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PRENATAL PREDICTION OF FETAL LUNG MATURITY BY MEASURING FETAL MAIN PULMONARY ARTERY DOPPLER INDICES

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ABSTRACT **Background:** Respiratory distress syndrome (RDS) is a leading cause of neonatal morbidity and mortality, particularly in preterm births. Non-invasive methods to predict fetal lung maturity are needed to guide obstetric decisions and reduce neonatal complications. Fetal main pulmonary artery (MPA) Doppler evaluation has been proposed as a promising tool. The present study aimed to evaluate the diagnostic performance of fetal MPA Doppler indices in predicting fetal lung maturity and neonatal RDS. **Methods:** This prospective observational study included 50 pregnant women between 28–40 weeks gestation at SAMC & PGI, Indore. All underwent real-time obstetric ultrasonography with MPA Doppler assessment (RI, PI, AT, ET, AT/ET ratio). Neonatal outcomes including birth weight, gestational age at birth, sex, NICU admission, and diagnosis of RDS were documented. Data were analyzed using SPSS v26.0, with calculation of sensitivity, specificity, PPV, and NPV for each Doppler parameter. **Results:** Of 50 neonates, 20 (40%) developed RDS. Mean birth weight (2055 ± 210 g vs 2265 ± 190 g, $p = 0.002$) and gestational age (33.1 ± 1.3 vs 34.3 ± 1.2 weeks, $p = 0.002$) were significantly lower in the RDS group. RDS-positive neonates had higher PI (2.01 ± 0.22 vs 1.78 ± 0.18, $p = 0.001$) and RI (0.83 ± 0.05 vs 0.79 ± 0.04, $p = 0.01$), and reduced AT (37.4 ± 3.2 vs 41.2 ± 2.8 ms, $p = 0.0005$) and AT/ET ratio (0.20 ± 0.02 vs 0.23 ± 0.02, $p < 0.001$). AT/ET ≤0.21 predicted RDS with sensitivity 85%, specificity 80%, PPV 77%, and NPV 87%. All RDS neonates required NICU admission compared to 20% of non-RDS neonates ($p < 0.001$). **Conclusion:** Fetal MPA Doppler, particularly AT/ET ratio, provides a reliable non-invasive method for predicting neonatal RDS and may improve prenatal risk stratification.

KEYWORDS : Fetal lung maturity, Respiratory distress syndrome, Doppler, Main pulmonary artery, Prenatal prediction

INTRODUCTION

Respiratory Distress Syndrome (RDS), also known as hyaline membrane disease, continues to be a significant cause of morbidity and mortality in neonates, particularly those born preterm [1]. The underlying mechanism involves surfactant deficiency in the pulmonary alveoli due to immaturity of type II pneumocytes, leading to increased alveolar surface tension, alveolar collapse during expiration, and impaired adaptation of the lungs from intrauterine to extrauterine life [1]. Despite substantial advances in perinatal care, RDS remains a leading cause of Neonatal Intensive Care Unit (NICU) admission and is associated with adverse neonatal outcomes [2].

Accurate prenatal prediction of fetal lung maturity is therefore crucial for guiding obstetric management and improving neonatal survival. Traditional invasive tests such as the lecithin–sphingomyelin ratio, phosphatidylglycerol estimation, foam stability test, and lamellar body count have long been considered the gold standards; however, they require amniocentesis, are invasive in nature, and have demonstrated only moderate specificity [3,4]. Non-invasive approaches such as estimating gestational age, placental grading, evaluation of fetal lung–liver echogenicity, fetal weight estimation, and monitoring of epiphyseal center appearance have also been studied, but their clinical application is limited due to variable accuracy [5,6]. This highlights the ongoing need for reliable, non-invasive alternatives.

In this context, fetal main pulmonary artery (MPA) Doppler assessment has emerged as a promising tool. Surfactant deficiency increases pulmonary vascular resistance, raising pulmonary arterial pressures that can be indirectly assessed by Doppler velocimetry [7]. Previous studies have demonstrated that fetal pulmonary artery Doppler indices correlate with gestational age, lung maturity, and neonatal outcomes, and may help in identifying neonates at risk of RDS [7,8]. Although research in this area remains limited, early findings underscore the potential of Doppler-based evaluation in fetal lung maturity prediction [7-9].

The present study was therefore designed to predict fetal lung maturity prenatally by measuring fetal MPA Doppler indices. Specifically, the study aims to explore the correlation between fetal lung maturity and MPA Doppler indices, evaluate their sensitivity, specificity, and predictive values, and determine their ability to identify fetuses at risk of developing neonatal RDS in preterm deliveries.

MATERIAL AND METHOD

After obtaining approval from the Institutional Ethics and Research Committee, this hospital-based prospective, observational, cross-sectional study was conducted in the Department of Radiodiagnosis, Sri Aurobindo Medical College and Post Graduate Institute (SAMC & PGI), Indore, Madhya Pradesh, over a period of 18 months, from 1st June 2023 to 30th November 2024.

A total of 50 pregnant women who met the eligibility criteria and consented to participate were prospectively enrolled. All participants underwent detailed obstetric ultrasonography with fetal main pulmonary artery (MPA) Doppler evaluation, and neonatal outcomes were assessed following delivery. Prior to enrollment, written informed consent was obtained from all participants. The study was carried out in strict accordance with ethical principles, ensuring patient confidentiality, autonomy, and the right to withdraw at any stage without prejudice.

Inclusion Criteria

- Women with singleton uncomplicated pregnancies.
- Gestational age between 28 and 40 weeks, calculated from last menstrual period (LMP) or confirmed by first-trimester dating scan.
- Fetuses delivered within 48 hours of ultrasound scan.

Exclusion Criteria

- Patients unwilling to participate or provide informed consent.
- Pregnancies complicated by hypertension, preeclampsia, diabetes mellitus, or autoimmune disorders.
- Multiple gestations, congenital fetal anomalies, macrosomia, or intrauterine growth restriction.
- Cases with incomplete imaging or neonatal follow-up data.

Procedure
All participants fulfilling the inclusion criteria underwent detailed history taking, including maternal age, parity, last menstrual period, history of chronic illnesses, and pregnancy complications. Obstetric ultrasonography was performed using GE Voluson E8 and GE Logiq P7 ultrasound machines with a 3.5–5 MHz curvilinear transducer. Standard real-time obstetric imaging included estimation of gestational age, biparietal diameter (BPD), femur length (FL), abdominal circumference (AC), amniotic fluid index (AFI), placental grading, expected fetal weight (EFW), and comparison of fetal lung-to-liver echogenicity.

Doppler Imaging Protocol
Color Doppler and pulsed Doppler studies were performed to assess the fetal MPA. The fetal heart was systematically evaluated in the four-chamber view, outflow tracts, and three-vessel view. The pulmonary artery was visualized in a short-axis view of the heart, traced cranially to its bifurcation. Pulsed Doppler sampling was applied at the MPA stem, avoiding overlap with the ductus arteriosus waveform.

The Doppler Parameters Recorded Included:
- Resistive Index (RI)
- Pulsatility Index (PI)
- Acceleration Time (AT)
- Ejection Time (ET)
- AT/ET ratio

Measurements were obtained at a physiologic fetal heart rate of 120–160 beats/min, avoiding maternal or fetal movement. Each variable was measured three times, and the average value was considered for analysis.

Postnatal Assessment
Following delivery, neonatal outcomes were recorded, including gestational age at birth, mode of delivery, birth weight, sex, and NICU admission. Neonatal respiratory distress syndrome (RDS) was diagnosed by pediatricians blinded to Doppler findings, based on clinical criteria including tachypnea, retractions, nasal flaring, supplemental oxygen requirement >24 hours, and chest X-ray findings consistent with RDS.

Statistical Analysis
All clinical, imaging, and neonatal outcome data were documented in a pre-structured proforma and compiled using Microsoft Excel. Statistical analysis was performed using IBM SPSS Statistics version 26.0. Descriptive statistics summarized maternal demographics and fetal variables, with categorical data expressed as frequencies and percentages, and continuous data as mean ± standard deviation (SD). The Chi-square test was applied to assess associations between Doppler indices and neonatal RDS. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and diagnostic accuracy of fetal MPA Doppler parameters were calculated. A p-value <0.05 was considered statistically significant.

RESULTS
A total of 50 pregnant women were included in the study. The mean maternal age was 26.4 ± 3.5 years, and the mean gestational age at the time of Doppler examination was 33.6 ± 1.3 weeks (range: 30–36 weeks). All participants delivered within one week of Doppler assessment.

Of the 50 neonates, 20 (40%) developed Respiratory Distress Syndrome (RDS), while 30 (60%) did not. The mean birth weight in the RDS group was 2055 ± 210 g, significantly lower than 2265 ± 190 g in the non-RDS group (p = 0.002).

Table 1: Comparison Of Neonatal Birth Weight Between RDS And Non-RDS Groups

Group	Number of neonates (n)	Mean Birth Weight (g) ± SD	p-value
RDS positive	20	2055 ± 210	0.002*
RDS negative	30	2265 ± 190	

*Statistically significant

Routine obstetric ultrasound parameters were also compared [Table 2]. RDS-positive neonates were found to have significantly lower GA, BPD, FL, AC, and EFW values. AFI did not differ significantly. Placental grading and lung–liver echogenicity showed predictive associations: most RDS neonates had Grade II placentas and iso/hypo-echogenic lungs, whereas non-RDS neonates more frequently had Grade III placentas and hyper-echogenic lungs.

Table 2: Comparison Of Routine Obstetric Parameters Between RDS And Non-RDS Groups

Parameter	RDS Positive (n=20) (Mean ± SD / %)	RDS Negative (n=30) (Mean ± SD / %)	p-value
Gestational Age at scan (weeks)	32.9 ± 1.2	34.2 ± 1.1	0.003*
Biparietal Diameter (mm)	81.2 ± 2.8	84.5 ± 3.1	0.002*
Femur Length (mm)	62.4 ± 2.5	65.1 ± 2.7	0.01*
Abdominal Circumference (mm)	285.3 ± 12.2	298.6 ± 13.4	0.004*
Estimated Fetal Weight (g)	2055 ± 215	2280 ± 205	0.001*
Amniotic Fluid Index (cm)	10.8 ± 1.9	11.2 ± 2.1	0.42
Placental Grading II	70%	40%	0.03*
Placental Grading III	30%	60%	0.03*
Lung–Liver Echogenicity: Iso/Hypo	75%	25%	<0.001 *
Lung–Liver Echogenicity: Hyper	25%	75%	<0.001 *

*Statistically significant

Fetal MPA Doppler indices were compared [Table 3]. PI and RI were higher in the RDS group, while AT and AT/ET ratio were significantly reduced. ET alone did not show statistical significance.

Table/3: Comparison Of Fetal MPA Doppler Indices Between RDS And Non-RDS Groups

Doppler Parameter	RDS Positive (n=20) (Mean ± SD)	RDS Negative (n=30) (Mean ± SD)	p-value
Pulsatility Index (PI)	2.01 ± 0.22	1.78 ± 0.18	0.001*
Resistive Index (RI)	0.83 ± 0.05	0.79 ± 0.04	0.01*
Acceleration Time (AT, ms)	37.4 ± 3.2	41.2 ± 2.8	0.0005*
Ejection Time (ET, ms)	180.6 ± 12.1	186.3 ± 11.5	0.08
AT/ET Ratio	0.20 ± 0.02	0.23 ± 0.02	0.0001*

*Statistically Significant

Postnatal Outcomes
- **Gestational Age At Birth:** Mean GA was significantly lower in the RDS group (33.1 ± 1.3 weeks) compared to the

non-RDS group (34.3 ± 1.2 weeks, $p = 0.002$).

- **Mode Of Delivery:** The majority of deliveries were by lower segment cesarean section (LSCS). In the RDS group, 70% were LSCS vs 60% in the non-RDS group, though the difference was not statistically significant.
- **Sex Distribution:** Male neonates constituted a higher proportion of the RDS group (60%) compared to the non-RDS group (46.7%).
- **NICU Admission:** All RDS neonates (100%) required NICU admission, whereas only 20% of non-RDS neonates required admission ($p < 0.001$).

Table 4: Postnatal Characteristics And Neonatal Outcomes

Parameter	RDS Positive (n=20)	RDS Negative (n=30)	p-value
GA at Birth (weeks)	33.1 ± 1.3	34.3 ± 1.2	0.002*
Mode of Delivery – LSCS	70%	60%	0.42
Mode of Delivery – Vaginal	30%	40%	0.42
Male Sex	60%	46.7%	0.31
NICU Admission	100%	20%	<0.001*

*Statistically significant

ROC curve analysis [Table 5] demonstrated that the AT/ET ratio was the most reliable Doppler parameter for prediction of neonatal RDS, with a cut-off ≤0.21 showing sensitivity 85%, specificity 80%, PPV 77%, and NPV 87%.

Table 5: Predictive Accuracy Of Fetal MPA Doppler Indices For Neonatal RDS

Doppler Parameter	Cut-off Value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
PI	≥1.90	70	72	65	76
RI	≥0.81	68	70	62	74
AT	≤38 ms	78	75	71	81
AT/ET Ratio	≤0.21	85	80	77	87

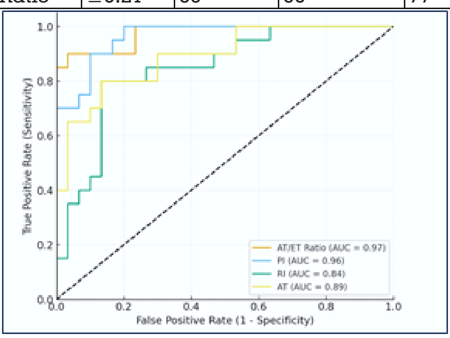

Figure 1. ROC Curves for Fetal MPA Doppler Indices in Prediction of RDS

DISCUSSION

Respiratory Distress Syndrome (RDS) is a leading cause of neonatal morbidity and mortality, with incidence rising sharply as gestational age decreases. Extremely preterm (<28 weeks) and very preterm (28–<32 weeks) neonates are at greatest risk, though RDS can also affect late-preterm and early-term infants [10]. Reliable non-invasive prediction of fetal lung maturity is therefore essential, especially in elective caesarean deliveries [10]. Doppler assessment of the fetal pulmonary artery offers promise, as studies by Kitabatake, Rasanen, and Fuke demonstrated correlations between Doppler indices, pulmonary vascular resistance, and lung maturity, supporting its clinical potential [11–13].

In our study, neonates with RDS had significantly lower mean birth weight (2055 ± 210 g) than those without RDS (2265 ± 190 g, $p = 0.002$). Gestational age was also lower in the RDS group (33.1 ± 1.3 weeks vs 34.3 ± 1.2 weeks, $p = 0.002$). These findings highlight the established inverse association between fetal maturity and RDS risk. Seth N et al. (2024) reported similar results, with lower birth weight and gestational age in RDS-positive neonates, reinforcing the reliability of these markers.[1] Comparable findings were also documented by Khalifa et al. (2021), who found that smaller fetuses delivered earlier were more likely to develop RDS [14]. Keshuraj et al. (2022) confirmed that early gestational age was strongly associated with lower AT/ET ratios and increased respiratory morbidity [9]. Classical studies by Moety et al. (2015) and Guan et al. (2015) further validated gestational age as a determinant of RDS [7,8].

In our cohort, RDS-positive neonates showed significantly smaller BPD, FL, AC, and EFW. Placental immaturity (Grade II) was more frequent in RDS cases, while non-RDS neonates more commonly exhibited Grade III placentas. Iso- or hypo-echogenic lungs relative to the liver were also strongly associated with RDS, whereas hyper-echogenic lungs were protective. Seth N et al. (2024) reported nearly identical findings, with reduced biometry, delayed placental maturation, and iso-/hypo-echogenic lungs in RDS-positive neonates. Khalifa et al. (2021) similarly found that combining placental grading and lung echogenicity with pulmonary artery Doppler improved diagnostic accuracy [14]. Moety et al. (2015) also demonstrated a strong correlation between placental maturity, lung echogenicity, and neonatal outcomes [8].

In our study, PI and RI were significantly elevated in RDS-positive neonates, while AT and AT/ET ratios were significantly reduced. Among these, AT/ET ratio emerged as the strongest predictor, with a cut-off ≤0.21 yielding sensitivity of 85% and specificity of 80%. Seth N et al. (2024) also reported similar results, identifying AT/ET as the most reliable parameter, with comparable sensitivity and specificity. [1] Hassan et al. (2023) confirmed AT/ET as the single most powerful Doppler predictor [15], while Keshuraj et al. (2022) reported robust associations across gestational age groups with slightly higher cut-offs (~0.29–0.32) [9]. Khalifa et al. (2021) emphasized the superiority of AT/ET compared to other indices [14].

Earlier foundational work by Moety et al. (2015) showed that an AT/ET ≈0.305 predicted RDS with high specificity [7], while Guan et al. (2015) also reported reduced AT/ET ratios in RDS-positive neonates [8]. Kim SM et al. (2013) and Schenone MH et al. (2014) further linked pulmonary artery Doppler indices to biochemical markers and neonatal outcomes [16,17]. Azpurua H et al. additionally demonstrated an inverse correlation between AT/ET ratio and amniotic fluid L/S ratio, supporting its role as a non-invasive surrogate [18].

More recently, Hassan et al. (2023) showed consistently lower AT/ET ratios among RDS fetuses across gestational subgroups, with an optimal cut-off of 0.305 (sensitivity 76.9%, specificity 84.1%) [15]. Taha HMG et al. reported slightly different thresholds, with sensitivity of 76.6% and specificity of 100% at a cut-off of 0.25 [19]. Such variations likely reflect differences in gestational ranges, Doppler settings, and populations studied [9,15,17].

In our study, all neonates with RDS required NICU admission compared to only 20% of non-RDS neonates ($p < 0.001$). Male neonates were slightly more affected (60% vs 46.7%), though not statistically significant. Mode of delivery did not influence outcome, with LSCS being the most common in both groups. These findings were consistent with Seth N et al. (2024), who also reported universal NICU admission among RDS neonates, with no significant effect of delivery mode. [1] Hassan et al. (2023) likewise reported higher NICU admissions in RDS-positive neonates with abnormal Doppler findings [15]. Keshuraj et al. (2022) also observed that neonates with reduced AT/ET ratios had longer NICU stays and greater need for respiratory support [9].

Our ROC curve analysis confirmed AT/ET ratio as the most accurate Doppler index for predicting RDS, outperforming PI and RI. The cut-off of ≤0.21 yielded sensitivity of 85% and specificity of 80%. Seth N et al. (2024) similarly identified AT/ET as the most reliable parameter with comparable diagnostic accuracy. [1] This parallels the findings of Keshuraj et al. (2022), who noted optimal cut-offs around 0.29–0.32 depending on gestational age, and Hassan et al. (2023), who validated AT/ET as the primary discriminator [9,15]. Earlier, Moety et al. (2015) and Guan et al. (2015) also concluded that AT/ET was the most reliable Doppler parameter [7,8].

The limitations of our study include its modest sample size and single-centre design, which may limit generalizability. Additionally, biochemical validation against amniotic fluid indices was not performed. Future research should involve larger, multicentric trials, standardized Doppler protocols, and integration with advanced techniques such as 3D ultrasound to establish widely applicable cut-offs.

CONCLUSION

This study demonstrates that fetal main pulmonary artery (MPA) Doppler indices, particularly the AT/ET ratio, serve as reliable non-invasive predictors of fetal lung maturity and the subsequent risk of neonatal respiratory distress syndrome (RDS). Elevated PI and RI with reduced AT and AT/ET ratios were strongly associated with RDS, while AT/ET ≤0.21 provided the highest sensitivity and specificity. Routine obstetric biometry, placental grading, and lung echogenicity further supported these findings. Incorporating MPA Doppler into obstetric ultrasound may enhance prenatal risk stratification and guide timely interventions, potentially reducing neonatal morbidity and improving perinatal outcomes.

REFERENCES

1. Seth N, Verma S. Foetal Pulmonary Artery Derived Doppler Parameters for Foetal Lung Maturity Assessment: An Observational Study. J Clin Diagn Res. 2024 Aug;18(8):TC01–TC05.
2. Wen SW, Smith G, Yang Q, Walker M. Epidemiology of preterm birth and neonatal outcome. Semin Fetal Neonatal Med. 2004;9(6):429-35.
3. Spong CY, Mercer BM, D'Alton M, Kilpatrick S, Blackwell S, Saade G. Timing of indicated late-preterm and early-term birth. Obstet Gynecol. 2011;118(2 Pt 1):323-33.
4. Ventolini G, Neiger R, Hood D, Belcastro C. Update on assessment of fetal lung maturity. J Obstet Gynaecol. 2005;25(6):535-38.
5. Tabsh KM. Correlation of ultrasonic epiphyseal centers and the lecithin: Sphingomyelin ratio. Obstet Gynecol. 1984;64(1):92-96.
6. Harman CR, Manning FA, Stearns E, Morrison I. The correlation of ultrasonic placental grading and fetal pulmonary maturation in five hundred sixty-three pregnancies. Am J Obstet Gynecol. 1982;143(8):941-43.
7. Moety GA, Gaafar HM, El Rifai NM. Can fetal pulmonary artery doppler indices predict neonatal respiratory distress syndrome? J Perinatol. 2015;35(12):1015- 19.
8. 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. 2015;43(6):375-83.
9. Keshuraj V, Prakash A, Boruah DK, Ramanna HC, Sowmyashree AR, Mithun SK. Validity of foetal doppler indices in predicting postnatal respiratory distress syndrome: A prospective study. Egypt J Radiol Nucl Med. 2022;53:183.
10. Ghafoor T, Mahmud S, Ali S, Dogar SA. Incidence of respiratory distress syndrome. J Coll Physicians Surg Pak. 2003;13(5):271-73.
11. Kitabatake A, Inoue M, Asao M, Masuyama T, Tanouchi J, Morita T, et al. Noninvasive evaluation of pulmonary hypertension by a pulsed doppler technique. Circulation. 1983;68(2):302-09.
12. Rasanen J, Wood DC, Weiner S, Ludomirski A, Huhta JC. Role of the pulmonary circulation in the distribution of human fetal cardiac output during the second half of pregnancy. Circulation. 1996;94(5):1068-73.
13. 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(1):228-33.
14. Khalifa YEA, Aboulghar MM, Hamed ST, Tomerak RH, Asfour AM, Kamal EF. Prenatal prediction of respiratory distress syndrome by multimodality approach using 3D lung ultrasound, lung-to-liver intensity ratio tissue histogram and pulmonary artery Doppler assessment of fetal lung maturity. Br J Radiol. 2021 Dec;94(1128):20210577.
15. Hassan HGEMA, Nagi MAMA, Salama AMM, Dawoud MOAEA, Elgendy GG, Abdelrahman AS. Sonographic prediction of fetal main pulmonary artery (MPA) Doppler indices of lung maturity and neonatal respiratory distress syndrome (RDS) development. J Ultrasound. 2023;26(2):525-33.
16. Kim SM, Park JS, Norwitz ER, Hwang EJ, Kang HS, Park CW, 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(10):805-12.
17. 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(3):208-14.
18. 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(1):40.e1-8. Doi: 10.1016/j.ajog.2010.01.075. Epub 2010 Apr 24.
19. Taha HMG, Al Ghorab NM, Al-Namory MM, Hussein NA. Role of fetal pulmonary artery doppler in prediction of neonatal respiratory distress in neonates of diabetic mothers. Int J Reprod Contracept Obstet Gynecol. 2022;11(12):3236- 41.