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Original article

Relation Between Fetal Doppler Pulmonary Artery Indices and Neonatal Respiratory Distress Syndrome In Term Neonates

Ahmed Mohamed Alsheikh; Ahmed Mohammed Elsadek; Samy Amin Gebreel

Department of Obstetrics and Gynecology, Faculty of Medicine, Al-Azhar University, Egypt.

Corresponding author: Ahmed Mohamed Alsheikh

Email: dr.ahmed.201053@gmail.com

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ABSTRACT

Background: Neonatal respiratory distress syndrome (RDS) is a common and challenging neonatal morbidity. Reliable prediction of the condition can improve management. Fetal pulmonary artery (PA) Doppler indices were suggested for prediction. However, the findings of different studies are conflicting.

Aim of the work: The present study aimed to assess the value of PA indices in the prediction of neonatal RDS in term babies.

Subjects and methods: This prospective study included 120 women with singleton term pregnancy. Assessed Doppler indices for the main pulmonary artery included pulsatility index (PI), resistive index (RI), peak systolic velocity (PSV), and the At/Et ratio. Upon delivery, the newborn babies were examined for RDS signs (tachypnea, retractions, and/or nasal flaring).

Results: Among the 120 delivered babies, there were 16 (13.3 %) with RDS. Comparison between neonates with RDS and neonates without showed significantly lower neonatal weight, higher pulmonary artery RI and PI, higher pulmonary artery PSV in neonates with RSD. Also, they had a significantly lower pulmonary artery at/et ratio when compared with normal babies. The pulmonary artery at/et ratio showed the best performance compared to other indices (sensitivity: 100.0 %, specificity: 50.0 %) at a cut-off (0.32).

Conclusions: The present study documented reliable predictive value of PA hemodynamic parameters including RI, PI, PSV, and at/et ratio in predicting neonatal RDS in term babies.

Keywords: Neonatal respiratory distress syndrome; Pulmonary artery; Fetal Doppler; Pulsatility index; Resistive index.

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* Main subject and any subcategories have been classified according to the research topic.

INTRODUCTION

Neonatal respiratory distress syndrome [RDS] is a commonly encountered clinical condition. It's considered one of the main reasons for neonatal diseases and mortality, particularly in preterm newborns [1].

The condition is primarily caused by immature lung development and deficient pulmonary surfactant production[2]. Risk factors include maternal drug administration[3], maternal diabetes[4], and genetic susceptibility[5]. The significant morbidity and mortality burden of neonatal RDS is mainly attributed to the complexity of the underlying pathology, challenging diagnosis in some cases, and lack of specific treatment methods[6].

Considering its clinical consequences and economic impact, prediction of RDS development may help to improve the management of the affected neonates. In this context, many biochemical and sonographic approaches were investigated. The former group included lecithin/sphingomyelin ratio and the lamellar body count [7], amniotic fluid surfactant/albumin ratio [8], amniotic fluid lamellar bodies count [9], and umbilical cord blood differentially expressed peptides [10].

Ultrasonographic imaging plays a significant role in diagnosing many fetal and neonatal conditions. Ultrasonographic parameters focused mainly on fetal pulmonary artery [PA] indices and fetal lung volume. The investigated PA indices included At/Et ratio[11-14], pulmonary artery resistive index [15].

AIM OF THE WORK

The present study aimed to uncover if there is any relation between the fetal PA doppler indices and the development of neonatal RDS and the outcome of the affected patients.

PATIENTS AND METHODS

Study design and setting

The current work is a prospective study performed at Al-Azhar University Hospitals, Cairo, Egypt. An approval to complete the study was gained from the local ethical committee [Approval number: 207/2/219], and all participants gave informed consent before enrollment in the study.

Inclusion and exclusion criteria

The study included 120 women with a singleton pregnancy. The sample size was calculated using G Power [University of Kiel, Germany] considering the data reported by the study of Buke et al., [2019] where the at/et ratio values in neonates with RDS and neonates without were 0.2965 ± 0.042 versus 0.386 ± 0.068 . Exclusion criteria were fetal anomalies, fetal distress, and post-term pregnancy.

General and ultrasonographic assessment

Upon admission, the included women were exposed to careful historical-taking and a full clinical and obstetrical examination. Assessed Doppler indices for the main pulmonary artery, including pulsatility index [PI], resistance index [RI], peak systolic velocity [PSV], and At/Et ratio. To get the At/Et, it was calculated as the period from the start of the ventricular systole to the reach of maximum velocity [At] divided by the period from the beginning to the termination of ventricular systole [Et]. Upon delivery, the newborn babies were examined for the signs of RDS [tachypnea, retractions and/or nasal flaring]. Doppler assessment was performed once, just before delivery.

Statistical analysis

The data were coded and analyzed via the statistical package SPSS version 25. The data was presented in the form of mean and standard deviation [SD] for quantitative variables and frequencies and percents for qualitative variables. Evaluation of numerical data was performed via an unpaired t-test. A comparison between the qualitative data was done by Chi-square [χ^2] test. ROC curve was made by analyzing the area under the curve. This was demonstrated to find the best cutoff -point of Sonar factors for diagnosis of RDS. At P-value < 0.05 were considered significant statistically.

RESULTS

The present study included 120 women with singleton pregnancy. Among the 120 delivered babies, there were 16 [13.3 %] with RDS. Comparison between neonates with RDS and neonates without RDS showed significantly lower neonatal weight [2969.0 ± 233.8 versus $3188.0 \pm$

372.3 grams; $p=0.004$], higher pulmonary artery RI [0.88 ± 0.05 versus 0.83 ± 0.06 ; $p=0.001$] and PI [1.9 ± 0.2 versus 1.74 ± 0.23 ; $p=0.014$], higher pulmonary artery PSV [88.1 ± 12.0 versus 77.4 ± 14.3 ; $p=0.005$] in neonates with RSD. Also, they had significantly lower pulmonary artery At/Et ratio [0.26 ± 0.03 versus 0.31 ± 0.07 ; $p<0.001$] when

compared with normal babies [Table 1]. The performance of various PA indices in the prediction of RDS was illustrated in table [2]. Pulmonary artery At/Et ratio showed the best performance in comparison to other indices [sensitivity: 100.0 %, specificity: 50.0 %] at a cut-off [0.32] [Fig.1-4].

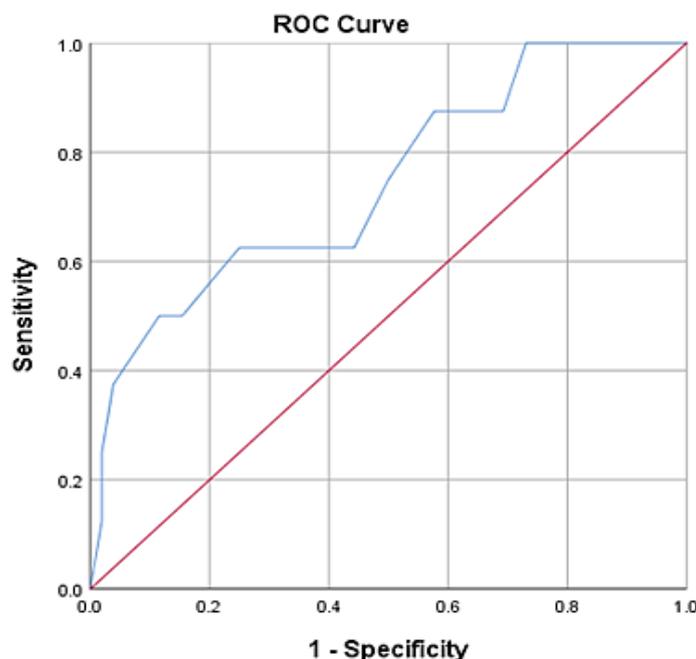
Table [1]: Maternal and neonatal characteristics in the studied neonates [n=120]

| | All neonates [N=120] | RDS + [n=16] | RSD -[N=104] | P value |
|------------------------------|----------------------|----------------|----------------|---------|
| Age [years] | 26.5 ± 5.1 | 28.1 ± 5.2 | 26.2 ± 5.0 | 0.17 |
| Parity | 1.7 ± 1.5 | 2.4 ± 1.5 | 1.6 ± 1.5 | 0.055 |
| Gestational age [weeks] | 38.4 ± 0.9 | 38.1 ± 0.8 | 38.4 ± 0.9 | 0.23 |
| Neonatal weight [gm] | 3159.0 ± 364.0 | 2969.0 ± 233.8 | 3188.0 ± 372.3 | 0.004 |
| Umbilical artery RI | 0.56 ± 0.06 | 56.0 ± 0.04 | 0.56 ± 0.06 | 0.96 |
| Pulmonary artery PI | 1.8 ± 0.23 | 1.9 ± 0.2 | 1.74 ± 0.23 | 0.014 |
| Pulmonary artery PSV | 78.8 ± 14.4 | 88.1 ± 12.0 | 77.4 ± 14.3 | 0.005 |
| Pulmonary artery At/Et ratio | 0.3 ± 0.07 | 0.26 ± 0.03 | 0.31 ± 0.07 | <0.001 |
| Apgar score 1 min. | 6.9 ± 1.5 | 4.5 ± 1.2 | 7.3 ± 1.1 | <0.001 |
| Apgar score 5 min. | 9.4 ± 0.8 | 7.8 ± 0.7 | 9.7 ± 0.5 | <0.001 |

RDS: Respiratory Distress Syndrome, RI: Resistive Index, PI: Pulsatility Index, PSV: Peak Systolic Velocity

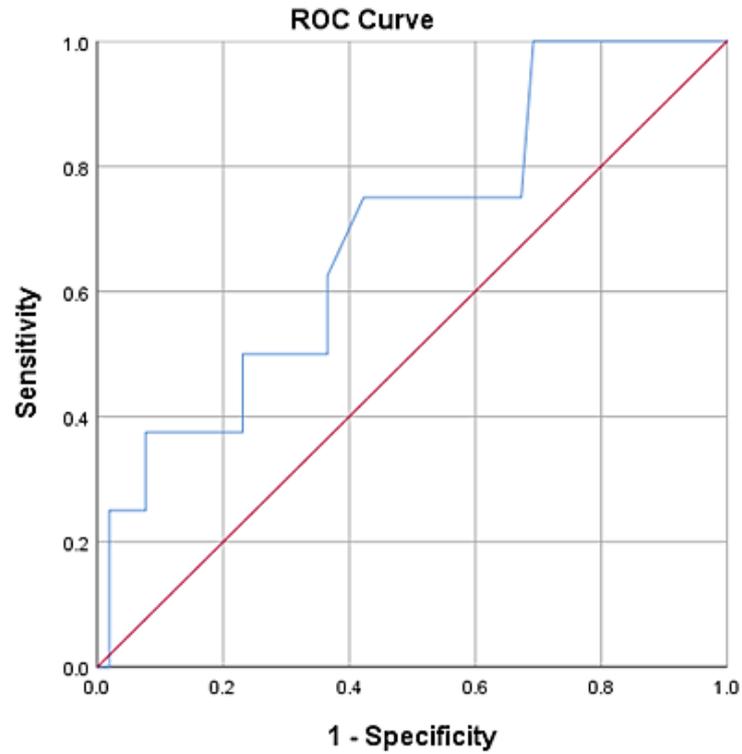
Table [2]: Performance of different pulmonary artery indices in the diagnosis of RDS

| | Cut-off | AUC | P | Sensitivity | Specificity |
|------------------------------|---------|------|-------|-------------|-------------|
| Pulmonary artery RI | 0.85 | 0.74 | 0.002 | 75.0 % | 50.0 % |
| Pulmonary artery PI | 1.79 | 0.69 | 0.014 | 75.0 % | 57.7 % |
| Pulmonary artery PSV | 78.5 | 0.7 | 0.01 | 75.0 % | 53.8 % |
| Pulmonary artery At/Et ratio | 0.32 | 0.73 | 0.004 | 100.0 % | 50.0 % |



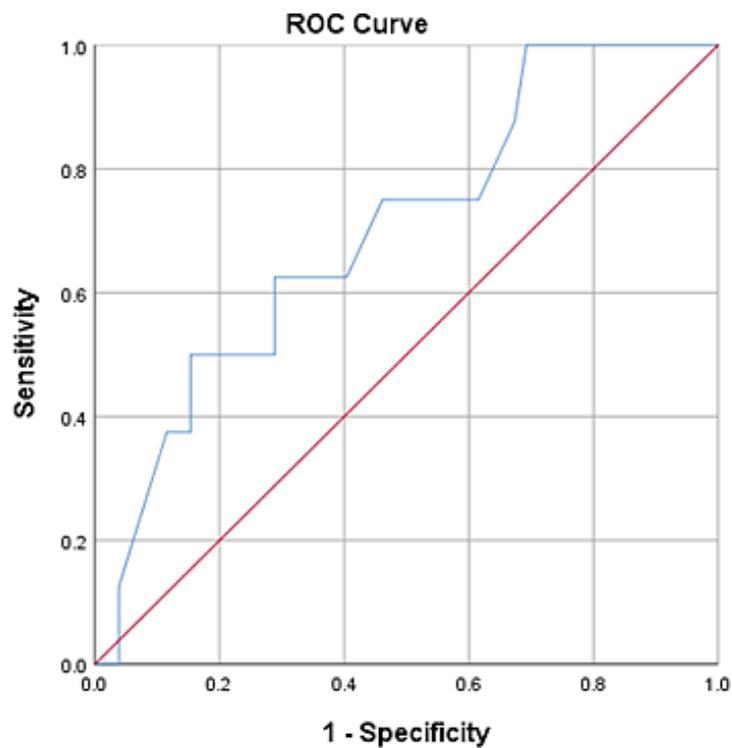
Diagonal segments are produced by ties.

Figure [1] ROC curve for pulmonary artery RI



Diagonal segments are produced by ties.

Figure [2]: ROC curve for pulmonary artery PI



Diagonal segments are produced by ties.

Figure [3] ROC curve for pulmonary artery PSV

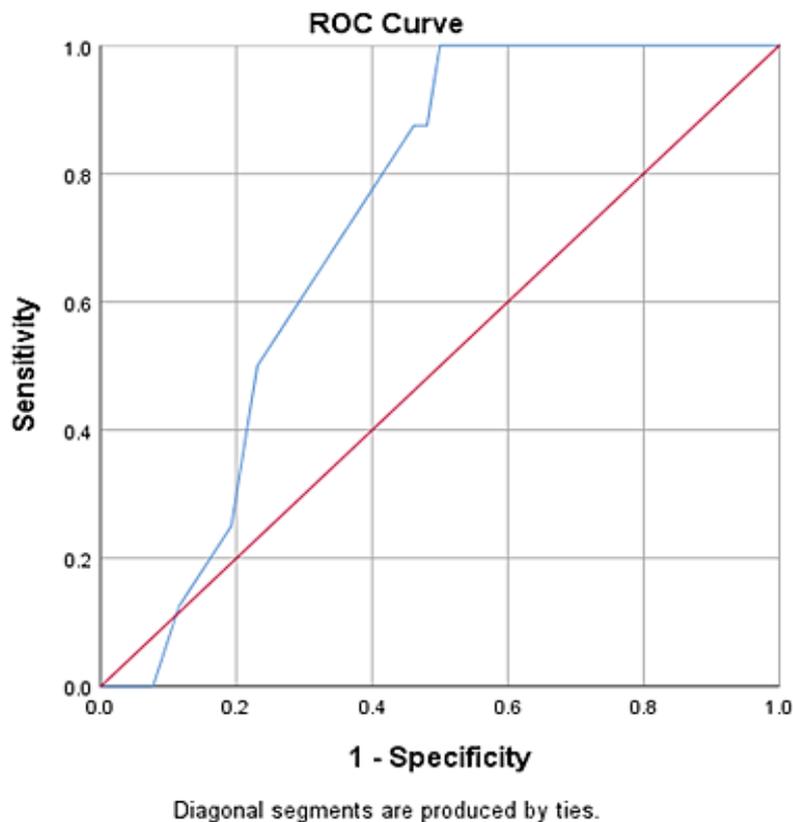


Figure [4] ROC curve for pulmonary artery At/Et ratio

DISCUSSION

In the current work, we assessed fetal pulmonary artery hemodynamic parameters' function in predicting neonatal RDS. The study found that all of the parameters, including pulmonary artery RI, PI, PSV, and At/Et ratio, showed good performance as predictors of RSD development in the studied neonates. In line with our conclusions, the study of Laban et al. [16] on 80 women. In their work, 13.8 % of delivered neonates had RDS. The authors acknowledged the value of PA-RI in predicting RDS in term neonates. They recognized pulmonary artery RI of ≤ 0.74 as a significant predictor of RDS. They added that fetal lung volume could be reliably also used for the same purpose. A subsequent study by the same group on another 80 women with 46.0 % of neonates with RDS reported similar conclusions in preterm neonates [15]. Moreover, they noted that combining both parameters resulted in better predictive value than single-use.

In another work, on a group of preterm and term babies [n=698], RDS was reported in 55 neonates. The authors reported significant predictive value of miscellaneous fetal main PA related parameters, including PI, RI, PSV, and PSV. However, the strongest correlation was found with At/Et [13].

In comparison, the study of Kim et al. [12] identified pulmonary artery At/Et ratio but not pulmonary artery RI and PI as a significant predictor of RDS in their study on 42 neonates, including 11 neonates who developed RDS. Of note, this study included a heterogeneous population of term and preterm babies delivered to singleton or twin pregnancies. Likewise, the study of Guan et al. [11] on 43 preterm neonates reported that only pulmonary artery acceleration time [at] and At/Et ratio could predict neonatal RDS. The predictive capability of pulmonary artery At/Et ratio was also appreciated by the recent works of Bke et al. [14] on 105 women and Duncan et al. [17] on 95 preterm neonates.

Interestingly and in support of our conclusions, the study of Azpurua et al.^[18] on 29 neonates documented an inverse relationship between the amniotic fluid lecithin/sphingomyelin ratio, a maturation marker of fetal-lung, and At/Et ratio in the fetal PA. This provides an explanation for the value of At/Et ratio in the prediction of RDS. It implies the role of poor fetal lung maturation in the pathogenesis of RDS.

In contrast to our findings and other studies, the study of Güngör et al.^[19] on 40 preterm babies failed to detect any significant differences between neonates who developed RDS and those who didn't regarding the fetal PA Doppler indices even after steroid administration. This may probably be attributed to the different demographic and clinical characteristics of the neonates included in different studies.

The present study isn't without limitations. It's a single-center study, and the sample size is relatively small. Further studies on larger and more diverse populations are strongly recommended.

Conclusions: In conclusion, the present study documented the reliable role of fetal PA-derived ultrasonographic parameters in predicting neonatal RDS in term babies. These parameters include RI, PI, PSV, and At/Et ratio.

Financial and Non-financial Relationships and Activities of Interest

None

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