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Prediction of neonatal respiratory distress syndrome by Quantitative ultrasound texture analysis of fetal lung Observational cross section study

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Abstract

To predict respiratory distress syndrome using a noninvasive method called quantitative ultrasonography study of fetal lung texture. A cohort of 304 cases and was conducted in the feto maternity unit of Minia Maternity and Children University Hospital over 3 years. Fetal lung images were used to develop a computerized method based on texture analysis and machine learning algorithms, trained to predict neonatal respiratory morbidity risk on fetal lung ultrasound images. In the Control group, the range of the Replication Index (RI) was between 0.58 and 1.04, with a mean ± standard deviation (SD) of 0.82 ± 0.1. In the RD group, the RI varied from 0.53 to 1.06, with a mean ± SD of 0.77 ± 0.13. There was a statistically significant difference (p= 0.002) between the two groups. There was no notable disparity observed in the texture lung analysis when utilizing automated tools between the two groups. The research showed a significant and meaningful difference between the groups regarding Doppler indices. There was no significant differenceThere was a significant difference in occupation between the two groups tested, with a p-value of less than .001. A significant discrepancy was observed between the two analyzed groups (p= <.001). Regarding Parity, there was no statistically significant difference seen between the two groups being analyzed (p= 0.057). The research showed a significant and meaningful difference between the groups being studied in terms of LMP GA (gestational age) and AFI. Specifically, the RDS group had a much lower AFI compared to the other groups regarding texture lung analysis.

Keywords: fetal lung maturity; image quantitative analysis; neonatal respiratory morbidity; texture analysis

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1. Introduction

Obstetricians and doctors have historically had difficulties in assessing the maturation of fetal lungs, especially in instances of preterm labor and preterm premature rupture of membranes (PROM). Neonatal respiratory morbidity, which includes respiratory distress syndrome or transitory tachypnea of the newborn, is the primary cause of death and illness related to premature birth [1]. Neonatal respiratory morbidity is not only found in babies born exceedingly prematurely, but also remains high in babies born before 39 weeks' gestation, including those born in the late preterm and early-term era [2]. The evaluation of fetal lung maturity (FLM) predominantly depends on the examination of pulmonary surfactant by laboratory assays performed on amniotic fluid [3]. In the past 25 years, scientists have been trying to predict the development of fetal lungs (FLM) using non-invasive methods. These methods include analyzing gray-level measures, lung tissue movements, and comparing lung-to-placenta or -liver images, among other techniques [4]. The investigation demonstrated a strong link with respiratory illness, but the diagnostic accuracy of the condition was insufficient for practical application in a clinical setting. The advancements in computer capacity and picture resolution have led to the development of robust quantitative methods for ultrasonic image processing throughout time [5]. Texture analysis procedures refer to computer tools that can analyze medical images and discover minor variations in appearance or texture that are imperceptible to the human visual system [6]. These linguistic patterns can be employed to teach computers in forecasting clinical data. The Doppler Effect enables the quantification of various parameters related to fetal blood flow. These measures have allowed for the analysis of several

blood arteries in the circulation between the mother and fetus, enabling the monitoring of the health and well-being of both the mother and fetus. The Doppler assessment of the primary pulmonary artery has proven to be valuable in examining the resistance of these blood vessels. It has been observed that alterations in these factors are associated with gestational age, fetal lung development, and neonatal results.

2. Materials and Methods

The research was conducted in the feto maternity section of Minia Maternity and Children University Hospital. The research population consisted of 304 cases who were hospitalized to the feto maternity unit at Minia Maternity and Children University Hospital. Upon receiving approval from the departmental scientific and ethical committee. The patients were categorized into two cohorts: a control group (A) and a case group (B) that exhibited respiratory distress syndrome (RD).

2.1. Selection criteria for admission into the research group

The gestational age was between 36 to 39 weeks. Conduct ultrasonography within 48 hours following delivery. singelton gestation. We exclude pregnant females with a gestational age below 36 weeks or above 40 weeks, Undergoing multiple pregnancies, Undetermined gestational age, Administer corticosteroids post-ultrasound but pre-delivery and congenital fetal malformation.

2.2. Methods

Patients were subjected to : Personal demographic details, including: Name, Age, marital status, address .The factors of interest encompass the birth mode, gestational age, gender, admission diagnosis, prenatal history, birth history, and postnatal history, Menstrual history include the onset of menstruation, any deviations from a typical menstrual cycle, dysmenorrhea, and any other symptoms related to menstruation. Historical account of the process of giving birth. History of medical background, encompassing any persistent medical conditions and the current drugs you are prescribed. The patient has a preexisting medical history of hypertension (HTN) and diabetes mellitus (DM). Existence of a familial history of the same illness or diabetes. The patient has undergone surgical intervention.

2.3. Evaluation

Comprehensive assessment: Evaluation of vital indicators including blood pressure, temperature, heart rate, and respiratory rate. Assessment for signs of paleness, bluish discoloration, yellowing of the skin, and swelling of lymph nodes. Assessment of the abdomen and specific areas of the body: Abdominal examination by Inspection ,fundal level ,fundal grip ,umbilical grip ,first and second pelvic grip and auscultation .

2.4. Study intervention

Our work consisted of systematically monitoring our patients by employing Doppler evaluation of the pulmonary artery in the pregnancy. Evaluation of fetal lung maturity with the utilization of quantitative ultrasonography and Perform a thorough evaluation of respiratory distress after childbirth utilizing clinical, radiographic, and chemical techniques.

2.5. Fetal pulmonary artery Doppler

The Doppler assessment was conducted by utilizing pulse wave Doppler to examine the fetal main pulmonary artery in close proximity to the pulmonary valve orifice. Following a standard ultrasound examination that involved measuring the size of the fetus, estimating its weight, and assessing the amount of amniotic fluid, the examiner proceeded to systematically evaluate the fetal heart. This included evaluating the four-chamber view, the outflow tracts, and the three-vessel view. The angle of incidence was consistently kept below 30 degrees. After acquiring the waves, the duration of acceleration of the fetal main pulmonary artery (FMPAT) was recorded in milliseconds using at least six waves, and an average value was computed. During the thorax axial view, while the fetus was not exhibiting any fetal breathing movements, the examiner traced the MPA until it reached a point halfway between the pulmonary valve and the bifurcation of the right and left branches. The Doppler gain and scale were modified to get an optimal depiction of the velocity waveform, allowing for clear visualization of the peak systolic velocity (PSV) and early diastolic notch. The MPA Doppler waveform exhibited its distinctive form, characterized by a strong systolic peak blood flow with a needle-like appearance, sometimes referred to as a 'spike and dome' pattern. At the end of the systole, a tiny area of flow in the opposite direction is also observed. The distinctive morphology of the MPA waveform is crucial for distinguishing it from the waveform of the ductus arteriosus, which exhibits a more rounded, voluminous, and triangular shape with increased diastolic flow. Eighteen once the ideal fetal MPA waveform was acquired, the appropriate Doppler velocity variables were manually traced three times and the average value was calculated. The variables comprised the S/D ratio, PI, RI, PSV, and the At/Et ratio. The At/Et ratio is calculated by dividing the time it takes for the ventricular systole to reach peak velocity (At) by the total duration of the ventricular systole (Et). The acceleration time is the duration between the start of systolic flow through the pulmonary valve and the highest systolic velocity. The FMPAT was used in the formula:

$$FMPAP=90 – (0.62\times FMPAT) \quad (19).$$

2.6. Quantitative ultrasound fetal lung maturity analysis

The objective is to conduct a quantitative analysis of prenatal lung maturity utilizing ultrasound imaging of the axial section of the fetal thorax at the level of the four-chamber view of the fetal heart. This analysis aims to provide an automatic assessment of the risk of neonatal respiratory morbidity. The quantitative ultrasound fetal lung maturity study was specially built to consist of two modules: a textural feature extractor and a classifier. The latter employs data from the retrieved characteristics to evaluate the likelihood of respiratory illness. This is considered as one of the computerized software intelligence system. Postnatal blind

neonatal evaluation of RDs clinically, radiologically and chemically.

3. Results and discussion

The delivery data for the study groups were shown in Table (1). The weight in group A ranged from 3055 to 3167, with an average ± standard deviation of 3097.57 ± 28. Conversely, the weight in-group B varied between 1896 and 2290, with an average ± standard deviation of 2139.22 ± 79.68. The two groups had a highly significant statistical difference ($p < .001$). The APGAR score at 1 minute in group A varied between 7 and 9, with an average value of 8.28 and a standard deviation of 0.55. The APGAR score at 1 minute in group B ranged from 6 to 8, with an average ± standard deviation of 7.08 ± 0.55. The two groups had a highly significant statistical difference ($p < .001$). The control group had APGAR scores ranging from 8 to 10 at the 5-minute mark, with a mean value of 9.16 ± 0.62, as shown by the standard deviation. The APGAR score at 5 minutes in group B varied between 6 and 8, with an average of 7.01 ± 0.7. The two groups had a highly significant statistical difference ($p < .001$). There was a significant statistical difference seen in the admission rates to the Neonatal Intensive Care Unit (NICU) between the two groups being studied ($p < .001$). Regarding gender, there was no statistically significant disparity seen between the two groups being analyzed ($p= 0.169$). Table 2 displayed the Fetal pulmonary artery Doppler measurements for the different study groups. In group A, the range of the RI was between 0.58 and 1.04, with a mean ± SD of 0.82 ± 0.1. In group B, the range of the RI was between 0.53 and 1.06, with a mean ± SD of 0.77 ± 0.13. There was a statistically significant difference ($p= 0.002$) between the two groups. The PI values in group A varied from 1.37 to 3.43, with a mean of 2.43 and a standard deviation of 0.46. In group B, the PI values ranged from 1.03 to 3.31, with a mean of 2.24 and a standard deviation of 0.56. There was a statistically significant difference ($p=0.001$) between the two groups. The AT/ET ratio in group A varied from 0.24 to 0.46, with a mean ± standard deviation of 0.34 ± 0.05. In group B, the AT/ET ratio ranged from 0.17 to 0.38, with a mean ± standard deviation of 0.27 ± 0.05. There was a highly statistically significant difference ($p < .001$) between the two groups. Neonatal respiratory distress syndrome [RDS] is a commonly seen medical condition. The primary cause of neonatal diseases and mortality, particularly in premature newborns, is mostly ascribed to this component [7]. The condition mostly arises from insufficient lung maturation and poor production of pulmonary surfactant. The risk factors for this condition include maternal drug administration, maternal diabetes, and genetic predisposition [8]. The significant morbidity and death rates linked to neonatal RDS mostly stem from the complex nature of the underlying condition, which poses challenges in its detection and restricts the range of targeted treatment choices [9]. An accurate assessment of fetal lung maturity is crucial in establishing the ideal timing for ending a pregnancy, with the goal of reducing the occurrence of respiratory distress syndrome (RDS). Nevertheless, all existing biochemical assessments for determining lung maturity necessitate amniocentesis, an invasive procedure that entails notable, albeit infrequent, hazards such as preterm premature rupture of membranes, preterm labor, placental abruption, fetomaternal hemorrhage, fetal injury, and exceedingly rare instances of fetal or maternal mortality. Therefore, it is preferable to have a test that does not require any intrusive procedures. The echogenicity of the fetal lung undergoes a regular pattern of change during pregnancy. The ultrasonographic measurements largely focused on assessing the fetal pulmonary artery [PA] and the functional capability of the fetal lung. The evaluated PA markers included the ratio of At/Et and the pulmonary artery resistance index.Previous studies have investigated the relationship between doppler waveforms in the fetal pulmonary artery and the presence of fetal pulmonary hypoplasia. In addition, as the lung progresses throughout gestation, the pulmonary vasculature also experiences growth and maturation. This entails an augmentation in the overall quantity of pulmonary arteries and a reduction in pulmonary artery vascular resistance [10]. Based on these facts, the application of fetal pulmonary artery doppler indices can help in identifying FLM [11]. The study conducted by Abdulla Elsayed et al. (2022) discovered a favorable relationship between the ratio of fetal pulmonary artery acceleration time to ejection time (At/Et) and both fetal gestational age and fetal lung maturity tests in amniotic fluid [12]. The aim of our study was to predict respiratory distress syndrome using the noninvasive technique of computer based artificial intelligence programs The study was carried out at Minia Maternity and Children University Hospital, namely in the feto maternity unit. The study had a sample of 304 participants who were categorized into two cohorts: a control group and a group afflicted with respiratory distress syndrome (RD). The inquiry yielded data about the demographic characteristics and occupational statistics of the mothers in the various groups under examination. The Control group consisted of individuals aged between 19 and 35, with an average ± standard deviation of 25.98 ± 4.33. The age range in the RD group was from 17 to 42, with an average ± standard deviation of 27.84 ± 6.89. A substantial statistical disparity ($p=0.005$) was observed between the two groups. The Body Mass Index (BMI) of the Control group ranged from 19 to 25.9, with an average value of 22.51 ± 1.7, representing the mean ± standard deviation. Conversely, the RD group had a Body Mass Index (BMI) that varied between 18.2 and 26, with an average ± standard deviation of 21.4 ± 1.68. The two groups exhibited a substantial and statistically significant difference ($p < .001$). Regarding residency, there was no statistically significant disparity seen between the two groups being examined ($p = 0.489$). Regarding Occupation, there was a highly significant disparity between the two groups under analysis ($p < .001$). Our findings challenge the conclusions of Khalil OA et al (2019) by demonstrating that there is no statistically significant difference in maternal age between the groups of fetuses diagnosed with newborn respiratory distress syndrome (RDS) and those without RDS [13]. Khalil OA et al. conducted a study in 2019 to investigate if doppler indices of the fetal main pulmonary artery (MPA) can be used as predictors for the incidence of respiratory distress syndrome (RDS). Out of the 40 fetuses investigated, 9 were found to be positive for RDS (RDS +ve group) and 31 were found to be negative for RDS (RDS -ve group).

Table 1. Delivery data among the study groups

	Control group A (n = 152)	**Case group B (n = 152)**	**Test of Sig.**	**p**
Weight			t = 139.904	<0.001
Mean ± SD.	3097.57 ± 28	2139.22 ± 79.68		
Median (IQR)	3094 (3073 - 3117.25)	2147.5 (2086.75 - 2195.75)		
Range (Min-Max)	112 (3055 - 3167)	394 (1896 - 2290)		
APGAR 1m			t = 18.969	<0.001
Mean ± SD.	8.28 ± 0.55	7.08 ± 0.55		
Median (IQR)	8 (8 - 9)	7 (7 - 7)		
Range (Min-Max)	2 (7 - 9)	2 (6 - 8)		
APGAR 5m			t = 28.467	<0.001
Mean ± SD.	9.16 ± 0.62	7.01 ± 0.7		
Median (IQR)	9 (9 - 10)	7 (7 - 7)		
Range (Min-Max)	2 (8 - 10)	2 (6 - 8)		
NICU Admission				<0.001
- **Yes**	15 (9.87%)	152 (100%)		
- **No**	137 (90.13%)	0 (0%)		
Gender			X2 = 1.896	0.169
- **Male**	72 (47.37%)	84 (55.26%)		
- **Female**	80 (52.63%)	68 (44.74%)		

χ2: Chi- Square test **SD:** standard deviation **IQR:** interquartile range
t: Independent T test **p**: p value for comparing between the studied groups

P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.001: Highly significant

Table 2. Fetal pulmonary artery Doppler among the study groups

	Control group A (n = 152)	**Case group B (n = 152)**	**Test of Sig.**	**p**
RI			t = 3.145	0.002
Mean ± SD.	0.82 ± 0.1	0.77 ± 0.13		
Median (IQR)	0.82 (0.75 - 0.88)	0.78 (0.67 - 0.85)		
Range (Min-Max)	0.46 (0.58 - 1.04)	0.53 (0.53 - 1.06)		
PI			t = 3.226	0.001
Mean ± SD.	2.43 ± 0.46	2.24 ± 0.56		
Median (IQR)	2.4 (2.12 - 2.75)	2.27 (1.9 - 2.62)		
Range (Min-Max)	2.06 (1.37 - 3.43)	2.28 (1.03 - 3.31)		
AT/ET			t = 12.28	<0.001
Mean ± SD.	0.34 ± 0.05	0.27 ± 0.05		
Median (IQR)	0.34 (0.3 - 0.37)	0.27 (0.23 - 0.3)		
Range (Min-Max)	0.22 (0.24 - 0.46)	0.21 (0.17 - 0.38)		

t: Independent T test **SD:** standard deviation **IQR:** interquartile range
p: p value for comparing between the studied groups
P-value > 0.05: Non significant; P-value < 0.05: Significant; P-value < 0.001: Highly significant

In addition, our findings are in direct opposition to the study done by Keshuraj V et al (2022), which aimed to evaluate the precision of prenatal doppler indicators in forecasting postnatal respiratory distress syndrome [14]. The researchers reported that 342 fetuses satisfied the requirements for the ultimate analysis. The study identified 47 instances of positive Respiratory Distress Syndrome (RDS) and 295 instances of negative RDS. The groups studied did not show any statistically significant difference in mother age, as indicated by a p-value of 0.398. Our findings diverged from the study conducted by Hassan HG et al. (2023), which sought to highlight the prognostic significance of perinatal fetal main pulmonary artery (MPA) doppler measures in the occurrence of newborn respiratory distress syndrome (RDS) [15]. Their study encompassed a sample size of 70 fetuses, out of which 26 were identified as positive for RDS, while the remaining 44 were identified as negative. Nevertheless, there was no noteworthy disparity found between the two groups for maternal age, as shown by a p-value of 0.985. Furthermore, our results challenge the findings of the study conducted by Khalifa YE et al (2021), which sought to investigate the correlation between different lung parameters assessed using three-dimensional ultrasound (3D US) and fetal lung maturity (FLM) in order to predict the likelihood of neonatal respiratory distress syndrome (RDS) [16]. According to their findings, 38 out of 143 fetuses (26.5%) were diagnosed with RDS. Nevertheless, no statistically significant disparity was detected among the groups under investigation for maternal age and BMI. The examination primarily examined the clinical data pertaining to the mothers in the study groups. A statistically significant disparity (p= <.001) was seen in the prevalence of medical conditions (such as diabetes mellitus, hypertension, thyroid illness, rheumatic heart disease, deep vein thrombosis, anemia, and epilepsy) between the two groups under evaluation. Regarding Parity, no statistically significant difference was seen between the two groups being studied (p=0.057).

4. Conclusions

Our analysis revealed a notable disparity between the groups we assessed in relation to gestational age (LMP GA) and AFI. More precisely, the RDS group had a much lower AFI in comparison to the other groups. Moreover, there was a significant discrepancy between the groups being studied in relation to the weight of newborns, with a particularly lower weight seen in the RDS group. Moreover, a significant and notable difference was noticed between the studied groups in relation to APGAR 1m and APGAR 5m, with the RDS group displaying considerably lower scores. There was a significant and statistically significant difference between the groups being tested in terms of AT/ET.A substantial statistical difference was seen between the examined groups in relation to RI&PI. There was no significant difference between the two groups regarding computer based lung texture analysis programs. Further investigation on a broader scope is required to authenticate our discoveries.

Recommendations

It is recommended to conduct further investigations using carefully designed randomized controlled trials or large, comparative observational studies. Ensure the incorporation of a varied and inclusive sample of patients that encompasses individuals with similar attributes, such as age, gender, and the severity of their ailment. Collecting data through the utilization of approved devices and methodologies at regular intervals following the surgical procedure. Future study should aim to have a suitably large sample size in order to assure statistically significant findings and to control for any potential confounding variables that may impact the results. In order to provide a more accurate assessment of long-term outcomes, it is necessary for research studies to include a prolonged period of follow-up. We recommend that future research should include multicenter trials to validate our findings.

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