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Original article

The Value of Doppler Indices in Prediction of Fetal Lung Maturity in Benha University Hospitals

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Abstract:

Background: Fetal lung maturity (FLM) determines whether a fetus may survive following birth. Despite developments in neonatal surveillance equipment, pulmonary hypoplasia still ranks as the top cause of newborn death and morbidity. This study aimed to X The function of ultrasonic imaging in forecasting FLM and its impact on fetal outcome can be evaluated by establishing the typical characteristics of fetal lung development at various gestational ages and investigating their relationship with gestational age. **Methods:** This prospective cohort study included 100 women coming at Benha University Hospitals & Benha Health Insurance Hospital. All patients were divided into 2 groups: Group I (N=35); Neonates with respiratory distress (RD), Group II (N=65); Neonates with non-respiratory distress (non-RD). **Results:** Sensitivity of acceleration time in RDS prediction was 83.6% versus 85.6% for ejection time, their specificity was 90.5% and 94.3% respectively, while AT\ET ration was higher in sensitivity and specificity (91.7% and 95.7% respectively) and 94% test accuracy. **Conclusion:** In newborns with high sensitivity and specificity, ejection-time (ET), acceleration-time, and acceleration-time/ejection-time ratio can help to predict FLM and respiratory distress syndrome. Neonates with RD may have low amniotic fluid index, resistance index, Bi-parietal diameter, femur length and abdominal circumference.

Keywords: Doppler Indices; Prediction; Fetal Main Pulmonary Artery; Fetal Lung Maturity.

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Introduction

If a fetus can survive after birth, it is determined by fetal lung maturity (FLM). The biggest risk to neonatal illness and death remains pulmonary hypoplasia, despite the fact that newborn monitoring technology has come a long way in the last several years. Both the pulmonary parenchyma and the pulmonary vasculature develop throughout fetal lung development [(1)].

Births occurring before 37 weeks of gestation are defined- by American Academy of Pediatrics and American College of Obstetrics and Gynecology- as preterm neonates. This group of newborns is diverse and includes a large range of gestational ages, each of which is linked to a unique set of results [(2)]. Human lung development starts during gestation and continues throughout childhood. Many things change in the last weeks of pregnancy, but one of the most important is the surfactant production, which is crucial for the baby's safe passage from the womb to the outside world [(3)].

When deciding when to give birth, it's crucial to think about the baby's lung maturity, especially in high-risk pregnancies. Significant neonatal morbidity, such as respiratory distress syndrome (RDS) or transient tachypnoea, can occur in babies whose lungs do not fully develop during pregnancy. Evaluate the foetal lung maturation to mitigate the perinatal mortality and morbidity associated with premature lung development when determining the due date of a high-risk pregnancy [(4)]. One feature of neonatal respiratory distress syndrome (RDS) is a compromised respiratory system either at or soon following birth. Lack of pulmonary surfactant produced by type II pneumocytes causes this condition, which prevents the collapse of the alveoli. This complicates one percent of live births and is more frequent in premature deliveries—before 34 weeks of gestation [(5)].

Various techniques have been employed to evaluate FLM, such as amniocentesis for biochemical markers, lamellar body counts, gray scale ultrasound scans, magnetic resonance imaging, and lecithin & sphingomyelin testing [(6)]. These days, ultrasound can measure the fetal lungs' area and diameter to see how the pulmonary parenchyma is developing. The location of fetal pulmonary vessels can be clearly demonstrated using color Doppler, which thereby clarifies the development of fetal pulmonary circulation and the fetal pulmonary maturity [(7)].

The aim of this work was to define the typical characteristics of fetal lung development at various gestational ages and investigate their association with gestational age, thereby evaluating the function of ultrasonicography in forecasting FLM and its effect on fetal outcome.

Patients and methods

This prospective cohort study included 100 women coming at Benha University Hospitals & Benha Health Insurance Hospital, from November2023 to November2024.

The patients responded with informed written consent. Every patient had a secret code number and an explanation of the goal of the research. Following approval by the Research Ethics Committee, Faculty of Medicine, Benha University, the study was undertaken. Approval code: 25-11-2023.

Inclusion criteria were All women who were pregnant with a healthy baby and had a straightforward one-time pregnancy are welcome to participate. The only criteria are that the pregnancy had an accurate gestational age (GA), which is determined by a specific last menstrual period, and that the baby was born within 24 hours of the mother's admission.

Exclusion criteria were subject's medical history, including but not limited to: previous administration of antenatal corticosteroids, multiple pregnancies, fetal

malformations, complications, macrosomic fetuses or intrauterine growth restriction (IUGR), meconium-stained fluid, antepartum hemorrhage, known fetal chromosomal abnormalities, or major structural abnormalities, patient's refusal to participate in the study.

Grouping:

All patients were divided into 2 groups: Group I (N=35): Neonates with RD and Group II (N=65): Neonates with non-RD.

All studied cases were subjected to the following: Full history taking including [patient identification and demographics (age, gravida, parity, gestational age at presentation), family history (preterm birth, fetal lung immaturity, congenital anomalies), presenting complaint, obstetric history (last menstrual period (LMP) and accurate dating of pregnancy, previous prenatal ultrasounds and their findings, history of complications), current pregnancy history (presence of symptoms, complications, obstetric interventions), past medical history (chronic conditions, previous surgeries, medications and allergies, and environmental and lifestyle factors. **Physical Examinations including: General examination [**patient's distress level, measure vital signs (blood pressure, temperature, heart rate, and respiratory rate)], **lower limb examination** (swelling or edema, **abdominal examination including** [measure fundal height to evaluate fetal growth and potential IUGR, determine fetal position and presentation, assess uterine tone and palpate for tenderness or signs of irritability, check for uterine contractions (palpable or painful)], **pelvic examination including** [examine cervical dilation, effacement, and consistency to assess preterm labor, check for vaginal discharge, bleeding, or ruptured membranes (PROM), fetal heart rate (FHR) monitoring: auscultate or use Doppler to assess FHR and patterns, perform a non-stress test to evaluate fetal well-being.]. **Routine laboratory investigations [**complete blood count, Random Blood Glucose level, and urine analysis]. **Imaging including** sonographical analyses- utilizing ultrasonic apparatus capable of high-density grayscale, pulsed-wave, and color Doppler modes- and FLM evaluation with a 3–5 MHz probe transducer.

Conventional 2D ultrasound: Between the outer border of the proximal parietal bone and the inner margin of the distal skull table, the bi-parietal diameter (BPD) was measured in a straight line perpendicular to the direction of the cerebral falx. If feasible, a transverse view of the foetal abdomen enabled the measurement of the abdominal circumference (AC) at the portal sinus, umbilical vein, and embryonic stomach, or at the skin line. To determine the length of the femur (FL), the distance between the two extremities of the diaphysis was measured. Finding the echogenic distal epiphyseal center of the femur and measuring it in the axial (anteroposterior) plane constitutes the epiphyseal ossification centers. In addition, the tibial end shows the location of the proximal echogenic epiphysis center. Once again, the axial (antero-posterior) plane was used to obtain the measurements.

Placental grading was conducted using the Grannum classification [(8)]. The grade 0 chorionic plate is flat and uniform. Grade I the chorionic plate, which is characterized by dispersed calcifications and undulations. A grade II calcification line is one that is not fully formed and does not extend to the basal plate. Chorionic plate indentation and basal plate calcification constitute Grade III.

The amniotic fluid index (AFI) was computed using the four-quadrant method. For every fluid pocket in every quadrant, this included determining their deepest, unobstructed vertical length in centimeters. AFI's usual range was 8–18. Four quadrants recorded the millimeter measurements of the linear densities (Vernix) of the amniotic fluid. The AF turbidity was calculated using the free-

floating particle count, size, and distribution in every one of the four quadrants. Their ability to move freely in response to a probe's light shaking of the mother's abdomen allowed them to be identified.

The thalamus echogenicity in relation to brain tissue was reported along with the millimeter-measured bi-parietal diameter (trans thalamic plane) using the ultrasonography. If the thalamus's echogenicity was consistent with that of the neighboring brain tissue, we would call it echogenic; otherwise, we would call it echo lucent.

Lung to liver echogenicity: We took thoracic and abdominal sections for our longitudinal sonograms. To keep the ribs from interfering too much, we were very careful not to image the lungs through the heart or the liver through a foetal stomach full with fluid. Since acoustic augmentation after these cystic forms would clearly produce falsely echogenic appearances of the organ parenchyma, we avoided doing this whenever possible. Towards the end of the second trimester, the liver parechyma should have a more consistent texture. To determine if the foetal lung was hypo-echoic, iso-echoic, slightly hyper-echoic, or certainly hyper-echoic, their echogenicity was compared to that of the foetal liver.

Density was used to grade the echogenicity of the meconium within the intestinal cavity. Comparatively to the echogenicity of the liver, the colons were assessed and graded: Grade 0: All abdominal contents appear to be the same; there is not any apparent colon. Identifying colonic haustra is possible and the contents of the colon do not appear to be echogenic, as is the case with the bladder and the stomach (Grade 1). Second year: Intermediate stage. Though less than the liver's, the echogenicity is more than that of the bladder. The echogenicity in third grade is somewhat similar to that of the liver.

Doppler examination

Flow velocity waveforms were obtained from the following arterial resistance indices: umbilical artery (UA), uterine artery (UtA), middle cerebral artery (MCA), and main pulmonary artery (MPA).

We placed the transducer on the mother's belly overlaying the fetus and symmetrically moved it to get the typical waveforms at the mid-section of a free loop of the umbilical cord. This let us quantify the UA Doppler.

Uterine artery: In order to locate the UtA, which was discovered just medial to the common iliac artery bifurcation, the probe was angled slightly towards the symphysis pubis after color flow imaging had identified it in the longitudinal segment. It was possible to ascertain the RI by recording waveforms from the uterine sides.

Middle cerebral artery : At the level of BPD, a cross-sectional image of the foetal brain was captured. To make the thalamus more visible, the transducer was subsequently moved caudally. Using color flow imaging, the main anterolateral branch of the circle of Willis (MCA) could be identified. At the point where the middle third of this artery meets the medial third, the pulsed Doppler sample gate was subsequently positioned. Midbrain, uterine, and umbilical artery waveforms were recorded. In addition to adjusting the gain, pulse repetition frequency, filter, and color box to suit the vessel width, it is recommended to keep the angle below 60 degrees. The absence of fetal breathing movements was taken into account in all measurements.

Main pulmonary artery: A systematic examination of the foetal heart, beginning at the MPA and continuing until the pulmonary valve and the bifurcation of the right and left branches, revealed that the foetus was at rest in the axial thoracic view, without breathing motions. A needle-like appearance was seen in the MPA Doppler waveform. There is a little depression where the flow is reversed at

the very end of the systole. Diastolic flow is higher in the ductus arteriosus wave compared to the MPA waveform, which is more rounder, fuller, and triangular.

The equipment computed RI electronically following the ideal fetal MPA waveform. Electronic calculations of the arterial RI and pulsatility index (PI) followed these formulae: RI = S − D/S, PI = S − D/A

S indicates peak systolic velocity; D, end diastolic velocity; and A, time averaged velocity.

The neonatal outcome

Upon delivery, the time interval between the ultrasound examination and delivery was recorded and if there was neonatal intensive care unit admission for RDS or not.

Sample size

The sample size calculation was performed using G. Power 3.1.9.2 (Universität Kiel, Germany). The sample size was calculated according to the mean fetal lung that was significantly higher in non-respiratory distress syndrome (non-RDS) neonates compared to RDS neonates (67.86 ± 2.86 vs. 60.67 ± 3.51, P<0.001) according to a previous study (4). Based on the following considerations: 0.05 α error and 90% power of the study, allocation ration 1:1. Eight cases were added to overcome dropout. Therefore, 100 patients will be allocated.

Statistical analysis

IBM Inc.'s SPSS v26, located in Chicago, IL, USA, will be used for statistical analysis. Numbers will be presented with the help of standard deviation (SD) and mean (MA). Frequency represented as a percentage will be used to display qualitative factors.

Results

Table (1) shows that the mean age of studied mothers was 28.6 years and their BMI was 28.5 ± 3.22 kg/m2, the mean of their gestational ages was 38.2 weeks, 60% of studied mothers were multigravida.

Table (2) shows a statistically significant correlation between neonatal RD with maternal and gestational ages, as mothers of RD neonates were older with lower gestational age. AFI, neonatal weight, APGAR score at 1 minute and APGAR at 6 minutes was statistically significantly lower among RD neonate.

Table (3) shows that BPD, FL and AC were statistically significantly lower among RD neonate. A statistically significant difference between neonates with RD and those without regarding doppler indices RI, ET, acceleration-time (AT) and acceleration-time/ejection-time ratio (AT\ET ratio), that all parameters was lowered among RD cases.

Table (4) shows that sensitivity of acceleration time in RDS prediction was 83.6% versus 85.6% for ejection time, their specificity was 90.5% and 94.3% respectively, while AT\ET ration was higher in sensitivity and specificity (91.7% and 95.7% respectively) and 94% test accuracy.

Table 1: Basic characteristics of the studied group.

		Group I N=100	
Age (years)		**28.6 ± 5.14**	
BMI (kg/m^2)		**28.5 ± 3.22**	
GA (weeks)		**38.2 ± 2.35**	
		N	**%**
Parity	**PG**	**40**	**40.0**
	MG	**60**	**60.0**
Mode of delivery	**Vaginal**	**45**	**45.0**
	Cesarean	**55**	**55.0**

Data presents as mean ± SD or frequency (%), BMI: Body Mass Index, GA: gestational-age, PG: Primigravida, MG: multigravida.

Table 2: Relation between neonatal respiratory distress and basic characteristics & between respiratory distress and fetal data among the studied group

			RD N=35	Non-RD N=65	t-test	P
			Mean ± SD			
basic characteristics	**Maternal age (years)**		**31.5 ± 4.11**	**28.3 ± 5.17**	**0.359**	**0.002***
	Gestational age (weeks)		**37.6 ± 1.16**	**38.4 ± 1.56**	**2.66**	**0.002***
	Parity	**PG**	**15 (42.9%)**	**25 (38.5%)**	1.57	0.602
		MG	**20 (57.1%)**	**40 (61.5%)**		
	Mode of delivery	**Vaginal**	**17 (48.6%)**	**28 (43.1%)**	0.874	0.223
		CS	**18 (51.4%)**	**37 (56.9%)**		
fetal data	**AFI (cm)**		**7.15 ± 1.98**	**11.3 ± 2.17**	**9.39**	**<0.001****
	Weight (gm)		**2127.6 ± 577.6**	**3338.4 ± 731.5**	**8.46**	**<0.001****
	APGAR 1 min.		**2.67 ± 0.87**	**5.33 ± 0.63**	**17.6**	**<0.001****
	APGAR 5 min.		**5.78 ± 0.65**	**7.88 ± 0.89**	**12.3**	**<0.001****
	Sex	**Male**	**15 (42.9%)**	**25 (38.5%)**	1.57	0.602
		Female	**20 (57.1%)**	**40 (61.5%)**		

Data presents as mean ± SD or frequency (%). PG: Primigravida, MG: multigravida, CS: Cesarean section. NS: P-value>0.05 is not significant, AFI: amniotic fluid index, APGAR: Appearance, Pulse, Grimace, Activity and Respiration. *: P-value<0.05 is significant. **: P-value<0.001 is high significant.

Table 3: Relation between BPD, FL, AC and neonatal respiratory distress & between MPA Doppler indices and neonatal respiratory distress among the studied group

		RD N=35	Non-RD N=65	t-test	P
		Mean ± SD			
BDP (mm)		**83.2 ± 7.18**	**89.5 ± 4.37**	**5.45**	**<0.001****
FL (mm)		**61.2 ± 3.29**	**68.9 ± 2.45**	**13.6**	**0.001****
AC (mm)		**258.7 ± 30.8**	**320.3 ± 22.6**	**11.6**	**<0.001****
MPA Doppler indices	**RI**	**0.79 ± 0.18**	**0.85 ± 0.17**	1.65	0.101
	PI	**2.26 ± 0.29**	**2.48 ± 0.45**	**2.61**	**0.01***
	ET (ms)	**108.7 ± 30.8**	**120.3 ± 22.6**	**2.16**	**0.03***
	AT (ms)	**302.8 ± 40.5**	**317.8 ± 33.9**	**2.33**	**<0.02***
	AT/ ET	**0.27 ± 0.03**	**0.41 ± 0.02**	**27.9**	**<0.001****

Data presents as mean ± SD or frequency (%). BDP: biparietal diameter, FL: femur length, AC: abdominal circumference. NS: RI: resistance index, PI: pulsatility index, ET: ejection time, AT: Acceleration time, At/Et ratio: Acceleration time/ejection time. . *: P-value<0.05 is significant. **: P-value<0.001 is high significant.

Table 4: Validity data of MPA doppler indices as predictors of neonatal RDS.

	Cut-off	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy	P
ET (ms)	>116.5	0.961	85.6%	94.3%	88.2%	92.4%	91%	**<0.001***
AT(ms)	>317.5	0.914	83.6%	90.5%	82.9%	90.8%	88%	**<0.001***
AT \ ET	>0.33	0.935	91.7%	95.7%	91.4%	95.4%	94%	**<0.001***

AUC: Area Under a Curve, p value: Probability value, NPV: Negative predictive value, PPV: Positive predictive value, ET: ejection time, AT: Acceleration time, At/Et ratio: Acceleration time/ejection time. *High statistically significant.

Case 1

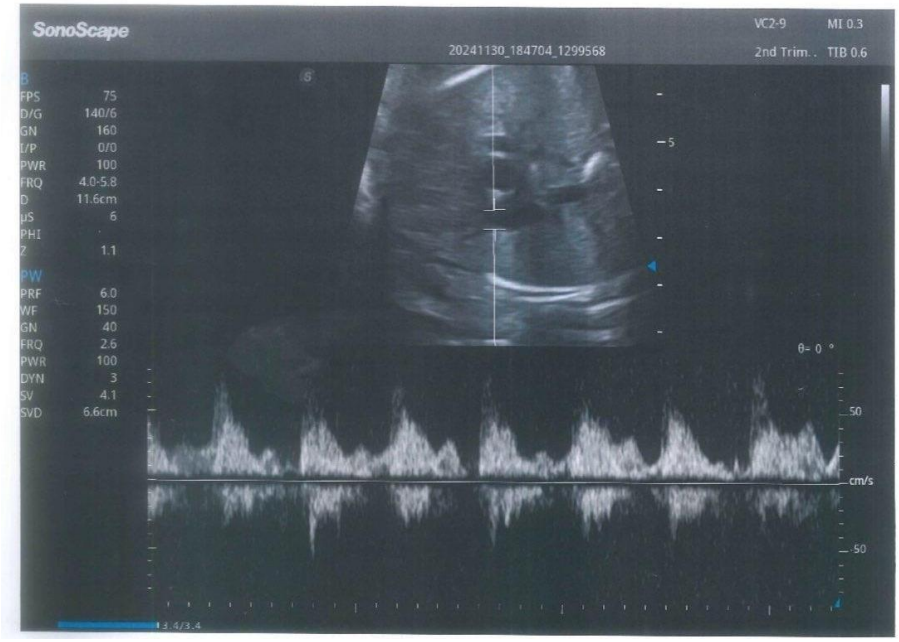

Figure (1): A 22 years old 2ndG, admitted for routine antenatal examination, GA38 weeks + 3days, SLF, HR (125 b/m), good perception of fetal movement, AFI(15), placental grading grade 3, colon grading grade 2, Doppler examination: MPA RI(0.71), PI(1.8), AT(60ms), ET(165ms), AT/ET(0.36), The neonatal outcome delivery 48 hours_ NICU admission for RDS (NO) **.**

Case 2

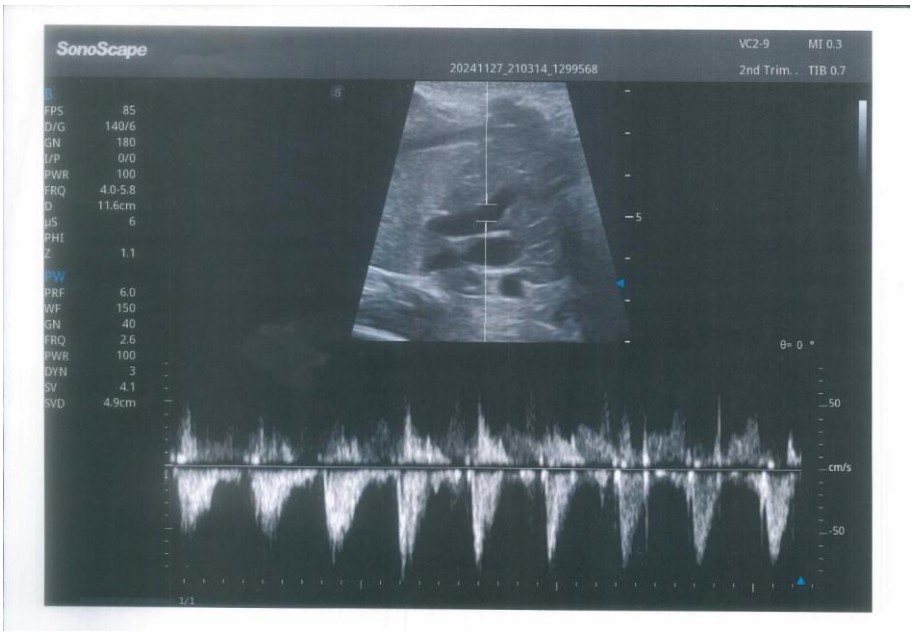

Figure (2):A 27 years old 3rdG, admitted for routine antenatal u/s evaluation, GA 39 weeks + 1day, SLF, HR (134b/m) with adequate movement, AFI (12cm), placental grading grade 3, colon grading grade 2, Doppler examination: MPA RI(0.75), PI(1.7), AT(57ms), ET(175ms), AT/ET(0.32), The neonatal outcome delivery within 24 hours after u/s examination _NICU admission for RDS (NO) **.**

Case 3

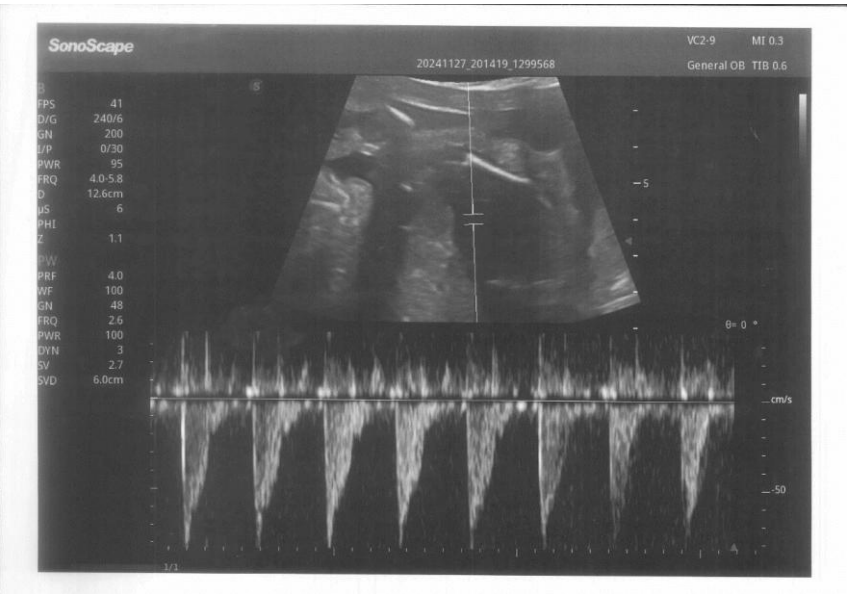

Figure (3):A 25 years old PG admitted for routine antenatal ultrasound examination , GA 38weeks+2 days, SLF , HR(130 bpm) with adequate movement, AFI(9cm), placental grading grade 3, colon grading grade 2, Doppler examination: MPA RI (0.73), PI (1.6), AT(53ms), ET(173ms), AT/ET(0.30),the neonatal outcome delivery within 24 hours after u/s examination, NICU admission for RDS (NO) **.**

Discussion

The lungs, the last fetal organ needed for extrauterine survival, reach functional maturation. Furthermore, causing newborn RDS is a lack of pulmonary surfactant [(9)]. Usually translucent to pale yellow in color, AF is the liquid that envelops a growing fetus in the amniotic sac. AF's makeup is complex and includes a wide range of mother and fetal elements. The structure of the AF depends on gestational age [(10)].

In our study, the mean age of studied mothers was 28.6 ± 5.14 years and their BMI was 28.5 ± 3.22, the mean of their gestational ages was 38.2 weeks, 60% of studied mothers were multigravida, 55% had cesarean delivery.

In alignment with our demographics, Kandil et al., [(11)] The average mother age was 27.89 years ± 4.37 years (range 20–37). With a standard deviation of 1.72, the average gestational age was 35.45 weeks—that is, between 30 and 37 weeks.

We found that there was a statistically significant difference between neonates with and without RD regarding maternal and gestational ages, as mothers of RD neonates were older with lower gestational age. While, no significant difference found in parity and mode of delivery.

In line with us, EL-omda and Elboghdady [(4)], their results showed that there was a statistically significant difference in gestational age between the RDS and non-RDS groups (P = 0.0005). Mother age, gravidity, parity, and termination (P value > 0.05) were not statistically significantly different between RDS and non-RDS pregnancies, nevertheless.

In contrast with our results, Kandil et al. [(11)] When the researchers compared the RDS status with the mother's age, gravidity, and parity, they did not find any statistical significance (P value greater than 0.05).

With no regard to age, our findings revealed that AFI, neonatal weight, APGAR score at 1 minute and APGAR at

6 minutes- was statistically significantly lower among RD neonate (p value < 0.001).

Apgar score was confirmed by a study of Wang et al. [12] those who suggested that a An Apgar score of 7 at 5 minutes postpartum showed a negative impact on RDS development and poor postpartum conditions owing to impaired respiratory function exacerbating hypoxia.

Also, Thavarajah et al. [13] infant problems including RD, feeding difficulties, hypothermia, and convulsions were significantly associated with both low and intermediate Apgar scores, according to the study.

The current study showed that BPD, FL and AC was statistically significantly lower among RD neonate with p value < 0.001 compared to non-RD neonates.

In addition, Kandil et al. [11] study found that BPD, AC, and FL were statistically significantly lower among RDS group compared to non RDS with p value = 0.001.

Next, we looked at the correlation between foetal MP Doppler indices and RD in neonates. We found that RD cases had lower values for all parameters (RI, ET, AT) and that there was a statistically significant difference between RD and non-RD neonates.

In alignment with the previous findings, Laban et al. [9] found that those who suffered RDS had a quite low pulmonary artery resistance index (PA-RI) (P-value = 0.02). Regarding AT and AT/ET ratio, the RDS and non-RDS groups had statistically significant variations.

Also, Moety et al. [14] Although the study revealed that AT/Et was much lower in fetuses that got RDS, they said that RI was much greater in fetuses that developed RDS, which deviates with our findings.

In difference, a previous study by Guan et al. [15] found that fetuses experiencing RDS have lower pulmonary vascular resistance, pressure, and blood flow than those not experiencing RDS.

This study showed that sensitivity of acceleration time in RDS prediction was 83.6% versus 85.6% for ejection time, their specificity was 90.5% and 94.3% respectively, while AT\ET ratio was higher in sensitivity and specificity (91.7% and 95.7% respectively) and 94% test accuracy, while accuracy of AT and ET was 88% and 91%. But ET parameter had the highest AUC (0.961) compared to AT (0.914) and AT\ET ratio (0.935).

In coherence with our study, Guan et al. [15] observed that AT alone itself has a 78.6% sensitivity and an 89.7% specificity, which would help to forecast RDS. With 71.4% sensitivity and 93.1% specificity, the AT/ET ratio may estimate RDS.

Additionally, Moety et al. [14] The development of RDS was anticipated by Sudy with a threshold value of 0.305; sensitivity was 76.4% and specificity was 91.6%. Compared to what we found, the sensitivity was low. One can predict how an infant's RDS would progress using the highly sensitive and specific MPA At/Et.

However, Schenone et al.[16] asserted that while the fetal major PATET cutoff of 0.3149 had a specificity of 93% and a sensitivity of 73%, the PATET could provide a noninvasive way to estimate FLM.

The limitations of the study were a non-randomized study had a relatively small sample size comparing to previous studies which may contributed to insignificant results and lacking of more related variable and assessing the outcome and mortality rate.

Conclusion

From our study results, in neonates with ET, the AT and At/Et can predict FLM and RDS in neonates with high sensitivity and specificity. Neonates with RD may have low AFI, RI, BPD, FL and AC.

Therefore, we recommend utilizing AT, ET, and AT\ET ratio in predicting FLM and RDS in neonates, conducting same study aim and methodology on larger

sample size and multiple centers and conducting more related variable and assessing the outcome and mortality rate will be advisable.

Conflicts of interest

No conflicts of interest

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