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Predictive Value of Pulmonary Artery Doppler Ultrasonography in the Evaluation of Neonatal Respiratory Distress Syndrome in Premature Births: A Retrospective Case Series Study

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ABSTRACT Objective: This study aimed to investigate the predictive value of pulmonary pressure parameters detected by Doppler ultrasonography for respiratory distress syndrome (RDS). **Material and Methods:** This study was conducted between January 2017 and December 2018. Twenty five newborns who were born before 37th gestational week without anomalies and had no pregnancy complications were included in the study. All pregnants were examined with Doppler ultrasonography in the last 3 days before birth. Pulmonary artery acceleration time (AT) and pulmonary artery ejection time (ET) were evaluated. Newborns were evaluated for RDS and divided into two groups as positive and negative. SPSS 25.0 program was used for statistical analysis. $p<0.05$ values were considered statistically significant. **Results:** Six newborns were diagnosed with RDS and 19 were not. The difference between the mean age of the mothers of the RDS (+) and RDS (-) groups was significant ($p<0.05$). However, there was no significant relationship between the groups in terms of height, weight, body mass index, gravida, and parity ($p>0.05$). For AT, ET, and AT/ET, statistical differences were observed between the groups ($p=0.003$, $p=0.012$, $p=0.001$). **Conclusion:** It showed an inverse correlation between fetal AT/ET and premature neonatal RDS. Fetal AT/ET ratio measurement may be a useful and reliable non-invasive method for predicting RDS.

Keywords: Neonatal respiratory distress syndrome; Doppler ultrasonography; pulmonary artery

Preterm birth is one of the most important factors that cause perinatal morbidity and mortality, which is still up to date in obstetrics despite technological advances. Preterm birth is defined as a birth before 37 gestational weeks that is irrelevant to the baby's birth weight.[1] Nowadays, the incidence of preterm birth varies between 10 and 12%.[2,3] There is also a familial predisposition. Furthermore, women with a history of premature birth have an elevated risk of premature birth.[4] Almost 75% of preterm births occur spontaneously after preterm labor and preterm membrane rupture; the remaining 25% are caused by medical or obstetric problems that put the fetus and mother at risk, such as maternal hypertension, diabetes, placenta previa, and intrauterine growth retardation. Prevention of preterm birth is based on the prevention and treatment of the underlying disease.[5]

One of the significant issues encountered in premature infants is respiratory distress syndrome (RDS), which results mainly from insufficient surfactant in the lungs. This deficiency results in an inadequate airflow in the lungs, thereby hindering the transition from intrauterine to neonatal life. Surfactant is a combination of phospholipids that reduces

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alveolar surface tension and maintains alveolar stability. The synthesis of surfactant starts in the fetus at around 26 weeks of pregnancy. The occurrence of RDS is more frequent in infants with lower birth weight and gestational age, with the highest incidence in babies born before 28 weeks. Race, gender, maternal diseases, and antenatal glucocorticoid treatment affect incidence.[6] Diagnosis requires tachypnea, retraction, cyanosis in the room air, and a characteristic chest radiograph. Clinical progression varies depending on the baby size, disease severity, surfactant treatment, the presence of infection, the degree of shunt formed by patent ductus arteriosus, and the initiation of ventilator therapy.[7,8] RDS is characterized by pulmonary edema caused by respiratory distress, impaired blood gas exchange, reduced static compliance, and impaired integrity of the alveolocapillary membrane due to surfactant deficiency.[9-11]

It is crucial to accurately determine fetal lung maturity during the prenatal period to prevent RDS. Several prenatal methods are used to evaluate fetal lung maturity. However, some of these methods are not sufficient for diagnosis, and some are invasive.[12,13] Therefore, the present study aimed to examine the predictive value of pulmonary pressure parameters detected by Doppler ultrasonography for RDS.

MATERIAL AND METHODS

The present study was carried out at Kartal City Hospital between January 2017 and December 2018. This is a case series comprised twenty-five newborns who were born before the 37th gestational week, had no congenital anomalies, and had no pregnancy complications. The study participants were classified into two groups: RDS (+) and RDS (-). This study was granted approval from the ethics committee of Kartal City Hospital (date: September 27, 2023, no: 2023/514/258/4) and the Declaration of Helsinki was followed.

All pregnants were examined with Doppler US in the last 3 days before birth. Verbal informed consent was taken from the patients prior to examinations. Ultrasonographic evaluation was performed by a gynecologist using VOLUSON E8 ultrasonographic (General Electric Healthcare, Little Chalfont, UK) device considering fetal movements and respiratory periods. To evaluate blood flow in the fetal pulmonary artery, measurements of several parameters were taken through three consecutive examinations, including the pulsatility index, systolic and diastolic ratio, peak systolic velocity, acceleration time (AT), ejection time (ET), and AT to ET of the main pulmonary artery. Care was taken to ensure precise measurements by magnifying the image and keeping the angle of insonation less than 20 degrees.

To diagnose RDS, in the absence of other causes of dyspnoea, fine granule densities, decreasing lung volume (inspired oxygen>0.4 fractional concentration) with increased oxygen demand were used. In addition, patient characteristics such as APGAR scores, and neonatal intensive care unit requirement were recorded.

STATISTICAL ANALYSIS

The SPSS 25.0 program (IBM, USA) was utilized to perform statistical analysis. Mean±standard deviation, median, range, and percentage (%) were used to present numerical and categorical data. The normality of variable distribution was assessed using the Shapiro-Wilk test. Comparisons between groups were made by using independent tests and the Mann-Whitney test. The Rho correlation coefficient of Spearman was used to determine any correlation between AT/ET value and RDS development. The defined variables were calculated to obtain the area under the curve (AUC) and the 95% confidence interval. Statistical significance was established as $p \leq 0.05$.

RESULTS

The study examined the medical records of six newborns with RDS, and 19 newborns who were not diagnosed with RDS. The mothers of RDS-positive newborns had a mean age of 28.35 years, while the mothers of RDS-negative newborns had a mean age of 33.68 years ($p<0.05$). No significant difference was found in height and weight between groups (Table 1). The groups did not differ significantly regarding parity and gravidity ($p=0.634$, $p=0.525$, respectively) or intensive care needs ($p=0.449$) (Table 2).

TABLE 1: Baseline characteristics of the study groups.

	RDS (+) (n=6)		RDS (-) (n=19)			
	X̄±SD	Minimum-Maximum	X̄±SD	Minimum-Maximum	t-test	p value
Age (year)	28.35±7.22	22-39	33.68±3.71	23-41	1.038	0.004
Height (cm)	163.22±8.27	153-178	159.22±6.39	151-171	3.647	0.228
Weight (kg)	71.47±6.41	61-78	75.98±8.39	57-97	4.120	0.497
Body mass index	26.75±3.54	22.1-28.3	29.44±4.17	21.5-41.4	1.087	0.551
Gravidity	2.15±1.63	1-5	2.37±1.58	1-7	-1.641	0.738
Parity	0.82±0.91	0-2	0.91±1.01	0-3	-0.937	0.772

RDS: Respiratory distress syndrome; SD: Sandard deviation.

AT was 77.81±11.88 sec in the RDS (+) group and 69.04±19.83 sec in the RDS (-) group. ET was 244.17±122.53 sec in the RDS (+) group and 258.41±42.28 sec in the RDS (-) group. AT/ET was found to be 0.36±0.17 in the RDS (+) group and 0.28±0.11 in the RDS (-) group (p=0.003, p=0.012, and p=0.001, respectively) (Table 3).

There was a significant difference between the 1st and 5th minute APGAR scores of RDS (+) and RDS (-) groups (p=0.001, p=0.004, respectively) (Table 4).

A negative correlation was found between the mean AT/ET value and RDS diagnosis (r=-0.666, p=0.001) (Figure 1). The study found that the optimal cut-off value for predicting RDS in newborns was 0.824 (AUC) and a cut-off (AT/ET) of 0.478. Sensitivity, specificity, and negative and positive predictive values were calculated as 94%, 72.2%, 95.9%, and 64.8%, respectively.

TABLE 2: Gravidity and parity values of patient groups.

		RDS (+) (n=6)		RDS (-) (n=19)			
		n	%	n	%	t-test	p value
Parity	0	3	12.00	9	36.00	-1.274	0.634
	1	2	8.00	6	24.00		
	2	1	4.00	1	4.00		
	3	0	0.00	3	12.00		
Gravidity	1	3	12.00	4	16.00	-1.058	0.525
	2	1	4.00	8	32.00		
	3	1	4.00	3	12.00		
	4	1	4.00	2	8.00		
	5	0	0.00	1	4.00		
	6	0	0.00	1	4.00		
	7	0	0.00	0	0.00		

RDS: Respiratory distress syndrome.

TABLE 3: Pulmonary artery AT, pulmonary artery ET and AT/ET values of the study groups.

	RDS (+) (n=6)		RDS (-) (n=19)		
	X̄±SD	Minimum-Maximum	X̄±SD	Minimum-Maximum	p=value
AT	77.81±11.88	66-92	69.04±19.83	39-105	**0.003**
ET	244.17±122.53	151-222	258.41±42.28	179-325	**0.012**
AT/ET	0.36±0.17	0.173-0.514	0.28±0.11	0.112-0.471	**0.001**

AT: Acceleration time; ET: Ejection time; RDS: Respiratory distress syndrome; SD: Standard deviation.

TABLE 4: APGAR scores and intensive care needs of groups.

		RDS (+) (n=6)		RDS (-) (n=19)			
		n	%	n	%	χ^2 test	p=value
APGAR score of 1-minute	7≥	4	16.00	9	36.00	33.21	**0.001**
	7<	2	8.00	10	40.00		
APGAR score of 5-minute	7≥	2	8.00	2	8.00	28.69	**0.004**
	7<	4	16.00	17	68.00		
Intensive care unit requirement	+	6	24.00	2	8.00	7.89	0.449
	-	0	0.00	17	68.00		

RDS: Respiratory distress syndrome.

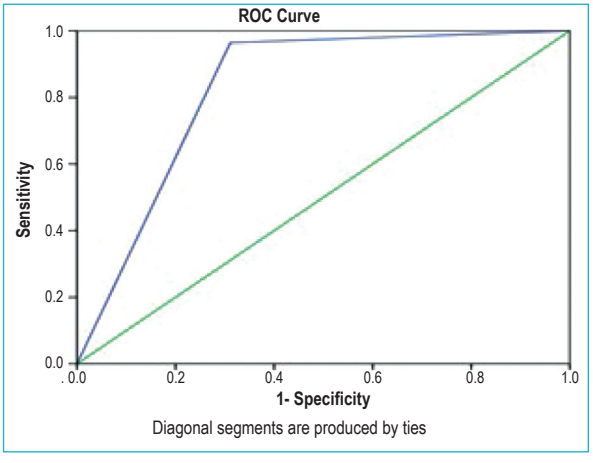

FIGURE 1: ROC curve for mean pulmonary artery acceleration time/pulmonary artery ejection time value and respiratory distress syndrome.

DISCUSSION

Although there were significant improvements in the prognosis of low birth weight infants with the development of newborn care facilities, preterm delivery rates could not be decreased.[14] A major cause of mortality and morbidity among newborns is RDS.

A recent study reported that the most powerful risk factor associated with preterm labor was maternal age. According to the same study, preterm labor has a moderate correlation with low weight gain during pregnancy and poor correlation with low socioeconomic status.[15] A study by Alvestad et al.reported that maternal folate deficiency increased the risk of preterm labor and birth in the third trimester.[16] RDS is closely associated with the gestational age of the newborn, with a higher incidence in premature births before the 28th week of gestation. The risk of RDS increases by 93% in such cases. The findings of the study showed that the average maternal age of newborns with RDS was 28.35±7.22 years, whereas the average maternal age of newborns without RDS was 33.68±3.71 years, which is consistent with existing literature. Studies have reported that only maternal age (<20 years) is important among sociodemographic factors in the etiology of spontaneous preterm delivery.[17,18] Perez et al. reported a significant increase in preterm labor rates in pregnancies under 20 years of age.[19]

Prior research found that the fetal lung maturity increases with an increase in the AT/ET ratio.[20] Similarly, Azpurua et al. indicated that despite an increased AT/ET ratio, the amniotic fluid lecithin/sphingomyelin ratio showed an inverse relationship with fetal lung maturation.[13] Kim et al. showed that as the AT/ET ratio increased, the fetal lung maturity decreased.[21] The result of the present study showed an inverse correlation between fetal AT/ET values and RDS. Eraslan Sahin et al. demonstrated that the risk of transient tachypnea of the newborn (TTN) increases in uncomplicated term small-for-gestational-age (SGA) fetuses (A).[22] In this study, a cut-off value of 0.298 was found to provide optimal specificity of 93.0% and sensitivity of 81.0% for the subsequent diagnosis of TTN in term SGA newborns in the neonatal period. The results of the study showed 72.2% specificity, 94.5% sensitivity, 95.9% negative predictive value, and 64.8% positive predictive value for neonatal RDS. Additionally, the current study indicates that fetal AT/ET measurements are a highly effective diagnostic test in predicting RDS. In practical terms, this test can predict

RDS with high specificity and sensitivity compared to our study data when the cut-off value is 0.478. This test can be a good alternative in predicting RDS with its easy applicability and high diagnostic accuracy in all neonatal units where ultrasonography is available.

CONCLUSION

The study concluded that measuring the fetal AT/ET ratio with Doppler US is a reliable and non-invasive method for predicting neonatal RDS.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Uğur Kemal Öztürk, Gökmen Sukgen;* ***Design:*** *Uğur Kemal Öztürk, Gökmen Sukgen, Ömer Kaya;* ***Control/Supervision:*** *Uğur Kemal Öztürk, Gökmen Sukgen, Murat Api;* ***Data Collection and/or Processing:*** *Uğur Kemal Öztürk, Gökmen Sukgen, Ömer Kaya;* ***Analysis and/or Interpretation:*** *Uğur Kemal Öztürk, Gökmen Sukgen, Ömer Kaya, Esra Keleş, Murat Api;* ***Literature Review:*** *Uğur Kemal Öztürk, Gökmen Sukgen, Ömer Kaya, Esra Keleş, Murat Api;* ***Writing the Article:*** *Uğur Kemal Öztürk, Gökmen Sukgen, Ömer Kaya, Esra Keleş, Murat Api;* ***Critical Review:*** *Uğur Kemal Öztürk, Gökmen Sukgen, Ömer Kaya, Esra Keleş, Murat Api;* ***References and Fundings:*** *Uğur Kemal Öztürk, Gökmen Sukgen, Ömer Kaya, Esra Keleş, Murat Api.*

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