

Value of Chest Ultrasound in Preterm Neonates with Neonatal Respiratory Distress Syndrome

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Abstract:

Background: The deficiency of surfactant, a lipoprotein material secreted by type 2 pneumocytes, is the cause of neonatal respiratory distress syndrome (NRDS), a common respiratory condition in neonates. This study aimed to detect the value of chest ultrasonography in the diagnosis of NRDS in preterm neonates for earlier and more accurate diagnosis and hence prompt management of the disease. **Methods:** This descriptive study encompassed 50 preterm neonates who were admitted to the Neonatal Intensive Care Unit of Ahmed Maher Teaching Hospital and exhibited clinical and radiological manifestations of respiratory distress syndrome. The patients were divided into two groups: group A (n=24) consisted of neonates with grade 3 respiratory distress and group B (n=26) consisted of neonates with grade 4 respiratory distress. **Results:** Sensitivity of lung ultrasound was 84.6%, its specificity was 100%, positive predictive value (PPV) was 100%, negative predictive value was 85.7% and accuracy was 92% in detecting NRDS. **Conclusion:** We concluded that chest ultrasonography has good sensitivity, specificity, PPV and accuracy in detecting NRDS. Also, it can detect the severity of neonatal RDS better than plain chest X-ray. **Keywords:** Neonatal Respiratory Distress Syndrome ; Preterm Neonates; Chest Ultrasound;

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Introduction

Neonatal respiratory distress syndrome is a common respiratory condition in neonates. It is caused by a deficiency of surfactant, a lipoprotein substance secreted by type 2 pneumocytes to allow the alveoli to expand during inspiration and prevent their collapse during expiration. The primary cause of NRDS in preterm neonates is the immaturity of type 2 pneumocytes. Males are much more susceptible to it than females ⁽¹⁾. The deficiency of surfactant, a lipoprotein material secreted by type 2 pneumocytes, is the cause of neonatal respiratory distress syndrome (NRDS), a prevalent respiratory disease ⁽²⁾.

Neonates are more susceptible to the latent effects of chest X-ray ("CXR") than other age groups as a result of their diminutive size and the proximity of radiosensitive tissues and organs. The presence of ionizing radiation during the procedure is the reason for this ⁽³⁾.

Chest ultrasonography has been implemented as a diagnostic tool for NRDS. Ultrasound (US) is a non-invasive and rapid procedure that can be repeated without causing any radiation-related side effects. In the event of an emergency, the utilization of ultrasound (US) is a practical alternative that enables patients to undergo examinations while receiving other treatments without the need to be transferred to the radiology room ⁽⁴⁾. Pulmonary US has a very high sensitivity ⁽⁵⁾ and reliability ⁽⁶⁾. RDS must be distinguished from pneumonia, neonatal transient tachypnea, and meconium aspiration syndrome in order to be diagnosed ⁽⁷⁾.

The purpose of this study was to determine the value of chest ultrasonography in the diagnosis of NRDS in preterm neonates for early and accurate diagnosis and hence prompt management of the disease.

Patients and methods

This **descriptive observational study** was conducted from March 1, 2022, to February 28, 2023, on fifty preterm

neonates with clinical and radiological manifestations of RDS admitted to the Neonatal Intensive Care Unit (NICU) of Ahmed Maher Teaching Hospital.

The patients' parents provided written consent that was informed. The purpose of the study was explained to each patient, and they were assigned a secret code number. The investigation was conducted with the approval of the investigation Ethics Committee, Faculty of Medicine, Benha University, and Ahmed Maher Teaching Hospital.

Inclusion criteria were RDS is administered to preterm neonates (28-36 weeks gestational age) within the first 24 hours of life. The diagnosis of RDS was made using a combination of clinical indicators (presentation, vital signs, and auscultation) and a plain chest x-ray. Preterm neonates with severe RDS, including those who received a single dose of artificial surfactant on the resuscitation table, were included.

Exclusion criteria neonates who were more than 36 weeks gestational age, neonates who did not exhibit any signs or symptoms of respiratory distress syndrome (RDS), neonates who had respiratory distress due to extrapulmonary causes, such as congenital heart diseases, renal failure, and early severe sepsis, neonates who had a history of maternal infection during pregnancy, clinical signs of congenital malformations, amniotic fluid stained with meconium, a pulmonary ultrasound done after a chest X-ray, and parents who opted out of the study.

Grouping: The patients were subdivided into group A (n=24): neonates with grade 3 respiratory distress and group B (n=26): neonates with grade 4 respiratory distress. During the lung ultrasound (LUS), we documented the following information for preterm neonates who fulfilled the inclusion criteria: gender, weight, gestational age, delivery mode, history of prenatal lung maturation, and type of breathing aid therapy (invasive or non-invasive).

Detailed history taking, clinical examination, routine investigations, oxygen support during NICU stay, plain chest X-ray in an anteroposterior position, and LUS in the supine and lateral decubitus positions were administered to all patients under investigation.

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Statistical analysis

We used IBM SPSS Statistics for Windows, Version 23.0, IBM Corp., Armonk, NY, USA, to compile, edit, and code the data that we then imported into the Statistical Package for the Social Sciences. Summary of the data: Number (n) of observations in each category or order for qualitative data. Quantity of data pertaining to each group or sequence. Numbers and statistics: To find the mean, add up all the values and divide them by the total number of observations. Due to its insensitivity to extreme values, the median is employed for the purpose of summarizing skewed data. Whether the data is presented in a descending or ascending order of magnitude, it is the middle observation in the collection. Distinction between means (SD): The square root of the variance and the dispersion are measured by it. The IQR, or inter-quartile range, is the set of values that fall somewhere near the center of the distribution of scores. "Range" means the range of values, or the distance between the two extremes. If the p-value is more than or equal to 0.05, the data is deemed non-significant, but if it is less than or equal to 0.05, the data is deemed significant⁽⁸⁾. A correlation between two qualitative variables can be discovered using Fisher's exact test (f) or the Chi-Square [X2] test. There are two tests that may be used to compare quantitative data across categories: the independent t-test and the Mann-Whitney U (also known as the Wilcoxon rank-sum test).

Results

(Table 1) demonstrated a statistically significant difference between the studied

groups as regards the demographic data. Patients in group A were older than patients in group B ($P<0.001$). Also, patients in group A had a higher weight when compared to patients in group B ($P<0.001$). Furthermore, 30.8% of the patients in group B were twins, while none of the patients in group A were twins ($P=0.004$). All the patients in group B were delivered by normal spontaneous vaginal delivery (SNVD) while only 8.3% of the patients in group A were delivered by SNVD ($P<0.001$). Regarding the maternal history, mothers of group A had significantly longer premature rupture of membranes (PROM) when compared to those in group B ($P=0.003$). Also, 16.7% of the mothers of group A had oligohydramnios, while none of those of group B had oligohydramnios ($P=0.04$). None of the mothers in group B received corticosteroid in comparison to 75% of those in group A ($P=0.008$).

(Table 2) shows that patients in group A had significantly higher oxygen saturation when compared to patients in group B ($P<0.001$) and that blenders were used for 16.7% of the patients in group A and for no one of the patients in group B ($P=0.046$).

(Table 3) shows statistically significant differences between the studied groups as regards chest x-ray findings, as 66.7% of the patients in group A showed a ground glass opacity in comparison to 7.7% of the patients in group B ($P<0.001$). Additionally, 33.3% of the patients in group A exhibited increased broncho-vascular markings, whereas none of the patients in group B exhibited such markings ($P=0.001$). Additionally, 92.3% of the patients in group B exhibited white lung, whereas none of the patients in group A exhibited white lung ($P<0.001$). In terms of RDS grade, 33.3% of the patients in group A had grade 2 RDS, whereas none of the patients in group B had grade 2 RDS ($P=0.001$). Finally, the percentage of patients in group A with grade 3 RDS was 66.7%, while the percentage of patients in

group B with grade 3 RDS was 7.7% ($P<0.001$). Furthermore, in group A, no patients were diagnosed with grade 4 RDS, whereas 92.3% of patients in group B had this condition ($P<0.001$). We found statistically significant differences between the studied groups as regards US positive findings and US score, as all the patients in group B showed air bronchogram, while most of the patients in group A (91.7%)

showed coalescent B lines in ($P<0.001$). As regards US score, all the patients in group B showed score 18, while 91.7% of the patients in group A had score 12 ($P<0.001$).

In assessing the severity of RDS in preterm neonates, the sensitivity of LUS was 84.6%, with specificity of 100%, PPV 100%, NPV 85.7% and accuracy 92%. (**Table 4**)

Table 1: Primary data among the studied groups

Variables		Group A (n=24)	Group B (n=26)	P Value
Gestational age (weeks)	Mean \pm SD	32.83 \pm 1.09	30.62 \pm 0.85	<0.00* ¹
	Range	(30 – 34)	(29 – 32)	
Weight (Kg)	Mean \pm SD	2.08 \pm 0.25	1.36 \pm 0.31	<0.001* ¹
	Range	(1.6 – 2.4)	(0.9 – 1.8)	
Gender (n. %)	Male	14 (58.3%)	12 (46.2%)	0.39 ²
	Female	10 (41.7%)	14 (53.8%)	
One of twins (n. %)		0 (0%)	8 (30.8%)	0.004* ³
Mode of delivery (n. %)	CS	22 (91.7%)	0 (0%)	<0.001* ³
	SNVD	2 (8.3%)	26 (100%)	
Maternal age (years)	Median (IQR)	23.5 (3.25)	22 (5)	0.06 ¹
	Range	(19 – 35)	(17 – 40)	
PROM (hours)	Median (IQR)	18 (1)	12 (9)	0.003* ¹
	Range	(16 – 20)	(3 – 20)	
	Diabetic	4 (16.7%)	2 (7.7%)	0.41 ³
	Hypertensive	2 (8.3%)	6 (23.1%)	0.25 ³
	Oligohydramnios	4 (16.7%)	0 (0%)	0.04* ³
	Uterine fibroid mass	2 (8.3%)	0 (0%)	0.23 ³
Prenatal Corticosteroids		6 (25%)	0 (0%)	0.008* ²

¹Student T-test, ²Chi-square test, ³Fisher exact test, PROM: Premature rupture of membranes, IQR: Inter-quartile range, SD: Standard deviation, SNVD: spontaneous vaginal delivery, CS: Cesarean section: significant as P value ≤ 0.05

Table 2: Oxygen saturation and ventilatory support during doing lung US among the studied groups

Oxygen saturation and ventilatory support			Group A (n=24)	Group B (n=26)	P Value
Oxygen saturation	Median (IQR)		90 (2)	72 (5)	<0.001*
	Range		(88 – 94)	(70 – 76)	
Ventilatory support	Nasal oxygen	Blender	4 (16.7%)	0 (0%)	0.046* ²
	P_{IP}/PEEP	Ambu bag	6 (25%)	4 (15.4%)	
		T- piece	6 (25%)	4 (15.4%)	0.39 ²
		CPAP	8 (33.3%)	14 (53.8%)	
Mechanical ventilation			0 (0%)	4 (15.4%)	0.14 ¹
					0.11 ²

*¹Chi-square test, ²Fisher exact test, IQR: Inter-quartile range, CPAP: Continuous positive airway pressure, P_{IP}: Peak inspiratory pressure, PEEP: Positive End-Expiratory Pressure, *: significant as P value ≤ 0.05

Table 3: Chest x-ray and ultrasound among the studied groups

Chest x-ray and ultrasound			Group A (n=24)	Group B (n=26)	P Value
Chest x-ray	Time (minutes)	Mean ± SD	29.2 ± 5.04	28.5 ± 4.19	0.59 ¹
		Range	(20 – 40)	(20 – 35)	
	Positive findings (n. %)	Ground glass	16 (66.7%)	2 (7.7%)	<0.001* ²
		Broncho-vascular mark	8 (33.3%)	0 (0%)	0.001* ²
		White lung	0 (0%)	24 (92.3%)	<0.001* ²
	RDS grade (n. %)	Grade 2	8 (33.3%)	0 (0%)	0.001* ²
		Grade 3	16 (66.7%)	2 (7.7%)	<0.001* ²
Grade 4		0 (0%)	24 (92.3%)	<0.001* ²	
Ultrasound	Time (minutes)	Mean ± SD	73.3 ± 28.1	63.1 ± 26	0.19 ¹
		Range	(40 – 120)	(40 – 120)	
	Positive findings (n. %)	Air bronchogram	2 (8.3%)	26 (100%)	<0.001* ²
		Coalescent B lines	22 (91.7%)	0 (0%)	
	Score (n. %)	12	22 (91.7%)	0 (0%)	<0.001* ²
	18	2 (8.3%)	26 (100%)		

*¹Student T-test, ²Fisher exact test, SD: Standard deviation. RDS: respiratory distress syndrome, *: significant as P value \leq 0.05.

Table 4: Validity of LUS in assessing the severity of NRDS in preterm neonates.

Chest US	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
	84.6%	100%	100%	85.7%	92%

Discussion

The primary cause of respiratory failure and mortality in infants within the first few days of life is NRDS⁽⁹⁾. It has an overall prevalence of 1.5 % and a mortality of 17 – 24 % in the NICUs⁽¹⁰⁾. It is a result of lacking lung surfactant that negatively impacts the normal lung functions⁽¹¹⁾. Lipids make up 90% of pulmonary surfactant, while proteins make up 10%. Its purpose is to reduce surface tension. Produced and released by type II alveolar cells, phospholipids account for 80-85% of the lipid mass⁽¹²⁾. A rise in the incidence of neonatal respiratory distress syndrome (RDS), one of the first lung diseases detected by ultrasound, has occurred concomitant with the use of LUS in the diagnosis of lung diseases in neonates. It was probable that RDS's US imaging features were erroneous due to an early

lack of in-depth understanding of the LUS⁽¹³⁾.

In our study, the gestational age was statistically significantly lower in the patients with severe RDS (30.62 \pm 0.85 weeks) than in the group with moderate RDS (32.83 \pm 1.09 weeks). This agreed with the study of Permana et al.⁽¹⁴⁾ who established a statistically significant correlation between gestational age and RDS. Babies born between 28 and 32 weeks of gestation have an RDS prevalence of 81%, compared to 52% and 50%, respectively, in babies born before 28 weeks of gestation and 33 to 36 weeks of gestation.

Babies that are born too soon have not had enough time to fully mature their surfactant and antioxidant systems. This occurs during the late saccular stage of development. Risk factors for respiratory distress syndrome (RDS), sepsis (blood infection), and birth asphyxia in premature

infants include an underdeveloped immune system, an inadequate respiratory center, and an immature lung with a surfactant deficiency ⁽¹⁵⁾. Gas exchange, surfactant absorption, and intrapulmonary fluid absorption are all negatively impacted by immature lung structure. Because the fetus starts to learn to breathe in rhythm and control during the final six weeks of pregnancy, the risk of respiratory distress syndrome (RDS) and sleep apnea increases with preterm delivery ⁽¹⁶⁾.

It was observed that infants born to mothers with severe RDS weighed significantly less (1.36 ± 0.31 kg) than those born to mothers with mild RDS (2.08 ± 0.25 kg). Additionally, infants who weigh less than 2500 grammes at birth are more susceptible to respiratory failure, as indicated by an additional investigation ⁽¹⁷⁾. Infants with low birth weight are a result of small gestational ages. Furthermore, both elements heighten the severity of RDS by causing immaturity in numerous organs, including the lungs. ⁽¹⁸⁾

In our study, all the patients in group B were delivered by normal vaginal delivery in comparison to only 8.3% of the patients in group A ($P < 0.001$). On the contrary, previous studies ⁽¹⁹⁻²¹⁾, The study suggested that the risk of neonatal RDS was increased in infants whose mothers underwent caesarean sections. As opposed to vaginal births, where surfactant is released into the airways in response to adrenergic stimulation and foetal lung fluid is removed through chest compressions, caesarean section babies secrete less surfactant into the alveolar space due to a larger residual volume of lung fluid and a smaller residual capacity ⁽²²⁾. In our study, absence of CS delivery in group B could be due to the small birth weight that facilitated the process of vaginal delivery.

While none of the mothers in group B received antenatal corticosteroids (ACS), 25% of the mothers in group A did ($P = 0.008$), which can be used to expedite

lung development. Consequently, the prevalence of RDS diminishes following the completion of an ACS course. The utilization of anti-ACSs medication results in a decrease in the duration of neonatal respiratory distress syndrome (RDS) episodes, a decrease in the need for respiratory support, and an overall decrease in the number of admissions to the NICU ⁽²³⁾.

Controversy surrounds the usefulness of ACSs during the gestational age range. Neither trials that lasted more than 36 weeks nor those that lasted less than 26 weeks were able to prove the product's efficacy. According to a recent study, the use of corticosteroids has been shown to have a clear positive impact on RDS starting at 34 weeks plus 0. There has been no change to the other main outcomes. As a result, the use of ACSs in women who are very late preterm (35 weeks + 0 days) must be assessed in the context of the balance of risks and benefits ^(24, 25).

In the present study, the majority of patients in group A (91.7%) exhibited coalescent B lines with a US score of 18 while all patients in group B and 8.3% of group A exhibited air bronchograms with a US score of 22 ($P < 0.001$). Sand et al. ⁽²⁶⁾ described the US findings in NRDS as bilateral compact B-lines, absent A-lines, and pleural line abnormalities. Moreover, patients with CXR classifications III and IV were reported to have lung consolidation. Vardar et al. ⁽²⁹⁾ shown that in the mild RDS group, the median and interquartile range (IQR) of LUS scores were 4 and 2-8, respectively, while in the severe RDS group, they were 10 and 9-12, with a p-value less than 0.01.

Liu ⁽¹³⁾ stated that the most critical factor in determining the severity of RDS when using ultrasound as a diagnostic instrument is the degree of consolidation in the lungs. Consolidation of the lungs in infants with moderate RDS occurs only in a small area immediately surrounding the pleura. However, in cases of severe RDS, the consolidation areas can spread to deeper

and bigger parts of the lungs, and they can even cause atelectasis in a large area^(27, 28).

In the current study, Sensitivity of US was 84.6%, its specificity was 100%, PPV was 100%, NPV was 85.7% and accuracy was 92% in differentiation between moderate and severe cases with RDS.

Liu and Hu.⁽³⁰⁾ The degree and severity of lung consolidation as well as the existence of significant complications allowed for the classification of RDS in LUS as mild, moderate, or severe. The ground glass sign is evident in mild RDS. In the early or recovery periods of moderate to severe RDS, it can also be observed. In moderate RDS, the snowflake sign is observed on US; however, it does not affect all lung zones. Symptoms of severe RDS include pneumothorax, extensive atelectasis, persistent pulmonary hypertension, pulmonary hemorrhage, or snowflake sign consolidation in all lung zones. The degree and extent of consolidation can also lead to other serious complications.

New research shows that the LUS score and consolidation areas can differentiate between RDS and non-RDS, determine the stages of NRDS, and foretell when mechanical ventilation will be necessary. Lung aeration is negatively correlated with the LUS score⁽³¹⁾.

Nevertheless, it is important to acknowledge that, despite the fact that US specialists believe that the LUS score may be beneficial, the score is of minimal importance from the clinic's perspective. The score system's scientific validity and accuracy have been called into doubt⁽³²⁾. Not only is the LUS score not reliable for determining the extent of neonatal lung disease, but it can also lead to significant differences in results⁽³³⁾.

The ability of US in diagnosing RDS has been more broadly studied than its role in diagnosing the RDS severity. For example, Shivani et al.⁽³⁴⁾ For the purpose of diagnosing respiratory distress, LUS was found to have a sensitivity of 95.9%, a specificity of 90.3%, a PPV of 94%, and an NPV of 93.3%. The researchers

performed a meta-analysis by Ma et al.⁽³⁵⁾. The study consisted of nine investigations that involved 703 infants. The aggregated specificity and sensitivity of LUS for the diagnosis of NRDS were 95% and 99%, respectively (CI: 0.92- 1.00). (confidence interval: 0.87 to 0.98). The mean area under the curve was 0.99 (0.98-1.0), indicating a high degree of diagnostic accuracy.

The nonionizing nature of LUS is a significant advantage over chest X-rays when it is necessary to conduct repeated evaluations to monitor the neonate's condition⁽⁶⁾. Furthermore, LUS can estimate the severity of the disease by calculation of LUS score and hence can guide the treatment^(31, 36).

The limitations of the study were the relatively small sample size and being a single center study. Also, the study lacks a control group and hence the value of different risk factors and US criteria couldn't be carefully assessed.

Conclusion

Our study found that when it came to evaluating the severity of neonatal RDS, LUS had excellent sensitivity, specificity, PPV, and accuracy. In addition to potentially improving the overall outcomes of neonatal RDS, performing LUS can reduce radiation exposure.

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Conflicts of interest

No conflicts of interest

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