk of neonatal RDS decreases as gestational age increases, because the lungs are the final fetal organs to functionally mature [1,2]. Therefore, neonatal RDS is often considered to be a disease of premature newborns, although it does not exclusively occur after preterm deliveries [1,2]. Biochemical tests have been developed to determine the risk of neonatal RDS and help obstetricians to decide when to deliver a neonate [2]. The chemical, biological, and physical properties of amniotic fluid represent the gold-standard measures of fetal lung maturity [2]. Nevertheless, amniotic fluid can be obtained only by performing amniocentesis, an invasive procedure that poses potential risks to the pregnancy, such as premature rupture of membranes, preterm labor, placental abruption, fetomaternal hemorrhage, fetal injury, and even fetal or maternal death [3]. Indeed, Grenache et al. [4] reported that the frequency of fetal lung maturity testing had decreased in the USA between 1998 and 2008, often because of concerns about amniocentesis.

A non-invasive test to assess fetal lung maturity would be a more acceptable option for pregnant women. Fetal lung maturity has been indirectly assessed by ultrasonic evaluation of gross morphology [5] and the use of Doppler blood flow waveforms [6]. However, as yet, there is no reliable non-invasive test to predict fetal lung maturity before delivery [7].

Measurement of fetal lung volume (FLV) and pulmonary artery pressure could potentially be used to predict neonatal RDS. Structural and functional progress of fetal lung development with increasing gestational age correlates with a change in the pattern of sonographic echogenicity of this organ [8]. Furthermore, fetal pulmonary artery flow velocity waveforms were found to change with increasing gestational age [9,10]. Finally, pulmonary artery pressure measured by Doppler decreased among newborns with RDS after administration of surfactant [11].

The aim of the present study was to develop reference cutoff values for mean FLV and pulmonary artery resistance index (PA-RI) as measures that could be used to predict the development of neonatal RDS in low-risk term pregnancies.

* Corresponding author at: Department of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, (Ramses Street), Al-Abbassia, 11566, Cairo, Egypt. Tel.: +20 1010042473; fax: +20 222705246.
E-mail address: laban63@yahoo.com (M. Laban).

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2. Materials and methods

A cross-sectional study was conducted at Ain Shams Maternity Hospital, Cairo, Egypt, between January 1, 2012, and July 31, 2013. Eligible women were aged 20–35 years and had been admitted for elective repeat cesarean at 37–40 weeks of pregnancy. Women with any pregnancy-related condition (e.g. hypertension, preeclampsia, or diabetes mellitus), autoimmune disorders, or twin pregnancies were excluded. Cases of congenital fetal anomaly, placental abnormality, macrosomia, and intrauterine growth restriction were also excluded. The present study was approved by the hospital research committee and informed consent was obtained from all participants.

A complete history was taken from all participants, and the first day of the last menstrual period was noted. Gestational age had been confirmed by ultrasonography between 9 and 12 weeks of pregnancy. Obstetric ultrasonography was performed by the second author (G.M.M.) using the Voluson E6 (General Electric Healthcare, Waukesha, WI, USA) before the elective cesarean delivery (but on the same day).

Two-dimensional (2D) ultrasonography was performed to record fetal biometry, placental site, and amniotic fluid index. A Doppler signal was introduced to assess umbilical artery resistance index and PA-RI. Three-dimensional (3D) ultrasonography was then used to estimate FLV. A longitudinal section of the fetal chest was obtained that clearly depicted the lung. A 3D window was activated and, after the complete electronic sweep and assurance of the absence of fetal or maternal movements to avoid motion artifacts, 3D mulitplanar view was then obtained. (A) Box was chosen as the active box. The virtual organ computer-aided analysis (VOCAL) program was activated and the manual option with 30° rotation steps was chosen. Drawing started from the apex to the base of the lung. After six steps of rotation in a longitudinal axis for each lung, FLV was automatically estimated for both lungs. The mean of the two volumes was calculated (Fig. 1). Measurement of FLV was performed two to four times by G.M.M. and little intra-observer variability was recorded.

To measure PA-RI, a three-vessel view of the fetal heart was obtained (Fig. 2A). Pulsed Doppler was introduced and the sample volume was focused on the pulmonary artery stem (Fig. 2B). Color Doppler was not used, because it causes blue and red overlapping colors, which would obscure the fetal pulmonary artery. Therefore, pulsed Doppler (no color) was preferred. The sample volume was placed over the artery directly depending on the sonographic anatomy. Umbilical artery resistance index was directly calculated by the computerized machine after using the marker at the peak systole and end diastole.

Neonatal outcome, including the need for admission to the neonatal intensive care unit, was assessed following cesarean delivery. In a previous study [12], FLV assessment had 83% sensitivity in the prediction of neonatal RDS. To calculate the necessary sample size for the present study, the reported 83% sensitivity plus or minus 12% was used with a 95% confidence level, a significance level of 0.05, and 80% power. The calculations yielded a sample size of 80.

Data were analyzed using SPSS version 15.0 (SPSS Inc, Chicago, IL, USA). Imaging data are presented as mean and 95% confidence interval (CI), and correlated with neonatal RDS using the Student *t* test. Demographic data are presented as medians with interquartile ranges, and were compared using the Mann–Whitney test. Receiver operating characteristic curves were constructed to select the optimal cutoff values for FLV and PA-RI. Odds ratios (ORs) with 95% CIs, and the likelihood ratio for a positive test result (LR+) were calculated and compared for the various cutoff values. $P < 0.05$ was considered statistically significant.

3. Results

A total of 80 women were included. Overall, 11 (14%) of the newborns exhibited neonatal RDS and were admitted to the

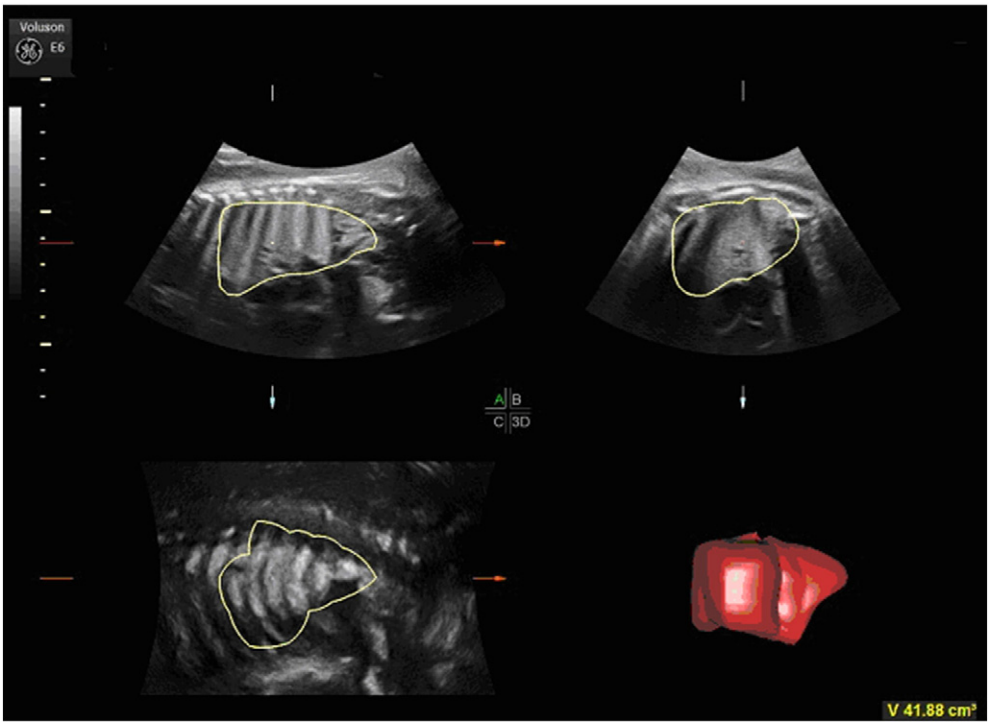

Fig. 1. Calculation of lung volume in a healthy fetus by virtual organ computer-aided analysis. The yellow line denotes the drawing of the fetal lung contour using manual option.