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Original article

Lung ultrasonography score as a predictor of RDS severity in premature infants

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Abstract. *Background and aim:* This study aimed to analyze lung ultrasound (USG) scores as a predictor of Respiratory Distress Syndrome (RDS) severity in premature infants. The research was conducted using an observational analytic method with a cross-sectional approach on 51 premature infants treated in the NICU at Dr. Soetomo Hospital, Surabaya. *Methods:* Data collection was performed by measuring lung USG scores at 0-3 hours and 12-24 hours after birth and analyzing the relationship between these scores and the severity of RDS based on chest X-rays, Downes Score, and Oxygen Saturation Index (OSI). *Results:* The study showed a significant positive correlation between lung USG scores at 12-24 hours and RDS severity based on chest X-rays (r=0.307, p=0.029). Additionally, there was a significant relationship between lung USG scores at 12-24 hours and Downes Score (r=0.355, p=0.011), while lung USG scores at 0-3 hours had a positive correlation with OSI (r=0.483, p=0.049). *Conclusions:* This study demonstrated that lung USG scores can be used as a predictor of RDS severity in premature infants, supporting the potential of lung USG as a non-invasive and effective method for early RDS assessment, which may assist in guiding clinical decisions related to surfactant administration and other interventions. (www.actabiomedica.it)

Key words: Lung ultrasound, predictor, premature infants, respiratory distress syndrome, severity, ultrasonography

Introduction

Premature birth is a challenge for developing countries including Indonesia, this can be seen from global data by WHO which states that in 2020 as many as 2.4 million babies died at the age of 1 month, which means as many as 6700 newborns died every day and resulted in a mortality rate of infants under 5 years of 47% (1,2).

The latest data in Indonesia from the Indonesian Ministry of Health shows that the incidence of premature infants is 12.7%, while the incidence of premature infants in East Java province is around 12.4% (3). Prematurity and LBW are also the highest contributors to the infant mortality rate under 1 year in Indonesia at 16.9 per 1000 live births according to data from the Central Statistics Agency (4), although the rate has decreased compared to the previous year, it is still high compared to other countries in Southeast Asia. There is a high imbalance between the life expectancy of premature babies in developing and developed countries, in developed countries as many as 9 out of 10 premature babies have a good life expectancy, while in developing countries the life expectancy of premature babies is only 1 in 10 babies.

Respiratory Distress Syndrome (RDS) is a common condition in premature infants, with a prevalence of approximately 20-30% and increasing to 50% in infants born before 28 weeks of gestation (5). Even up to 44.15% of infants born before 37 weeks experience complications, with a staggering increase of 60% for those born before 28 weeks (6). RDS is also a leading cause of premature infant mortality, contributing to nearly 30% of total deaths, with mortality rates in some regions reaching 60%. Infants who survive RDS are at risk for long-term complications such as bronchopulmonary dysplasia (BPD) in 25-30% of cases, as well as chronic lung disorders that increase the risk of asthma and lifelong lung function decline (7,8). From an economic standpoint, RDS results in significant financial burden as affected infants require intensive care in the NICU for weeks to months, ultimately impacting both the healthcare system and the family's finances (5). Furthermore, long-term complications resulting from RDS necessitate ongoing medical monitoring and care, impacting the quality of life of both the infant and their family (9).

One of the most severe and most common complications is complications due to respiratory disorders in premature infants known as respiratory distress syndrome (RDS) (10). This disorder is caused by respiratory tract immaturity and surfactant deficiency, which results in respiratory distress that occurs immediately after birth. Infants with RDS in developed countries have a high life expectancy due to advances in science and knowledge and a better health system than developing countries, one of which is due to the administration of surfactant to newborns with RDS (11). The obstacle of surfactant administration in developing countries such as Indonesia is the economic aspect, because most of the financing of preterm infant care is borne by the state so that a cheap and accurate diagnostic tool is needed for the accuracy of indications for surfactant administration.

One of the diagnostic tools that is now recommended is lung ultrasound examination. Lung ultrasound examination is considered an economical, accurate and repeatable examination so it is said to be better than thoracic photo examination which is said to be the gold standard of RDS diagnosis and can be done for monitoring in critically and non-critically ill infants because it can be done bedside or next to the patient (12). another advantage of lung ultrasound examination is that it can be done quickly, easily, can be repeated, is not invasive and safe from radiation hazards, but one of the disadvantages is that there is still high variability between examiners and is subjective (13).

Lung ultrasound examination is a good predictor for evaluating increased oxygen demand as a marker of severity in RDS because there is a moderate correlation with Oxygen saturation index (p=0.52 (95% CI, 0.30-0.70) (14) and a significant correlation in the PaO2/FiO2 ratio (r=-0.55; 95% CI = -0.69 - -0.35; p<0.0001) (15). The use of scores from lung ultrasound as a predictor of surfactant administration differs depending on the lung area examined, a study by (16). stated that a score of > 7 in 6 lung areas gave 94% sensitivity and 60% specificity, while a study by (17). examining 6 lung areas showed that a score of more than 4 could predict the need for surfactant administration (96% sensitivity and 100% specificity). Until now, there are still limited studies in Indonesia that examine the relationship between lung ultrasound scores and increased oxygen demand as predictors of RDS severity in premature infants.

This study aims to analyze lung ultrasound (LUS) scores as a predictor of respiratory distress syndrome (RDS) severity in premature infants. Specifically, the study aims to: (1) analyze LUS scores as a predictor of RDS severity, (2) evaluate the relationship between LUS scores and Downes Scores in infants using CPAP, and (3) analyze the relationship between LUS scores and the Oxygen Saturation Index (OSI) in infants using NIPPV and mechanical ventilators.

Research Methodology

This cross-sectional observational analytical study examines the association between elevated oxygen requirements and lung ultrasound (LUS) scores, which are markers of the severity of respiratory distress syndrome (RDS) in premature infants. Research on vulnerable groups, such as premature infants with a gestational age of ≤34 weeks and a birth weight of ≤2500 grams, will be carried out in the NICU emergency room of Dr. Soetomo Hospital in Surabaya.

Inclusion and Exclusion Criteria

Infants diagnosed with RDS, those with a gestational age of ≤34 weeks, those weighing ≤2500 grams at birth, and those on mechanical ventilation or non-invasive ventilation support are all eligible to participate in the study. On the other hand, the exclusion criteria include infants with severe infections like sepsis, serious congenital abnormalities that impair respiratory function, parents who decline study participation, and infants who are unable to undergo lung ultrasonography because of life-threatening conditions like shock or severe hypothermia. Furthermore, for a variety of reasons, such as parental refusal or withdrawal from the study without medical consent, subjects may be excluded at the researcher's discretion.

Sample Size Calculation

The study's estimated sample size of 51 participants was calculated using a four-month sampling period from February 2024 to May 2024, an RDS incidence ratio of 23%, an absolute precision of 0.12, and a 95% confidence level.

Data Collection Instruments

Data will be collected using a number of important tools, including the Oxygen Saturation Index (OSI), RDS intensity as shown by chest X-rays, and LUS scores. A 15 MHz micro linear probe will be used in the Philips Epic device used for the ultrasound evaluation. Assessments conducted longitudinally throughout the anterior and lateral lung regions will be the main focus of the LUS evaluation.

Ethical Considerations and Informed Consent

Prior to participation, informed consent will be obtained from the parents or guardians of the infants. Ethical permission will also be secured from the Health Research Ethics Committee of Dr. Soetomo Hospital. Comprehensive explanations of the study, including any associated risks and benefits, will be provided to the parents/guardians, ensuring a clear understanding before consent is documented.

Data monitoring and Analysis

Initial LUS scores will be assessed within a few hours post-birth, followed by chest X-ray examinations and OSI measurements. Continuous monitoring of LUS and oxygen saturation levels will also be conducted. Data collection will be thorough, leveraging NICU documentation and personal assessments, and recorded utilizing standardized forms.

Descriptive analyses will be employed to characterize the sample and evaluate the incidence of RDS, utilizing frequency distributions and cross-tabulation tables. To assess the relationship between the variables, Spearman's correlation test will be utilized, enabling comprehensive analysis of the data collected.

Study Objectives

The main objective of this research is to scrutinize the relationship between LUS scores and increased oxygen requirements, functioning as indicators of RDS severity. This analysis is aimed at yielding valuable insights into the utility of LUS as a clinical tool for assessing the severity of RDS in premature infants, thereby potentially enhancing clinical decision-making processes.

Research Results

Sample characteristics

This study will be conducted in the NICU Emergency Room of RSUD Dr. Soetomo, Surabaya, from March 4, 2024, to July 18, 2024. A total of 51 subjects meeting the inclusion and exclusion criteria will participate in the study until completion.

Based on the analysis presented in Table 1, the demographic characteristics of the research subjects

Table 1. Characteristics of research subjects based on demographic data.

Characteristic	Category	Total	Percentage
Gender	Male	19	37,3
	Female	32	62,7
Delivery Method	C-Section	49	96,1
	Spontaneous	2	3,9
Gestational Age (weeks)	31,3 mgg		
Birth Weight	BW < 1000 g	8	15,7
	BW 1000-1499 g	20	39,2
	BW 1500 – 2500 g	23	45,1
Birth Weight Classification	Small for gestational age (SGA)	14	27,5
	Appropriate for Gestational Age (AGA)	37	72,5
	Large for Gestational Age (LGA)	0	0
Lung Maturation	Not given	20	39,2
	Once	11	21,6
	Twice or more	20	39,2
Apgar Score (mean)	1st Minute	4,37 (± 1,854)	
	5th Minute	5,96 (± 1,766)	
Surfactant	Given	13	25,5
	Not given	38	74,5
RDS Degree Based on Chest X-ray	No RDS	21	41,2
	Degree 1	20	39,2
	Degree 2	8	15,7
	Degree 3	2	3,7
	Degree 4	0	0
Initial Oxygenation	CPAP	33	64,7
	NIPPV / NIV	8	15,7
	Mechanical Ventilation	10	19,6

Source: Prepared by the author (2024).

show notable differences in proportions, such as the predominance of female subjects (62.7%) and the high rate of cesarean section deliveries (96.1%). The average gestational age of the subjects was 31.3 weeks, indicating a premature birth group. In terms of birth weight distribution, the category between 1500 g and 2499 g was the most dominant, with 23 subjects (45.1%), followed by 20 subjects (39.2%) weighing between 1000 g and 1499 g, and 9 subjects (15.7%) weighing less than 1000 g.

When classified by birth weight, the majority of subjects, 37 (72.5%), were born appropriate for gestational age (AGA), while 14 subjects (27.5%) were small for gestational age (SGA).

Regarding antenatal corticosteroid administration for lung maturation, 20 subjects (39.2%) had not received this treatment, while others had received it twice or more. In terms of early respiratory support, the majority of subjects (64.7%) started treatment with Continuous Positive Airway Pressure (CPAP).

Table 2. Normality test of lung ultrasound score with RDS severity from thoracic photographs.

Ultrasound Score	RDS Degree	Kolmogorov-Smirnov			Shapiro-Wilk		
0 – 3 hours		Statistic	df	Sig.	Statistic	df	Sig.
	,00	,147	21	,200*	,940	21	,223
	1,00	,181	20	,087	,938	20	,219
	2,00	,227	8	,200*	,906	8	,326
	3,00	,260	2				
12 – 24 hours	,179	21	,076	,858	21	,006	,179
	,155	20	,200*	,900	20	,042	,155
	,215	8	,200*	,941	8	,618	,215
	,260	2					,260

Source: Prepared by the author (2024).

Meanwhile, 10 subjects (19.6%) required mechanical ventilation, and 8 subjects (15.7%) used Non-Invasive Positive Pressure Ventilation (NIPPV). Most subjects (74.5%) did not receive surfactant after birth, compared to 13 subjects (25.5%) who did. The average Apgar score at the first minute was 4.37 (±1.854), indicating that the infants might need further medical attention. At the fifth minute, the Apgar score increased to 5.96 (±1.766), improving the infants' condition.

Regarding the proportion of RDS (Respiratory Distress Syndrome) severity based on chest X-ray, the majority of subjects did not have RDS (41.2%), while 39.2% had RDS degree 1, 15.7% had RDS degree 2, and 3.9% had RDS degree 3.

Relationship between lung ultrasound score and RDS severity based on chest X-ray

Table 2 shows the normality test of lung ultrasound scores and RDS severity based on chest X-rays, and the data for the USG score at 0-3 hours follow a normal distribution according to both tests.

Following the normality test, an ANOVA analysis was performed on the total USG score at 0-3 hours and 12-24 hours to determine the agreement of RDS severity diagnosis based on chest X-rays.

Based on the ANOVA analysis, there is no sufficient evidence to state that there is a significant difference in RDS severity diagnosis based on chest X-rays (Table 3).

To determine the relationship between the total score of ultrasounds which is categorically classified into mild category (total score 0-6), moderate category (total score 7-12) and severe category (total score 13-18) with RDS severity based on thoracic photos using the Spearman Rank test.

The results of the Spearman Rank correlation analysis between the total categorized ultrasound (USG) score show a significant positive correlation between the USG score at 12–24 hours and the RDS diagnosis, with a correlation coefficient of 0.307 and a p-value of 0.029 (Table 4).

Relationship between lung ultrasound score and downes score

The normality test between the 0-3 hour and 12-24 hour ultrasound scores and the Downes score shows a significance value of less than 0.05 so that the null hypothesis of normality can be rejected, which means that the data does not follow a normal distribution, while the Kolmogorov-Smirnov test result is 0.150 and the Shapiro-Wilk test is 0.935 which supports the conclusion of non-normality. Based on data that is not normally distributed, Spearman's correlation will be used (Table 5).

The correlation test between ultrasound score at 0-3 hours and Downes Score (Table 6) showed a weak correlation coefficient of 0.145, which was not statistically significant (p=0.308). This indicates that in this

Table 3. ANOVA Test of lung ultrasound score with RDS severity from thoracic photographs.

Anova	Sum of Squares		df		Mean Square		F		Sig.	
	0 – 3 hours	12–24 hours	0–3 hours	12–24 hours	0 – 3 hours	12 – 24 hours	0–3 hours	12–24 hours	0–3 hours	12–24 hours
Between Groups	45,743	49,277	3	2	15,248	24,639	,906	1,489	,445	,236
Within Groups	791,002	760,968	47	46	16,830	16,543				
Total	836,745	810,245	50	48						

Source: Prepared by the author (2024).

Table 4. Spearman Rank Test between categorical lung ultrasound score and degree of RDS from thoracic photographs.

Spearman Rank		Total Score Categorical		RDS Degree	
		0-3 hours	12-24 hours	0-3 hours	12-24 hours
Total Score Categorical	Correlation Coefficient	1.000	1.000	.022	.307*
	Sig. (2-tailed)	.	.	.880	.029
	N	51	51	51	51
RDS Degree	Correlation Coefficient	.022	.307*	1.000	1.000
	Sig. (2-tailed)	.880	.029	.	.
	N	51	51	51	51

Source: *Correlation is significant at the 0.05 level (2-tailed).

Table 5. Normality test of lung ultrasound score with Downes score.

Tests of Normality						
	Kolmogorov-Smirnova			Shapiro-Wilk		
	Statistic	df	Sig.	Statistic	df	Sig.
Downes Score Test 1	,150	51	,006	,935	51	,008
Downes Score Test 2	,265	51	,000	,840	51	,000

Source: Prepared by the author (2024).

Table 6. Spearman rank test of lung ultrasound score with Downes score.

Spearman Rank		Total Score		Downes Score	
		0-3 hours	12-24 hours	0-3 hours	12-24 hours
Total Score	Correlation Coefficient	1,000	1,000	,145	,355*
	Sig. (2-tailed)	.	.	,308	,011
	N	51	51	51	51
Downes Score	Correlation Coefficient	,145	,355*	1,000	1,000
	Sig. (2-tailed)	,308	,011	.	.
	N	51	51	51	51

Source: Prepared by the author (2024).

Table 7. Spearman rank test of lung ultrasound score with OSI value.

Spearman Rank		Total Score		OSI	
		0-3 hours	12-24 hours	0-3 hours	12-24 hours
Total Score	Correlation Coefficient	1.000	1.000	.483*	.045
	Sig. (2-tailed)	.	.	.049	.848
	N	51	51	17	21
OSI	Correlation Coefficient	.483*	.045	1.000	1.000
	Sig. (2-tailed)	.049	.848	.	.
	N	17	21	17	21

Source: Prepared by the author (2024).

early period, the changes detected by lung ultrasound are not associated with the measured Downes score.

As for the correlation test results between the Ultrasound Score at 12-24 hours and Downes Score, there was sufficient evidence of a significant relationship characterized by a moderate positive correlation coefficient of 0.355, which was also statistically significant (p=0.011).

Relationship between total USG score and Oxygen Saturation Index (OSI)

Spearman's correlation test between ultrasound score values at 0-3 hours and OSI (Oxygen Saturation Index) values in subjects using mechanical ventilation and NIV (Table 7) showed sufficient evidence with a moderate positive correlation with a correlation coefficient of 0.483, which was also statistically significant (p=0.049). However, in the 12-24 hour lung ultrasound examination, there was no significant correlation with OSI with a correlation coefficient of 0.045, which was also not statistically significant (p=0.848), indicating that the relationship was not aligned with the time of measurement.

Discussion

Characteristic

Based on the above study, it has been shown that there are significant differences in the gender distribution within the examined sample population. Specifically, the cumulative percentage of female subjects is 62.7% of the total sample size, clearly indicating dominance compared to males. Consequently, this difference may lead to substantial imbalances in how accurately the sample reflects the larger population being studied, raising concerns about potential bias in the research results and necessitating careful consideration of generalizing the findings to other contexts or populations. Furthermore, existing literature has established that gender significantly influences the incidence and severity of Respiratory Distress Syndrome (RDS) in premature infants, indicating that male premature infants have a relatively higher risk of developing RDS compared to female premature infants. This phenomenon is attributed to various factors, including slower lung development in male infants, which can result in inadequate surfactant production, essential for maintaining alveolar stability. Additionally, the presence of estrogen in females has been shown to accelerate lung maturation and surfactant production, further contributing to the observed differences in outcomes between genders (18). Finally, it is crucial to consider the impact of various genetic factors that may also significantly influence the differential vulnerability of male and female infants to disease severity.

Prematurity, or preterm birth, is the leading cause of infant morbidity and mortality worldwide, making its causes and prevention a long-standing challenge for both researchers and clinicians. According to the World Health Organization (WHO), preterm neonates are infants born before 37 weeks of gestation. There are several subcategories of prematurity based on gestational age, including extremely preterm (<28 weeks), very preterm (28 to <32 weeks), and moderate to late preterm (32 to <37 weeks. Prematurity can also be classified by birth weight into low birth weight (1,500–2,499 grams), very low birth weight (1,000–1,499 grams), and extremely low birth weight (<1,000 grams) (19).

The research also states that the average gestational age is 31.3 weeks, which falls into the very preterm category, where this group of gestational age often experiences RDS. The incidence of RDS decreases as gestational age increases. A total of 45.1% (23 subjects) weighed 1500-2499 grams, categorized as low birth weight (Low Birth Weight/LBW), and 72.5% (37 subjects) were born appropriate for gestational age (Appropriate for Gestational Age/AGA), indicating that although premature, most infants have a weight that corresponds to their gestational age. This suggests that the factors causing premature birth may not significantly affect intrauterine growth. Premature birth is an important factor in the incidence of respiratory distress syndrome (RDS) in neonates, with gestational age and birth conditions playing crucial roles.

RDS is the most common condition requiring admission of newborns to the Neonatal Intensive Care Unit (NICU). It is characterized by breathing difficulties immediately after birth due to lung immaturity, which results in impaired gas exchange and acute lung damage (20). The severity of symptoms depends on a combination of constitutional, genetic, and environmental factors influencing treatment. Current risk factors have diminished due to improved prenatal care for preterm births, pharmacological interventions for fetal lung maturation, and early management at birth.

Infants born at a gestational age of less than 28 weeks have a high incidence of RDS due to their underdeveloped lungs. A study from West Java found that RDS was observed in 64.68% of premature infants, with the highest incidence (81%) in those born between 28 and 32 weeks (21). The incidence of RDS decreases as gestational age increases. For instance, infants born at 34 weeks have a higher rate of RDS (15%) compared to those born at 35-36 weeks (4%). There is a correlation between lung ultrasound scores and increased oxygen requirements as an indicator of RDS severity in premature infants.

In the context of early respiratory support for patients at risk of respiratory failure, Continuous Positive Airway Pressure (CPAP) emerged as the most frequently used treatment modality for 33 subjects (64.7%). This highlights the important role of CPAP in managing respiratory disorders, as maintaining airway patency and adequate ventilation is crucial. CPAP has proven effective in reducing respiratory failure and mortality rates, particularly in premature infants with respiratory distress syndrome, demonstrating its broad application across various patient populations (22). Conversely, mechanical ventilation was necessary for 10 subjects (19.6%), reflecting the more severe clinical conditions of these subjects, making non-invasive oxygenation unfeasible. Mechanical ventilation is often required in cases of acute respiratory failure, where respiratory mechanics are vital for patient management. Timely use of mechanical ventilation can significantly reduce morbidity in patients at risk of damage, emphasizing the need for careful assessment and early intervention. Additionally, 8 subjects (15.7%) received Non-Invasive Positive Pressure Ventilation (NIPPV), serving as an alternative for patients with severe clinical conditions who do not yet require invasive support. NIPPV has gained recognition for its effectiveness in treating acute respiratory failure, especially when initiated early; its use can improve patient outcomes by providing ventilation support without the complications associated with invasive procedures, making it a valuable option in respiratory management. The integration of these various forms of respiratory support illustrates a stepped approach to managing respiratory failure, with the provision of CPAP as the first line of defense, transitioning to mechanical ventilation or NIPPV guided by the patient's clinical status and response to initial care (23).

The diagnosis of Respiratory Distress Syndrome (RDS) in premature infants is significantly informed by chest imaging, particularly chest radiography. Key findings in these images include bilateral fine granular opacities, hypo-aeration, and air bronchograms, which are indicative of RDS. In severe cases, total opacity of both lung fields may be observed as the main radiological marker for the condition (24). Additionally, interstitial edema is often noted in chest examinations, present in 50% of moderate cases and 14 out of 18 severe cases. These abnormalities, along with hypervascularization, play a key role in the diagnostic process, reflecting the underlying pathophysiology of surfactant deficiency, which is the main cause of RDS. This correlation is critical when interpreting chest images, as the findings can vary significantly based on the infant's gestational age. For instance, the degree of hypo-aeration and opacity may indicate the urgency of the intervention required, particularly in the context of surfactant replacement therapy, which has been shown to improve lung function and reduce mortality in affected newborns. Moreover, clinical signs of RDS, such as increased respiratory rate, grunting, nasal flaring, and cyanosis, often accompany radiological findings (25). These clinical indicators, combined with imaging results, provide a comprehensive view of the infant's respiratory status, aiding in timely and effective management.

Chest X-rays remain the standard for diagnosing RDS in neonates because they provide detailed images that help identify characteristic RDS patterns, such as hypo-inflation, diffuse granularity, and air bronchograms (26). Despite its usefulness, chest X-rays expose infants to radiation, which may have long-term negative effects. Therefore, while essential, there is a push to find alternative methods that reduce radiation exposure (27). Chest radiography has limitations in sensitivity and specificity. For RDS, sensitivity is reported at 35% and specificity at 82%, indicating a significant risk of misdiagnosis (28). Radiographic patterns can vary significantly, and atypical presentations may lead to misdiagnosis, such as surfactant administration producing non-typical RDS radiographic patterns, complicating the diagnosis (29). Interpreting neonatal chest radiographs requires specialized expertise and experience, which may not always be available in all healthcare facilities. Factors such as infant positioning, imaging techniques, and image quality can also affect diagnostic accuracy. Given these limitations, there is a need to develop more accurate and safer diagnostic methods for detecting RDS in newborns.

The use of ultrasound in clinical medicine has been known for over 20 years and is referred to as Point-of-Care Ultrasonography (POCUS). It initially began with adult patients and has since been applied to critically ill pediatric and neonatal populations (30). POCUS refers to the use of ultrasound equipment within the treatment space by clinicians, other than radiologists or cardiologists, to assist with medical procedures and assess patients quickly to identify pathological processes for resuscitation and life-saving interventions.

POCUS is not intended to replace radiologists or cardiologists but to answer clinical questions and assist in management through serial examinations, monitoring disease progression, and evaluating responses to treatment quickly and efficiently (31).

Previous studies have demonstrated the effectiveness of lung ultrasound scores in diagnosing and predicting the severity of respiratory distress syndrome (RDS) in various neonatal populations. For instance, research has shown that lung ultrasound can accurately predict the need for surfactant therapy and correlate with clinical parameters like oxygenation indices. Moreover, comparisons with traditional radiological methods, such as chest X-rays, have highlighted the potential of lung ultrasound as a reliable, radiation-free alternative.

However, earlier studies have several limitations. Many had small sample sizes, affecting the generalizability of their findings. Additionally, the lack of standardized protocols for performing and interpreting lung ultrasound has led to inconsistent results. Most studies focused on specific populations, leaving gaps in knowledge for other gestational age ranges.

Notably, there is a scarcity of research conducted in Indonesia and similar developing countries, which may impact the applicability of findings in these regions. Furthermore, the existing resear lacks sufficient focus on the temporal aspects of measurements, such as the relationship between the timing of ultrasound assessments and the incidence or severity of RDS.

This study aims to address these gaps in the literature by examining the effectiveness of lung ultrasound scores in predicting RDS severity in a specific population and exploring the impact of timing on ultrasound assessments. The need for ongoing research in this domain is emphasized, as while lung ultrasound shows promise, there are still unanswered questions regarding its implementation and effectiveness across diverse clinical settings.

Results from the Analysis of Variance (ANOVA) test on the relationship between lung ultrasound scores and RDS severity showed an F value of 0.906 and a probability (p-value) of 0.445 at the 0–3-hour age test, indicating no significant difference between groups during that period. Similarly, lung ultrasound scores at 12-24 hours produced an F value of 1.489 and a probability (p-value) of 0.236, also showing no significant difference during that period. The above analysis does not demonstrate statistical significance, indicating several things: the observed differences between the groups during both periods are most likely due to chance or random variation and not due to treatment effects; there is insufficient statistical evidence to reject the null hypothesis; the treatment does not have a large enough effect to be statistically detected. This could be due to the need for a larger sample size and suggests important variability within the system, necessitating further research with a stronger design and larger sample size.

The use of lung ultrasound scores generally shows a significant correlation with the oxygenation status of premature infants with RDS. Additionally, this tool is useful for predicting the development of bronchopulmonary dysplasia (32). The lung ultrasound score also demonstrates high sensitivity (98%) and specificity (92%) for detecting pulmonary manifestations of RDS in premature infants, making it a reliable alternative for diagnosis and monitoring treatment responses (33). Although the lung ultrasound score provides significant advantages in assessing the severity of RDS, it cannot fully replace conventional radiology. Instead, this method serves as a complementary tool that reduces radiation exposure and provides a rapid assessment of the patient's clinical condition. The accuracy of the lung ultrasound score in predicting surfactant needs and other interventions still requires further (34). A study in Australia mentioned that lung ultrasound scores cannot replace radiological examinations in measuring lung volumes but only provide a very weak correlation with the oxygenation status of premature infants (35). Although lung ultrasound scores have high diagnostic value and are safe from radiation, they have shortcomings such as high false positives due to artifacts and other lung abnormalities such as pneumonia and Transient Tachypnea of the Newborn (TTN). Additionally, the level of variability and standardization of the examination protocols also plays a role.

Nevertheless, lung ultrasound remains important in the initial evaluation of the lung condition of premature infants. This technique can provide real-time information about dynamic changes in the lungs and assist in monitoring disease progression. However, to obtain more accurate and comprehensive results, a combination of lung ultrasound and conventional radiological examinations may be necessary in managing premature infants with respiratory issues.

In the study, further analysis was conducted by categorizing the total lung ultrasound scores into three groups: mild, moderate, and severe, which were then analyzed using the Spearman Rank test. The results showed a weak relationship between the ultrasound score at 12-24 hours and the RDS diagnosis based on thoracic imaging, with a correlation coefficient of 0.307 and a p-value of 0.029. This indicates a moderate positive correlation when measuring the score at 12-24 hours; the higher the score, the greater the severity of RDS. The lack of significance in the results at 0-3 hours may be due to variations in physiological changes immediately after birth and the adaptation process, requiring more time to assess RDS severity with lung ultrasound. Additionally, the late onset of RDS symptoms, which may only be detectable after 12 hours, and the varying time intervals of thoracic examinations necessitate further research with uniform imaging timing and a narrow time frame of less than 5 hours with lung ultrasound. Therefore, clinicians are advised to carefully consider the optimal timing for lung ultrasound assessments in evaluating RDS in neonates. Although early monitoring remains important, comprehensive assessment and determination of RDS severity should be conducted during the 12-24 hour period post-birth to obtain a more accurate and informative picture, which in turn can aid in making more precise therapeutic decisions.

An analysis was conducted to examine the relationship between lung ultrasound scores at 0-3 hours and 12-24 hours with the Downes score. The analysis was performed using the Spearman correlation test, and the results indicated that the lung ultrasound score at 0-3 hours showed no significant correlation with the

Downes score, with a significance value of 0.308 and a low correlation coefficient (0.145). This suggests that the influencing factors tend to be independent or influenced by other unmeasured variables in this study. Meanwhile, the correlation between the total lung ultrasound score at 12-24 hours and the Downes score showed a significant positive correlation with a correlation coefficient of 0.355 and a significance value of 0.011. The strength of this relationship is categorized as moderate, indicating that increases in the total score are likely accompanied by increases in the Downes score or vice versa.

The difference in results between these two time periods may indicate dynamic changes in the influencing factors between the lung ultrasound score and the Downes score over time. The significance of the correlation during the 12-24 hour period suggests that the scores tend to move in the same direction. This has important implications in the context of research or clinical applications. The lung ultrasound examination during the 12-24 hour period may be more informative in assessing the severity of respiratory disturbances compared to the examination at 0-3 hours, due to the development of the disease's pathophysiology or the response to medical interventions occurring during that interval. Therefore, continuous monitoring using lung ultrasound and the Downes score can provide a more comprehensive view of the progressiveness of respiratory disturbances in patients.

The use of lung ultrasound scores for neonatal respiratory distress syndrome (RDS) is a valuable tool for diagnosing and managing the severity of the disease, while the Downes score is generally used to assess the severity of RDS in premature infants. The lung ultrasound score offers a more direct and accurate method for evaluating lung involvement. Lung ultrasound scores can assist in monitoring RDS progression, guiding treatment decisions, and potentially reducing the need for mechanical ventilation and surfactant therapy. Therefore, utilizing lung ultrasound scores alongside the Downes score can enhance overall assessment and management of RDS in premature infants (15). The relationship between lung ultrasound scores and the Downes score in premature infants with RDS is aligned; lung ultrasound scores assess lung aeration, correlating with surfactant activity and lung mechanics. While lung ultrasound can be reliable, it depends on the type of probe or the operator's skill and experience. It accurately evaluates lung function, reflecting the lung volume available for gas exchange, which is directly related to surfactant activity. Thus, lung ultrasound scores provide valuable insights into the lung status of premature infants with RDS (36). The use of lung ultrasound scores can also reduce the misdiagnosis of RDS by 30.1% compared to diagnoses based solely on thoracic imaging (37).

An analysis was conducted to examine the relationship between total lung ultrasound scores and the Oxygen Saturation Index (OSI) in infants receiving oxygen assistance with NIPPV or mechanical ventilation. The analysis was performed using the Spearman test to measure the strength and direction of the relationship between the two ranked variables, which are non-parametric and do not assume normal data distribution.

The Spearman test results between the lung ultrasound score at 0-3 hours and OSI, with a sample size of 17 subjects, showed a moderate positive correlation (0.483) and statistically significant (0.049), indicating a positive relationship between the lung ultrasound score and OSI at 0-3 hours. An increase in the total score tends to be followed by an increase in OSI values and vice versa. Meanwhile, the relationship between total lung ultrasound scores at 12-24 hours in 21 subjects with OSI did not show a significant correlation (0.848).

The significant relationship in the early period may reflect the initial clinical condition of premature infants with RDS, where total scores and OSI are closely correlated. The loss of correlation in the subsequent period may indicate other influencing factors such as medical interventions or the development of the infant's clinical condition. Thus, further analysis is needed to identify factors causing changes in the relationship between total scores and OSI from the initial to the subsequent period. Additionally, advanced statistical methods such as longitudinal regression analysis should be considered to evaluate changes in relationships between variables over time. The small sample size should also be considered for further research to enhance the reliability of results in this analysis.

The non-invasive measurement of OSI has clinically proven to have a positive correlation with the Oxygenation Index (OI) in neonates with respiratory distress and can be used to monitor lung disease severity and prevent occurrences of sepsis and iatrogenic anemia (38). A large cohort study showed that non-invasive OSI values could serve as a reliable substitute for OI (39). An OSI value with a cutoff > 8 has a sensitivity of 100% and specificity of 98% for predicting neonates with severe respiratory failure (40). The ideal time for OSI examination is <72 hours, considering factors such as the infant's clinical condition and the early phase of respiratory failure, while the provision of oxygen assistance such as CPAP and surfactant administration will affect OSI values (41, 42). This may explain why the lung ultrasound score at 12-24 hours was not significant with OSI values due to changes in clinical conditions and management of infants with RDS (41). Further research with a larger sample size and a longer observation period may provide deeper insights into the relationship between lung ultrasound scores and OSI in premature infants with RDS. Additionally, other factors that may influence OSI values, such as the type and intensity of medical interventions administered during treatment, should be considered. More comprehensive multivariate analyses may also help identify other contributing variables affecting changes in OSI values and lung ultrasound scores in premature infants with RDS.

This research is related to lung ultrasonography scores and their correlation with the severity level of RDS, consistent with previous studies that highlight the effectiveness of lung ultrasonography as a diagnostic tool for neonatal respiratory distress syndrome (RDS) (33). However, the findings of this research, such as the lack of significant correlation in the 0-3 hour period, differ from other studies that suggest that early ultrasonography assessment may be more predictive of the severity of RDS (34). This discrepancy may be attributed to variations in sample size, assessment timing, or methodological differences, highlighting the need for standardized protocols in the use of lung ultrasonography.

Furthermore, it is imperative to acknowledge the presence of confounding variables that may impact outcomes, such as gestational age variability, birth weight, and timing of medical interventions like CPAP or surfactant therapy (22,40). These factors can influence an infant's response to treatment, which in turn impacts the observed lung ultrasonography scores and oxygen saturation index (OSI). The limitations of this study, including a small sample size and lack of long-term follow-up, also need to be addressed to provide a clearer understanding of the reliability and applicability of these findings. A more comprehensive multivariate analysis with a larger cohort is required to confirm these results and explore the broader implementation of lung ultrasonography in the management of RDS in various clinical settings (39,42).

This study is subject to certain limitations, particularly the small sample size of 51 subjects, which inhibits the ability to generalize findings. There is a need for validation of the LUS score threshold and the development of practical guidelines, especially for facilities with limited resources. It is recommended to conduct a multi-center study with a larger sample size to improve diagnostic accuracy and reduce interpretational errors. Strengthening these methodologies is expected to enhance the role of LUS in managing RDS in premature infants.

Conclusion

Research shows that there is a moderate positive correlation between the ultrasound score at 12-24 hours post-birth and the severity of RDS, as measured through chest X-rays. However, a significant correlation was not found during the initial examination (0-3 hours). This is suspected to be due to physiological changes immediately after birth, assessing RDS severity more accurate after 12 hours.

The correlation between lung ultrasound scores at 12-24 hours and the Downes Score shows a significant relationship, while the examination at 0-3 hours does not show a significant correlation. This indicates that assessments at 12-24 hours are more informative in evaluating the severity of RDS compared to the early period.

This research has effectively demonstrated a strong positive relationship between lung ultrasonography scores and the degree of respiratory distress syndrome (RDS) in premature infants, highlighting the significance of evaluations carried out 12 to 24 hours postpartum. Significant clinical ramifications result from these findings, indicating that routine lung ultrasonography evaluations beyond the first few hours after delivery may offer important new information on the development of RDS. Clinicians may be better able to customize therapeutic interventions with this approach, which could lessen the need for more intrusive procedures like mechanical ventilation. In this susceptible population, prompt interventions that improve oxygenation and overall clinical outcomes can be facilitated by early and accurate evaluation of lung ultrasonography scores. Lung ultrasound scoring should be incorporated into clinical protocols for monitoring premature infants, as evidenced by the correlations found between the scores and recognized indicators of RDS severity. Lung ultrasound assessments may offer a non-invasive way to improve monitoring procedures and, consequently, promote better respiratory distress management when incorporated into routine clinical workflows. To confirm that lung ultrasonography scores can accurately predict outcomes in a variety of settings and populations, more multicenter research is necessary. This will help create a standardized method for using lung ultrasonography in neonatal care in addition to supporting our findings. Finally, our results highlight how important lung ultrasonography is for tracking RDS. Beyond the first 12 hours after delivery, ongoing evaluation is essential for the prompt identification and treatment of seriously impacted infants, improving the standard of care given to this susceptible population.

Ethics Committee: Not required as this study collected an anonymous questionnaire without any sensitive questions and the manuscript does not include details, images, or videos related to patients.

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References

1. Wulandari RD, Laksono AD, Matahari R. Policy to decrease low birth weight in Indonesia: who should be the target? Nutrients. 2023;15(2):465. doi: 10.3390/nu15020465
2. Ledinger D, Nußbaumer-Streit B, Gartlehner G. WHO-Leitlinie: Versorgung von Frühgeborenen und Neugeborenen mit niedrigem Geburtsgewicht. Dtsch Gesundheitswes. 2024;86(4):289-93. doi: 10.1055/a-2251-5686.
3. Kemenkes RI. Profil Kesehatan Indonesia 2021. Jakarta: Pusdatin Kemenkes; 2022. Available from: https://repository.kemkes.go.id/book/828.
4. G B, F G, S N, et al. Indonesia Demographic and Health Survey 2017: adolescent reproductive health. Key indicators report. Iran J Pediatr. 2018;27(5). doi: 10.5812/ijp.11523
5. Pholanun N, Srisatidnarakul B, Longo J. The incidence and factors predicting survival among preterm infants with respiratory distress syndrome admitted to neonatal intensive care unit. J Ners. 2022;17(2):138-43. https://doi.org/10.20473/jn.v17i2.36860.
6. Dyer J. Neonatal respiratory distress syndrome: tackling a worldwide problem. P T. 2019;44(1):12-4. Available from: https://pmc.ncbi.nlm.nih.gov/articles/PMC6336202/
7. Thébaud B, Goss KN, Laughon M, et al. Bronchopulmonary dysplasia. Nat Rev Dis Primers. 2019;5(1):78. doi: 10.1038/s41572-019-0127-7
8. Yadav S, Lee B, Kamity R. Neonatal respiratory distress syndrome. [Internet]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK560779/
9. Widiastari EF, Graha WA, Pardede M. Lung bullae due to septic pulmonary embolism in a 4-year-old child: a case report. Comorbid Orthop Illn Details. 2022;1(3):15-20. doi: 10.55047/comorbid.v1i3.355.
10. Sweet DG, Carnielli VP, Greisen G, et al. European consensus guidelines on the management of respiratory distress syndrome: 2022 update. Neonatology. 2023;120(1):3-23. doi: 10.1159/000528914.
11. Chen IL, Chen HL. New developments in neonatal respiratory management. Pediatr Neonatol. 2022;63(4):341-7. doi: 10.1016/j.pedneo.2022.02.002.
12. Ferdian H, Wahid DI, Samad S, Wardani AE, Alam GS, Moelyo AG. Lung ultrasound in diagnosing neonatal respiratory distress syndrome: a meta-analysis. Paediatr Indones. 2019;59(6):340-8. doi: 10.14238/pi59.6.2019.340-8.

13. Norman M, Jonsson B, Wallström L, Sindelar R. Respiratory support of infants born at 22-24 weeks of gestational age. Semin Fetal Neonatal Med. 2022;27(2):101328. doi: 10.1016/j.siny.2022.101328.
14. Zong H, Huang Z, Zhao J, et al. The value of lung ultrasound score in neonatology. Front Pediatr. 2022;10:791664. doi: 10.3389/fped.2022.791664
15. Sett A, Rogerson SR, Foo GWC, et al. Estimating preterm lung volume: a comparison of lung ultrasound, chest radiography, and oxygenation. J Pediatr. 2023;259:113437. doi: 10.1016/j.jpeds.2023.113437
16. Raimondi F, Migliaro F, Corsini I, et al. Neonatal lung ultrasound and surfactant administration. Chest. 2021;160(6): 2178-86. doi: 10.1016/j.chest.2021.06.076.
17. Perri A, Fattore S, D'Andrea V, et al. Lowering of the neonatal lung ultrasonography score after nCPAP positioning in neonates over 32 weeks of gestational age with neonatal respiratory distress. Diagnostics (Basel). 2022;12(8):1909. doi: 10.3390/diagnostics12081909.
18. Stewart DL, Elsayed Y, Fraga MV, et al. Use of point-of-care ultrasonography in the NICU for diagnostic and procedural purposes. Pediatrics. 2022;150(6):e2022060053. doi: 10.1542/peds.2022-060053.
19. Vardar G, Karadag N, Karatekin G. The role of lung ultrasound as an early diagnostic tool for need of surfactant therapy in preterm infants with respiratory distress syndrome. Am J Perinatol. 2020;38(14):1547-56. https://doi.org/10.1055/s-0040-1714207.
20. Basso O, Wilcox A. Mortality risk among preterm babies. Epidemiology. 2010;21(4):521-7. doi: 10.1097/ede.0b013e3181debe5e.
21. Liu J, Yang N, Liu Y. High-risk factors of respiratory distress syndrome in term neonates: a retrospective case-control study. Balkan Med J. 2014;33(1):64-8. https://doi.org/10.5152/balkanmedj.2014.8733.
22. Permana I, Judistiani RTD, Bakhtiar B, Alia A, Yuniati T, Setiabudiawan B. Incidence of respiratory distress syndrome and its associated factors among preterm neonates: study from West Java tertiary hospital. Int J Trop Vet Biomed Res. 2022;7(1). doi: 10.21157/ijtvbr.v7i1.27043.
23. Urs PS, Khan F, Maiya PP. Bubble CPAP - a primary respiratory support for respiratory distress syndrome in newborns. Med J Armed Forces India. 2009;65(5):409-11. https://pubmed.ncbi.nlm.nih.gov/19179737.
24. Gorman EA, O'Kane CM, McAuley DF. Acute respiratory distress syndrome in adults: diagnosis, outcomes, long-term sequelae, and management. Lancet. 2022;400(10358): 1157-70. doi: 10.1016/s0140-6736(22)01439-8.
25. Liszewski MC, Stanescu AL, Phillips GS, Lee EY. Respiratory distress in neonates. Radiol Clin North Am. 2017;55(4): 629-44. doi: 10.1016/j.rcl.2017.02.006.
26. Marzani AB, Hartono ARS, Monalisa C, et al. Hyaline membrane disease in preterm newborn. Med Clin Updat. 2022;1(1):44-5. doi: 10.58376/mcu.v1i1.14.
27. Zerbarani WO. Perbandingan antara Foto Thorax dan Ultrasonografi Thorax dengan Gambaran Klinis pada Pasien Hyaline Membrane Disease [thesis]. Makassar: Universitas Hasanuddin; 2022. Available from: https://repository.unhas.ac.id/id/eprint/22848/2/C125172005_tesis_20-06-2022%201-2.pdf.
28. Hiles M, Culpan AM, Watts C, Munyombwe T, Wolstenhulme S. Neonatal respiratory distress syndrome: chest X-ray or lung ultrasound? A systematic review. Ultrasound. 2017;25(2): 80-91. doi: 10.1177/1742271x16689374.
29. Dr Mz, Dr Nsm, Dr Ah, et al. Evaluation of oxygenation index compared with oxygen saturation index among neonates admitted to the NICU. Acta Med Iran. 2021;59(6). doi: 10.18502/acta.v59i6.6896.
30. Buonocore G, Bracci R, Weindling M. Neonatology. Cham: Springer; 2018. doi: 10.1007/978-3-319-29489-6.
31. Elsayed Y, Wahab MGA, Mohamed A, et al. Point-of-care ultrasound (POCUS) protocol for systematic assessment of the crashing neonate—expert consensus statement of the international crashing neonate working group. Eur J Pediatr. 2022;182(1):53-66. doi: 10.1007/s00431-022-04636-z.
32. Dumpa V, Avulakunta I, Bhandari V. Respiratory management in the premature neonate. Expert Rev Respir Med. 2023;17(2):155-70. doi: 10.1080/17476348.2023.2183843.
33. Raimondi F, Yousef N, Migliaro F, et al. Point-of-care lung ultrasound in neonatology: classification into descriptive and functional applications. Pediatr Res. 2018;90(3):524-31. doi: 10.1038/s41390-018-0114-9.
34. El-Malah HEDGM, Hany S, Mahmoud MK, Ali AM. Lung ultrasonography in evaluation of neonatal respiratory distress syndrome. Egypt J Radiol Nucl Med. 2015;46(2): 469-74. doi: 10.1016/j.ejrnm.2015.01.005.
35. De Martino L, Yousef N, Ben-Ammar R, et al. Lung ultrasound score predicts surfactant need in extremely preterm neonates. Pediatrics. 2018;142(3):e20180463. https://doi.org/10.1542/peds.2018-0463.
36. Liu J. Ultrasound diagnosis and grading criteria of neonatal respiratory distress syndrome. J Matern Fetal Neonatal Med. 2023;36(1). doi: 10.1080/14767058.2023.2206943.
37. De Luca D, Ojembarrena AA, Raimondi F. Scientific evidence is the only common ground for the debate on neonatal lung ultrasound. Neonatology. 2023;120(3):402-3. doi: 10.1159/000530023.
38. Fernández S. Basic notions of lung ultrasound in neonatology. Arch Argent Pediatr. 2022;120(6):e246. https://doi.org/10.5546/aap.2022.eng.e246.
39. Ashwini K, Badiger S, S ST. Utility of oxygen saturation index (OSI) over oxygenation index (OI) in monitoring of neonates with respiratory diseases. Res Sq [Preprint]. 2024. doi: 10.21203/rs.3.rs-3880807/v1.
40. Muniraman HK, Song AY, Ramanathan R, et al. Evaluation of oxygen saturation index compared with oxygenation index in neonates with hypoxemic respiratory failure. JAMA Netw Open. 2019;2(3):e191179. doi: 10.1001/jamanetworkopen.2019.1179.
41. Tana M, Tirone C, Aurilia C, et al. Respiratory management of the preterm infant: supporting evidence-based

practice at the bedside. Children (Basel). 2023;10(3):535. doi: 10.3390/children10030535.
42. Khalesi N, Choobdar FA, Khorasani M, Sarvi F, Aski BH, Khodadost M. Accuracy of oxygen saturation index in determining the severity of respiratory failure among preterm infants with respiratory distress syndrome. J Matern Fetal Neonatal Med. 2019;34(14):2334-9. doi: 10.1080/14767058.2019.1666363

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