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"Role of Lung Ultrasonography to Evaluate Surfactant Need in Preterm Neonates in Suez Canal District"

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Abstract:

Background

Respiratory distress syndrome (RDS) continues to represent a crucial problem for preterm neonates despite the new advancement in its management. Currently, management of RDS is mainly through using early continuous positive airway pressure (CPAP) in the management of preterm neonates since birth together with early selective administration of surfactant. Lung ultrasound (LUS), as a simple and non-invasive diagnostic technique with no exposure to ionizing radiation, can be used as a reliable diagnostic tool for diagnosis of neonatal respiratory distress syndrome with good sensitivity and specificity.

Aim

Assess the applicability of lung ultrasonography for early prediction of the surfactant need in preterm neonates ≤ 34 weeks treated with CPAP.

Patients /Methods

We studied 60 neonates ≤ 34 weeks treated with early CPAP; LUS was done in the first 2 hours of life. 16 neonates received surfactant therapy according to European guidelines 2019 update. We assess reliability of LUS score for prediction of surfactant treatment.

Results

The result of our study shows that in the group received surfactant the median LUS score was 10, While in the group didn't need surfactant therapy the median LUS score was 4. About reliability of LUS score for prediction of surfactant treatment. Our results showed that LUS score at a cut off value of ≥ 6 has a sensitivity of 93.8 % and specificity of 84.1 %. while Chest X ray score at a cut off value of ≥ 5 has a sensitivity of 81.3 % and specificity of 77.3 %.

Conclusion

LUS score is a useful tool in early prediction of need for surfactant administration in preterm neonates on CPAP.

Key words: Lung ultrasonography, respiratory distress syndrome, surfactant.

Introduction:

Respiratory distress syndrome (RDS) continues to represent a crucial problem for preterm neonates despite the new advancement in its management over the last years which leads to improved survival for extreme preterm neonates but with increased incidence of bronchopulmonary dysplasia [1].

Overall, incidence of RDS is affected by gestational age; occurring in about 45% of early and moderate preterm neonates (24-33 weeks), reduced to 4% in late preterm neonates (34-36 weeks) and less than 1% in full term neonates [2].

Management of prematures with RDS should begin even before their birth. Prenatal corticosteroids given to pregnant women who were expecting preterm birth improved survival and decreased the risk of RDS, necrotizing enterocolitis (NEC), and intraventricular hemorrhage. [3], also extremely preterm neonates should be born in centers with tertiary neonatal intensive care unit (NICU) to receive their initial neonatal care with better long term outcomes [4].

Early selective surfactant administration for preterm neonates with signs of RDS is very important, it improves the outcome and decrease risk for air leak syndromes, neonatal mortality and chronic lung diseases compared to delayed administration after worsening of RDS [5].

Lung ultrasound (LUS) can be used in diagnosis of RDS with high sensitivity and specificity, as reported in a literature review, about 97% and 91% respectively [6]. When lung consolidation, pleural line abnormalities, and either bilateral white lung or A-line disappearance are found at the same time, RDS can be diagnosed with 100% sensitivity and specificity [7]. It can also predict the need for surfactant [8–10].

LUS can be used in diagnosis of RDS complication with better detection, compared to Chest X-ray, of consolidation and sub-pleural atelectasis [11–13]. It can be used also in follow up and early assessment of the response to surfactant replacement therapy [11,14].

In this study we assessed the applicability of lung ultrasonography to evaluate the surfactant need in preterm neonates ≤ 34 weeks treated with early continuous positive airway pressure (CPAP) according to European guidelines 2019 update.

Methods:

This study is cross sectional analytic study on premature neonates ≤34 week admitted to Neonatal Intensive Care Unit (NICU) and treated on positive continuous airway pressure (CPAP) according to European guidelines 2019 update. Exclusion criteria includes congenital pneumonia, complex congenital malformations or chromosomal aberrations, meconium aspiration syndrome, congenital lung diseases, severe neonatal sepsis and septic shock and surfactant administration in delivery room as per European guidelines 2019 update [15]. We used convenience sampling. Sixty neonates admitted to the NICU in AL Salam Port said hospital and suez canal university hospital eligible for the study`s criteria between October 2020 and April 2022 were chosen.

In details, according to European guidelines 2019 update, preterm neonates who doesn't respond to bag& mask ventilation and require intubation received surfactant in the delivery room and excluded from the study. Spontaneously breathing preterm neonates were stabilized with early CPAP of 6 cm H_2O. LUS was done in the first 2 hours of life. Surfactant was administered whenever fraction of inspired oxygen (Fio_2) requirements exceeds 0.30 through INSURE technique [intubate-surfactant-extubate] [15].

A high-resolution linear transducer with a frequency of 9 MHz was used in this study. The images were obtained using GE LOGIQ e linear probe 9L. LUS was performed by a single performer (neonatologist trained on neonatal LUS and had 3 months of hands-on experience under supervision before the study) within the first 2 hours of admission before surfactant administration. While in a quiet state, neonates are positioned in a supine and lateral position, each lung was divided into 3 areas (anterior, lateral, posterior). When using the LUS approach, the anterior lung area was examined between the sternum and the anterior axillary line, the lateral lung area was examined between the anterior and posterior axillary lines, and the posterior lung area was examined between the posterior axillary line and the spine. In the supine position, the anterior and lateral lung areas were assessed, and the posterior lung areas were examined in the lateral decubitus positions. (0-3) point score was given for each lung area (total score ranging from (0-18) in both lungs).

The result of lung ultrasound was masked to clinicians who decided whether to use surfactant or not and the LUS performer wasn't involved in decision-making in treating the preterm neonates. In the neonates who received surfactant replacement therapy, another LUS assessment was done within 2 hours after surfactant administration.

The LUS score was modified from a score proposed for adult patients [16]. It was used in a previous study on neonates to evaluate surfactant need, it includes the full spectrum of possible conditions; normal lung aeration, interstitial pattern, alveolar pattern and consolidation [17–19].

In details, LUS is designed as follows:

- 0 score for A-pattern (indicates presence of A lines only).
- 1 score for B-pattern (indicates presence of ≥ 3 well-spaced B-lines).
- 2 score for severe B-pattern (indicates presence of crowded and coalesced B-lines with or without subpleural consolidations).
- 3 score for extended consolidations.

the chest x ray score (0-8 points), which was adapted from [20] (0 = normal radiolucent lung fields with sharp cardiac and diaphragmatic margins; 1 = slightly reduced radiolucency with still sharp cardiac and diaphragmatic margins; 2 = noticeably reduced radiolucency with retained cardiac and diaphragmatic margins; 3 = significantly reduced radiolucency with air bronchogram and blurred cardiac and diaphragmatic margins; 4 = nearly completely white lung fields with or without air bronchogram. [17,20]

The statistical package for social science (SPSS) for Windows version 25 was used for the statistical analysis. The computer statistical package was used to enter the collected, coded data.

Approval from the research ethics committee in faculty of medicine Port said university was obtained in May 2020. Administrative permissions were requested from the hospitals in which the study was performed. Informed consent was obtained from the parents.

Results:

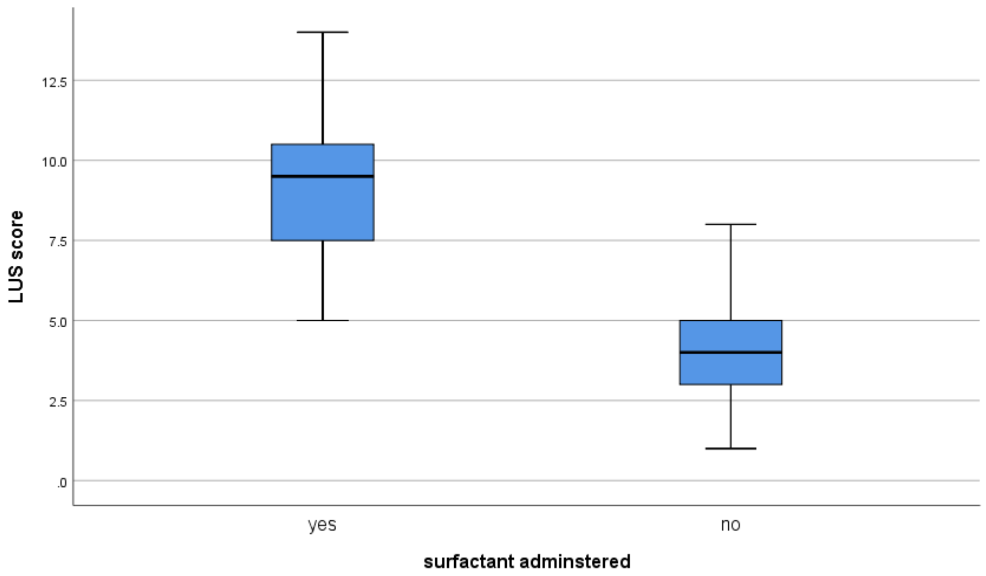

Figure 1: shows the median value, 25th percentile, 75th percentile, upper and lower limit of LUS score in the different groups whether received surfactant or not.

In the group received surfactant the median LUS score was 10. 7 and 11, respectively, were the 25th and 75th percentiles. The median LUS score for the group, which did not require surfactant therapy, was 4, while the 25th and 75th percentiles were 3 and 5, respectively.

Table 1: shows difference in LUS score mean value, standard deviation and range between

	Lung ultrasonography score		
	Mean ± standard deviation	Range	P-value
NO surfactant	4 ± 2	(1 - 8)	
One dose of surfactant	8 ± 2	(5 – 10)	<0.001*
Two doses of surfactant	11 ± 2	(9 – 14)	

groups.

* Significant statistically at p<0.05

The mean was highest in the neonates needed 2 doses of surfactant followed by these needed one dose of surfactant and it was lowest in neonates didn't need surfactant. (P value ≤ 0.001)

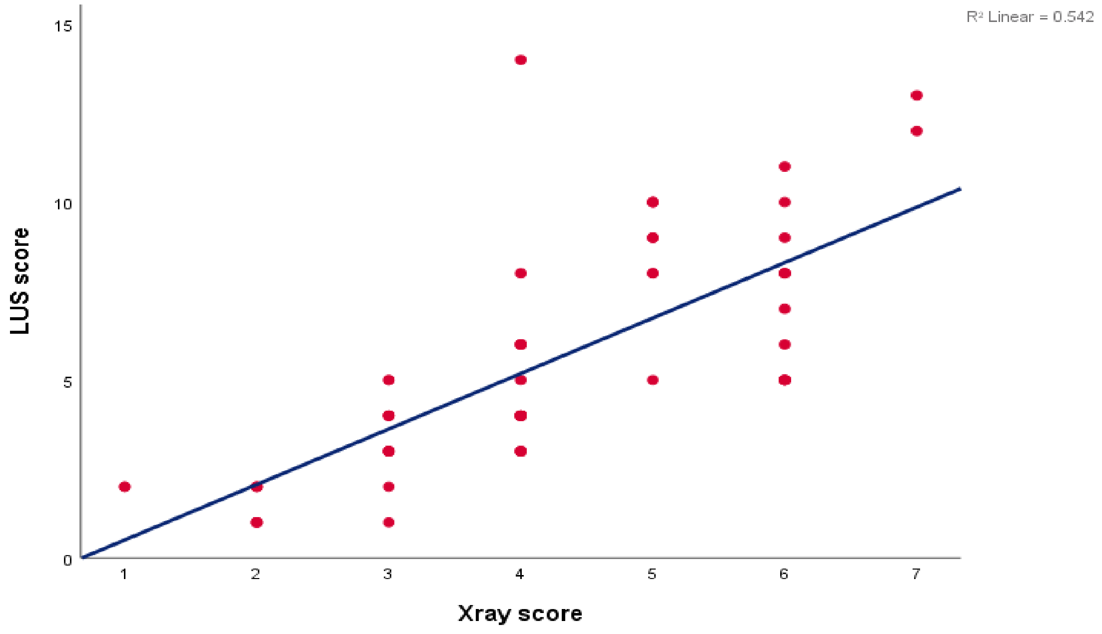

Figure 2: Scatter plot shows correlation between chest x ray score and LUS score.

This figure shows the strong positive Correlation (r = 0.736) between chest x ray score and LUS score. correlation is statistically significant (P=<0.001).

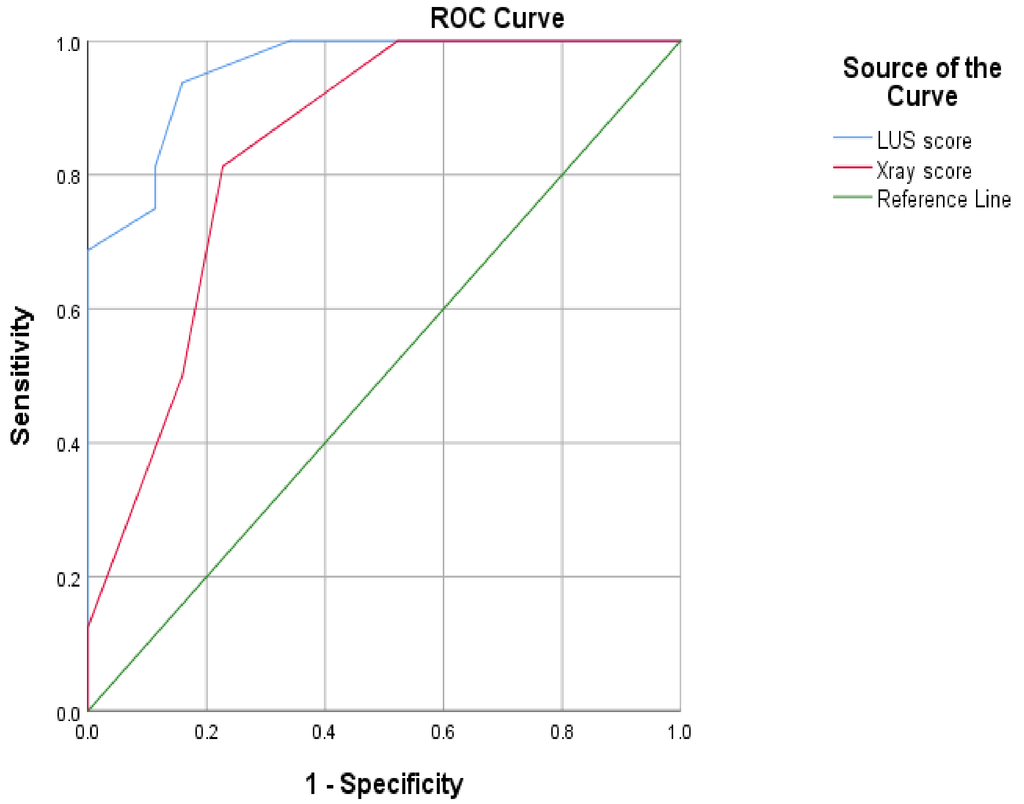

Figure 3: ROC (receiver operating characteristic) analysis for the prediction of surfactant treatment using LUS score and X ray score.

	AUC	P value	95% confidence interval		Best cut off value
			Lower Bound	Upper Bound	
LUS score	0.947	<0.001*	0.896	0.988	≥ 6
X ray score	0.829	<0.001*	0.741	0.917	≥ 5

* Statistically significant at p<0.05

ROC analysis for the prediction of surfactant treatment using LUS score and X ray score shows an area under curve (AUC) of 0.947 for LUS and AUC of 0.796 for X ray score. Both are

statistically significant (p=<0.001).

Table 2: Reliability of LUS score and X ray score for prediction of surfactant treatment.

	Best cut off value	Sensitivity	Specificity	+ve predictive	-ve predictive
LUS score	≥ 6	93.8 %	84.1 %	68.2 %	97.4 %
X ray score	≥ 5	81.3 %	77.3 %	56.5 %	91.9 %

This chart shows how well the LUS and X-ray scores predict the need for surfactant therapy. At a cutoff value of 6, the sensitivity and specificity of the LUS score are 93.8% and 84.1%, respectively. At a cutoff value of 5, the chest X-ray score has a sensitivity of 81.3% and a specificity of 77.3%.

Discussion:

Respiratory distress syndrome (RDS) continues to represent a crucial problem for preterm neonates despite the new advancement in its management [1]. Currently, management of RDS is mainly through using early continuous positive airway pressure (CPAP) in the management of preterm neonates since birth together with early selective administration of surfactant [21]. On the other hand, surfactant prophylaxis is no longer indicated for preterm neonates stabilized by non-invasive respiratory support [22].

New methods in diagnosis for assessment of endogenous surfactant and lung maturity as lamellar bodies count present in gastric aspirate are now available to help in detecting preterm neonates need early surfactant administration [23]. However these methods can't be widely adopted because of technical difficulties, and there is an increasing needs for a simple bedside test that can be done within the NICU [22]. LUS may be a helpful tool [15].

In this study we assessed the applicability of lung ultrasonography to evaluate the surfactant need in preterm neonates ≤ 34 weeks treated with early CPAP according to European guidelines 2019 update. We also assessed response need for second dose of surfactant.

We studied 60 neonates ≤ 34 weeks treated with early CPAP; LUS was done in the first 2 hours of life. 16 neonates received surfactant therapy according to European guidelines 2019 update. LUS was repeated after the surfactant within 2 hours. 7 neonates received second dose of surfactant if the oxygen needs remained high ≥10 hours (the median half-life of surfactant) after the first administration.

The median LUS score in the group that received surfactant was 10, and the 25th and 75th percentiles were 7 and 11, respectively. Although the median LUS score for the group did not require surfactant therapy was 4, the 25th and 75th percentiles were 3 and 5, respectively, which is consistent with the results reported by **Vardar *et al.* 2021** [24] when they found that The LUS score ranged from 2 to 8 with median of 4 for those with mild RDS and from 9 to 12 with median of 10 for those with severe RDS. In the RDS group that received surfactant treatment, the median LUS score was 9 (8–10) while it was only 2 (1-4) in the untreated group.

Also **Gregorio-Hernández *et al.* 2020** [8] reported that The median score for the initial ultrasound in the surfactant-treated group was 16 points (13–18), compared to 7 points (6–10) for the non-surfactant group. These results are in accordance with our study in that the group received surfactant has higher median while the difference in values between the 2 studies occurs due to the difference in LUS maneuver.

Our study shows a significant strong positive Correlation (r = 0.736) between LUS score and chest x ray score. This is in agreement with the cited study of **Aldecoa-Bilbao *et al.* 2021** [17] who found a correlation with statistical significance between LUS score and chest x-ray score ($r = .55$; $p < .001$). also **Vardar *et al.* 2021** [24] reported that The LUS scores showed a significant correlation with X-ray stages.

We define the ability of LUS score to predict surfactant need using ROC curve analysis to further elucidate the findings of the current study and compare it with the chest x ray score and we found an area under curve (AUC) of 0.947 for LUS and AUC of 0.796 for X ray score. Both are statistically significant (p=<0.001). At a cutoff value of 6, the sensitivity and specificity of the LUS score are 93.8% and 84.1%, respectively. At a cutoff value of 5, the chest X-ray score has a sensitivity of 81.3% and a specificity of 77.3%. This is in accordance with what is published by **Perri *et al.* 2018** [20] who found that AUC values of 0.94 and 0.80 were obtained from ROC analyses of the LUS and chest x-ray scores, respectively. A chest x-ray score of four or higher showed an 82% sensitivity and 76% specificity, whereas a LUS score of five or higher showed an 86% sensitivity and 88% specificity.

This is in agreement with **Aldecoa-Bilbao *et al.* 2021** [17] who reported that ROC analysis of chest x-ray scores and LUS score to determine the need for surfactant revealed an AUC for LUS score = 0.95 and a cut-off point > 8 with sensitivity of 87% and specificity of 83%. The AUC for CXR score was 0.81 and a cut-off point of more than 3 with sensitivity of 56% and specificity of 87% .

Also **Raimondi *et al.* 2021** [25] studied the role of LUS score in surfactant prediction and reported AUC of 0.86, at cutoff value of 9, AUC of 0.86, specificity of 0.83%, positive predictive value of 0.79 and negative predictive value of 0.82%. Sensitivity was about 79%.

In accordance with our results, other study done by **De Martino *et al.* 2018** [26] published that LUS score showed AUC of 0.94 for prediction of surfactant need, whereas a subgroup analysis revealed AUCs of 0.93 for infants of ≤28 and 0.98 for infants >28 weeks. The AUCs for these 2 subgroups did not show statistically significant difference (P = .328).

In another study published by **Vardar *et al.* 2021** [24], results showed The ROC analysis for LUS score produced an AUC of 1, a 95% confidence interval of 0.99 to 1, and a p-value of < 0.01. With LUS score of four, the need for the initial dose of surfactant therapy can be predicted with 96% sensitivity and 100% specificity. while this variance in values from our study occurs due to the difference in LUS maneuver.

A systematic review published by **Razak and Faden 2020** [10] showed that studies using a higher LUS score threshold of >5–6 had more accurate diagnostic results than those using a lower threshold of >4. Infants with LUS scores >5–6 had a significantly higher risk of needing surfactant treatment or mechanical ventilation than infants with LUS scores <5–6.

There were few limitations to our study. First, there are different maneuvers to perform LUS. Also, the results of LUS are operator and equipment dependent. This affects the ability to generalize of the results of our study.

Second, we used high frequency liner probe in performing this study which limits number of fields we can examine in preterm neonates.

Conclusion:

In conclusion, LUS score is useful tool in early prediction of need for surfactant administration in preterm neonates on CPAP. LUS score at a cut off value of ≥ 6 has a sensitivity of 93.8 % and specificity of 84.1 % for prediction of need for surfactant treatment.

Abbreviations:

AUC: area under curve; **CPAP**: continuous positive airway pressure; **LUS**: lung ultrasound; **NEC**: necrotizing enterocolitis; **NICU**: neonatal intensive care unit; **RDS**: respiratory distress syndrome; **ROC**: receiver operating characteristics; **SPSS**: statistical package for social science.

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